Antarctic marine benthic invertebrates: chemical ecology, bioactivity and biodiversity

Invertebrados bentónicos marinos de la Antártida: ecología química, bioactividad y biodiversidad

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Memoria presentada por

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VISTO BUENO
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Parece que han pasado siglos desde que me imaginara delante de esta pantalla y este teclado escribiendo estas líneas. Finalmente llega el momento y reconozco que me invade un poco el miedo. Miedo básicamente por enfrentarme a lo poco que queda ya para completar esta tesis; miedo que se confunde, claro está, con la incertidumbre de lo que el futuro me tenga que deparar. Se cierra un capítulo importante de mi vida y se tiene que abrir otro todavía más importante (o al menos eso espero). Sea como sea, lo que realmente importa es que aquí estoy haciendo balance de todo un período queriendo rendir un pequeño homenaje con estas palabras a todos aquellos que han contribuido en menor o mayor manera, de forma directa o indirecta, a que haya podido completar finalmente esta tesis doctoral. Para todos ellos ahí van mis agradecimientos.

Ha llovido bastante ya desde que empecé a trabajar con Conxita, la Jefa. Tras mis inicios en el CEAB con Rafa Sardá, quien me introdujo, para mi bien, en el maravilloso mundo de los anélidos poliquetos, el destino quiso que fuera a caer en el grupo de investigación de Conxita que, por aquel entonces, andaba escasito de personal. Recuerdo como si fuera ayer cuando me leí con detenimiento las tareas que, como técnico de laboratorio del proyecto, tenía que desempeñar: algo así como "muestreo y experimentación en la Antártida durante la campaña 2005–06". Sin quererme creer que era yo el que se iba a embarcar en una aventura de ese calibre me dirigí al despacho de Conxita para salir de dudas. Su respuesta acompañada de una sonrisa burlona fue algo así como: "En principio eres tú pero si no quieres venir pues tendremos que buscar a otra persona…". Sobra decir que no me opuse a esta invitación… ¿Alguien rehusaría? Seguramente pocos o muy pocos. La cuestión es que mi primer trabajo de técnico (ni por supuesto los sucesivos) nunca se redujo a una relación laboral estándar. Y ahí es donde tengo tanto que agradecer a Conxita, ya que me animó desde el principio a que desempeñara labores de investigación de forma paralela a mi trabajo como técnico del proyecto. Sin su confianza y manga ancha en este sentido nunca habría llegado a evolucionar en lo científico como creo que he hecho. De hecho, aún recuerdo la conversación que tuve con ella tras conseguir financiación para un contrato de varios años de duración. Tras pensármelo detenidamente le propuse (pedí) poder hacer la tesis doctoral de forma paralela a mi trabajo de técnico. Ella me dijo algo como: "¡Ya pensaba que no me lo ibas a pedir!". Sea como sea, y a pesar de mi imposibilidad genética para recordar literalmente las frases que me marcan, la cuestión es que fue entonces (corría el año 2007 si no me falla la memoria) cuando me aventuré en esto de hacer la tesis. Desde aquello se han sucedido otras dos campañas más (con muchos momentos buenos y con algunos pocos momentos malos, para qué negarlo) y mis intereses científicos se han diversificado. Por todos esos momentos en los que siempre he sentido tu respaldo ahí va ese GRACIAS por tu confianza sin límites Conxita.

Ya he dicho que he estado en tres expediciones antárticas, cosa que creo que habrá poca gente que no sepa, pues me resulta un tema muy socorrido en cualquier cena para "romper el hielo"… Nunca está de más recordarlo una vez más. Pero es que este tipo de expediciones marcan profundamente. Isla Decepción, nuestro destino

antártico “preferido”, es un lugar que difícilmente pueda llegar a definir con palabras. Hace falta algo más que unas fotos o unos vídeos para poderse hacer una idea de lo que es trabajar y vivir en un lugar tan privilegiado como nuestra Isla. Cuando alguien me pregunta cómo es vivir por unas semanas en un lugar así, casi siempre recurro al símil del “Gran Hermano” antártico (sin ánimo de darle ni el menor mérito al programa de televisión, Dios me libre). Y en gran medida es así gracias a la gente con la que acabas conviviendo día y día (no se hace de noche prácticamente). Tres campañas dan para muchos agradecimientos pues son muchas las personas que acaban pasando por la Base: desde los propios compañeros del grupo de investigación (con los que luego me extenderé como la ocasión merece), pasando por los demás científicos que comparten campaña, y acabando por el personal militar y de la UTM. Todos ellos han ayudado durante nuestros muestreos, durante el procesado de las muestras, durante los experimentos. Pero también todos ellos han contribuido a hacer que nuestras campañas sean un recuerdo imborrable para mí que me llevaré siempre. Así que para todos ellos, aunque no quiera personalizar aportando sus nombres, un GRACIAS tan grande como el sombrero de un picaor.

Justo antes mencionaba fugazmente a mis colegas de trabajo. Ahora les doy nombre y les atribuyo méritos. Aunque en los últimos tiempos hayamos tenido nuestras diferencias, Laura siempre ha estado ahí. Parte de esta tesis se la debo a ella, por el trabajo conjunto que hicimos en dos de los artículos que componen esta tesis, pero sin duda gran parte de los momentos de disfrute y locura también se los debo a ella. ¿¡Qué decir de Jenny!? (“MI Jenny” o “Jinni” como la llamaba Alaa) Pues que me siento afortunado de haberla conocido y que pasara de ser “la noia rossa” cuando la conocí en el CEAB, a ser la persona que ahora mismo representa para mí. Se podría resumir con un “soy fans tuyo” pero aún así lo voy a redondear con un “¡Te quiero, Morena!”. Jenny le va a la zaga al siguiente personaje al que tantas cosas debo. A Cristobo lo conocí en la primera campaña antártica en el 2005-06 cuando él justo se iniciaba en esto del “buseo polá”. Desde entonces nos hemos hecho inseparables aunque, todo hay que decirlo, una vez rehusara compartir conmigo cama de matrimonio en un hotel de Punta Arenas: “¡Por ahí sí que no paso!”, fueron sus palabras (eso sí que lo recuerdo literalmente), lo cuál entiendo por que es un tipo casado y no quería caer en la tentación… Bromas aparte, Cristobo ha sido para mí, además de un amigo incondicional (una suerte de hermano mayor), una pieza esencial dentro del engranaje del grupo sin el que muchos de mis experimentos nunca habrían salido como estaba previsto. Blanca (Blanqueeee) también me ha ayudado lo suyo y la verdad es que es un encanto de persona que espero que pronto se encuentre delante de un documento como éste escribiendo los agradecimientos de su tesis. Más tarde llegaron Carlitos y Juan, que también me han ayudado un montón y que siempre se han prestado a ayudarme a lo que fuera, aunque para ello tuvieran que bucear en las “frías” aguas de Blanes en el mes de Abril. Y también, como no, María Bas, que ha aguantado estoicamente sesiones interminables de poliquetos cuando a ella lo que más le gusta son los cetáceos… No me quiero olvidar tampoco de los que pasaron por nuestro grupo: para Yvonne, Michela y Ximena, que tomaron ya otros caminos, también un pedazo de esta tesis. En este apartado de agradecimientos no me gustaría dejar de mencionar a Manuel Ballesteros. Gracias Manuel por abrirme las puertas de tu despacho, por escuchar mis lamentos en más de una ocasión y por echarme una mano en lo que hiciera falta. Tampoco me quiero olvidar de otras personas que hace

ya tiempo que aportaron a la causa sus conocimientos en la taxonomía de diferentes grupos de invertebrados marinos antárticos. Gracias a Javier Cristobo, Pilar Ríos, Laura Núñez, Mercedes Varela, Alfonso Ramos, Neus Campanyà, Juan Moles, Manuel Ballesteros, Blanca Figuerola, Aina Bosch y Meritxell Edo por aportar su granito de arena. Mención especial para Luis Laria del CEPESMA de Luarca (Asturias), quién nos acogió con los brazos abiertos a Cristobo y a mi y nos cedió generosamente la osamenta de un rorcual aliblanco que tenía en su jardín. Para cerrar esta parte no debería olvidar la siempre necesaria ayuda económica recibida durante todos estos años a través de diferentes proyectos de investigación: ECOQUIM (REN2003-00545, REN2002-12006-E ANT), ECOQUIM-2 (CGL2004-03356/ANT), ACTIQUIM (CGL2007- 65453/ANT), ACTIQUIMWHALES (CTM2008-03135- E/ANT) y ACTIQUIM-2 (CTM2010-17415). También el departamento de Biología Animal me concedió varias bolsas de viaje para asistir a congresos y la Unión Europea me concedió una beca del programa SYNTHESYS para llevar a cabo una estancia en el Museo de Historia Natural de Londres. Recordar también que la empresa PharmaMar aportó también fondos a través de varios proyectos y que la Unidad de Tecnología Marina (UTM) nos cedió material oceanográfico en varias campañas antárticas.

Aunque ahora parezca que mi tesis se hizo solo en Barcelona, es justo recordar que sus inicios fueron en el CEAB. Como en el caso de las campañas antárticas no quería personalizar demasiado pero algo sí que creo que debiera. Mil gracias a Ramón (por solucionar los centenares de problemas informáticos con infinita paciencia), a Angel (por ayudarme con cuestiones logísticas sin poner una pega), a Carmela y Gemma (por ayudarme a hacer cientos de gestiones con la mejor de las sonrisas). Mención aparte para Rafa Sardá de nuevo, quién, aparte de introducirme, como ya he dicho, en el mundo de los poliquetos, siempre ha estado ahí cuando he necesitado que me echaran un cable. Que el resto de ceabinos no se sienta olvidado con estas palabras. Gracias a toda la familia del CEAB por compartir este período de mi vida conmigo.

Pero sí, efectivamente, gran parte de mis tesis la he desarrollado en el Departamento de Biología Animal y en la Facultad de Biología. La vida hubiera sido poco menos que imposible sin la inestimable ayuda de las chicas de administración: Raquel (que ya no está en el departamento y a la que echamos mucho de menos), Victoria, Isabel, Maria José y Judit. Su diligencia en el trabajo y su trato cercano y amistoso las distinguen. No me querría tampoco olvidar de Joan, quién también me ha ayudado lo suyo en gestiones de todo tipo. Mención aparte para los “Guassos” (Jordi-1, Jordi-2, David…), que siempre me han prestado la herramienta que me hacía falta (aunque en muchos casos no supiera ni como utilizarla) y me han ofrecido su disponibilidad e imaginación para solucionar lo que para mí eran problemas insuperables.

Esta tesis no se hubiera podido acabar si no me hubiera rodeado de colegas-amigos y excelentes científicos quienes me han ayudado en el sprint final de los últimos meses. Gonzalo Giribet me acogió en su laboratorio (a cuyos miembros aprovecho desde aquí para agradecer la ayuda que me prestaron) como uno más lo que me permitió dar un paso de gigante en un par de artículos que están ya a punto de ver la luz. Además con él compartí varias alegrías que el Barça nos quiso brindar durante el año 2011, que no es poca cosa… During my one-month stay at the National

History Museum of London, Adrian Glover greatly helped me to finish some “encysted issues” in my thesis. I would also like to thank Thomas Dahlgren, who helped me a lot in the experimental design of the whale bone experiment. Helena Wiklund, passionate for polychaetes in general and for members in the genus *Ophryotrocha* in particular, deserves a special mention since her expertise and courage have been decisive for me to finish some parts in this thesis. Jim Blake and Stacy Doner are also greatly acknowledged because they shared with me their infinite knowledge in the taxonomy of cirratulids. Aunque finalmente no vaya a incluir en esta tesis el estudio en el que estamos trabajando, mi agradecimiento a Juan Junoy por haberme invitado sin reparos a hacer una breve estancia en la Universidad de Alcalá y por el pacharán casero con etiquetado personalizado que me regaló. Finally, I would like to mention Brigitte Ebbe. Thanks to the workshop she organized in Woods Hole in 2010 I could meet the great experts in Antarctic polychaetes. Without the collaborations I established there the present PhD would not had been the same.

Momento ahora para acordarme de los amigos. Antes de ir más allá, unas líneas para disculpar mis ausencias prolongadas (y creo que justificadas) en el sprint final para acabar esta tesis. Ya sé que son cosas que se entienden pero no por ello al causante (o sea yo mismo) le dejan de pesar. Sea como sea hay muchas personas a las que me gustaría mencionar aquí, para dejar constancia de lo importantes que han sido en mi día a día. Me gustaría empezar por Carmen. AMIGA con mayúsculas que se ha preocupado por mí y que incluso en los últimos momentos de la tesis, cuando más he desconectado del mundo, no se ha olvidado de que seguía estando ahí. Me acuerdo que cuando llegó a Blanes, en su primera fiesta en la playa le dije algo así como que era un “gran fichaje”… La verdad es que, ni que decir tiene, que tengo buen ojo para estas cosas. El maestro Joao Gil, reciente doctor y “Grande de los Poliquetos”, me ha iluminado el oscuro sendero de la taxonomía de los anélidos proporcionándome innumerables artículos de su extensa y excelsa biblioteca. Además hemos compartido muy buenos ratos (la dragaaaaaaaaaaaaa…!) y muchos poliquetos bajo la lupa. Con Oriol, el Torras, la Gemma, Paoletta, Susana Pinedo, Jean Cris (el francés más majete que conozco), Guillermo (por cierto desde aquí gracias por cederme el honor de acabar la tesis antes que tú… te debo una… te llamo yo…)… la relación ha sido un poco menos metafísica y más de bares, de fútbol playa, de calçotadas y demás historias, lo cuál es tan importante o más que el resto de cosas. Con la Hierbas, ahora que vivimos relativamente lejos (interesante recordar aquí que para alguien de pueblo como yo el concepto “lejos” abarca a todo aquello que está más allá del río Tordera) nos vemos menos, pero cuando estuvo por el pueblo pos mucho más animada la cosa, vamos que yo he notado mucho tu ausencia. Algo parecido a lo que ha pasado con Adri (Tutuki), que ahora que no está y que se fue a aprender a hacer pasta con pesto, se la echa mogollón de menos. La verdad es que pocos hay que se rieran de mis chorradas como tú (“¿Eso son unas Niki Jordan?... Ay! Me las dejas veeeeeeeeeeeeeeer!!”). Muy agradecido por eso y por la tesis que nos regalaste que me ha venido de perlas para encontrar la inspiración que me hacía falta en los asteroideos mediterráneos. A “mis chicas” del departamento Rocío (reciente blandense de adopción) y a Mari Carmen (la belleza andaluza) les tengo que agradecer la compañía en las comidas en la facultad y que aguantaran mis chapas en los malos momentos, entre otras muchas cosas, claro está. Fuera del país me tengo también que acordar también de Alicia, quién me acogió como a un padre una

temporadilla en la mítica casa de Leland. Siguiendo con otros con los que coincidí en Boston, no puedo dejar de acordarme de Jan y Júlia, de Marta (la chica con los infinitos recursos de laboratorio), de Elena (o "esa persona que nunca pierde al Trivial") y, cómo no, de la Susi (que quiere bailar la salsa). Volviendo a Blanes, con Carlo y Carol nos hemos pegado muy buenas cenas (y más que vendrán); con Dani y Eva hemos disfrutado y sufrido a partes iguales viendo los partidos de nuestro Barça; y con el Torras, la Gemma, el Francis, el Torio, el Domin, la Carol, el Alfon, la Cristis, Vir, Jorge… hemos compartido, más antes que en los últimos tiempos, un montón de eventos lúdico-festivos. Para el final de este repaso me dejo al Juanico (y a la Patri, claro está). Esta parejita se ha preocupado de mí como si fuera de la familia y no han parado de demostrarme lo que les importo. En especial el Juanico se ha convertido en mi inseparable compañero de inmersiones en aguas "chocolate", pareja de cursos de inmersión incompletos y aprendiz de forense de cetáceos, solo por mencionar algunas cosillas. A todos vosotros un millón de gracias y un grande perdón a los que os prometí ir a pescar calamardos y nunca os llevé… Me puede la boca, lo sé… ;-).

Me toca acordarme ahora de la familia, o esas personas que te quieren por imperativos genéticos y que se ven obligados a entenderte a pesar de que aún no sepan muy bien en qué ando liado y para qué sirve lo que hago (sobretodo en el caso de mi padre o de mi hermano Manel). Mi padre y mi madre siempre han estado ahí. Como suele decirse en lo bueno y en lo malo, y qué duda cabe que sin sus ánimos, sus "vente a comer/cenar a casa si no tienes nada en la nevera", sus ayudas económicas a fondo perdido (?), su apoyo incondicional y un sinfín de otras historias, no habría podido completar este trabajo. Espero que ellos se puedan llegar a sentir tan orgullosos de mí como yo lo estoy de ellos, así que en gran medida este trabajo se lo dedico a ellos. Como no acordarme también del Esteban, que me ha prestado su ayuda y su barca para lo que hiciera falta, siempre con la mejor de las sonrisas, siempre dispuesto a echar una mano, siempre con ganas de ir a pescar calamardos… Mi hermano Manolillo también me ha ayudado lo suyo aunque con cuestiones más alejadas del mundo marino. Tampoco puedo olvidarme de los padres de Ana, Fernando y Maite, quienes me han ayudado tanto en sus visitas a Blanes como cuando he visitado yo Madrid. ¿Y qué hubiera sido de todo esto sin mis Peques? Aunque probablemente ellas no se hagan a la idea, mi Carla y mi Lucía me han devuelto muchas veces la ilusión y me han arrancado casi siempre una sonrisa. Han sido indispensables y esenciales para mí durante este período y ojalá lo sigan siendo, y no dudo que así lo serán, en el futuro. Ahí queda este "¡Os quiero con locura, Peques!" u "¡Os quiero más que a un perchico!"

Como se suele decir, lo mejor (o en este caso mejor dicho "la mejor") para el final. Ana ha sido la compañera perfecta para este largo y duro viaje. Hace ya algunos años era yo el que recibía un montón de merecidos (momento modestia) elogios en su tesis y ahora me toca reconocerle lo importante que ha sido en mi vida y todo lo que me ha ayudado en estos años que hemos compartido. Da igual que haya estado demasiado lejos demasiado tiempo, o que haya estado cerca y demasiado ocupada. Siempre me ha hecho sentir valorado, siempre me ha hecho sentir importante, siempre me ha hecho sentir especial. En grandísima medida muchas de las cosas buenas que se puedan apreciar en este trabajo son fruto de sus ánimos, de sus correcciones, de sus ideas, de sus sugerencias. Contigo, Ana, me he vuelto mejor en muchos aspectos.

Por citar un par de ejemplos ya no combino el chándal con los relojes metálicos (aunque podríamos decir que ya no me pongo chándal y acabábamos antes) o ya no invierto/pierdo tanto tiempo mirando a esos que dan patadas a un balón y que destacan solo por que llevan calcetines de rayas o no. También contigo aprendí que se puede hacer feliz a una persona reptando en el suelo de la cocina por una causa noble o que se puede robar una sonrisa bailando el "Oba-oba" o haciendo el tonto en modo Luisma sin venir a cuento. Mis agradecimientos a Ana son prácticamente infinitos. De hecho en un principio pensé en escribir un capítulo de la tesis tan solo de agradecimientos a Ana, lo que pasa es que tras unas semanas de darle vueltas a la idea me di cuenta de que no había manera humana de encajarlo dentro del hilo conductor de la tesis y tuve que desistir. Una pena. Sea como sea creo que con este "¡Te quiero, Bouse! ¡Eres la mejor!" se puede resumir en unas pocas palabras lo que representas para mí.

Finalmente, quede aquí un último recuerdo para todos los invertebrados marinos bentónicos que han donado, desinteresadamente y sin el consentimiento de padres y/o familiares responsables, parte de sus cuerpos o directamente sus cuerpos enteros por el bien de la ciencia y de mi carrera científica. Sin su aportación esta tesis no se hubiera podido llevar a cabo.

Sergi Taboada
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Contenido

General Introduction and Objectives

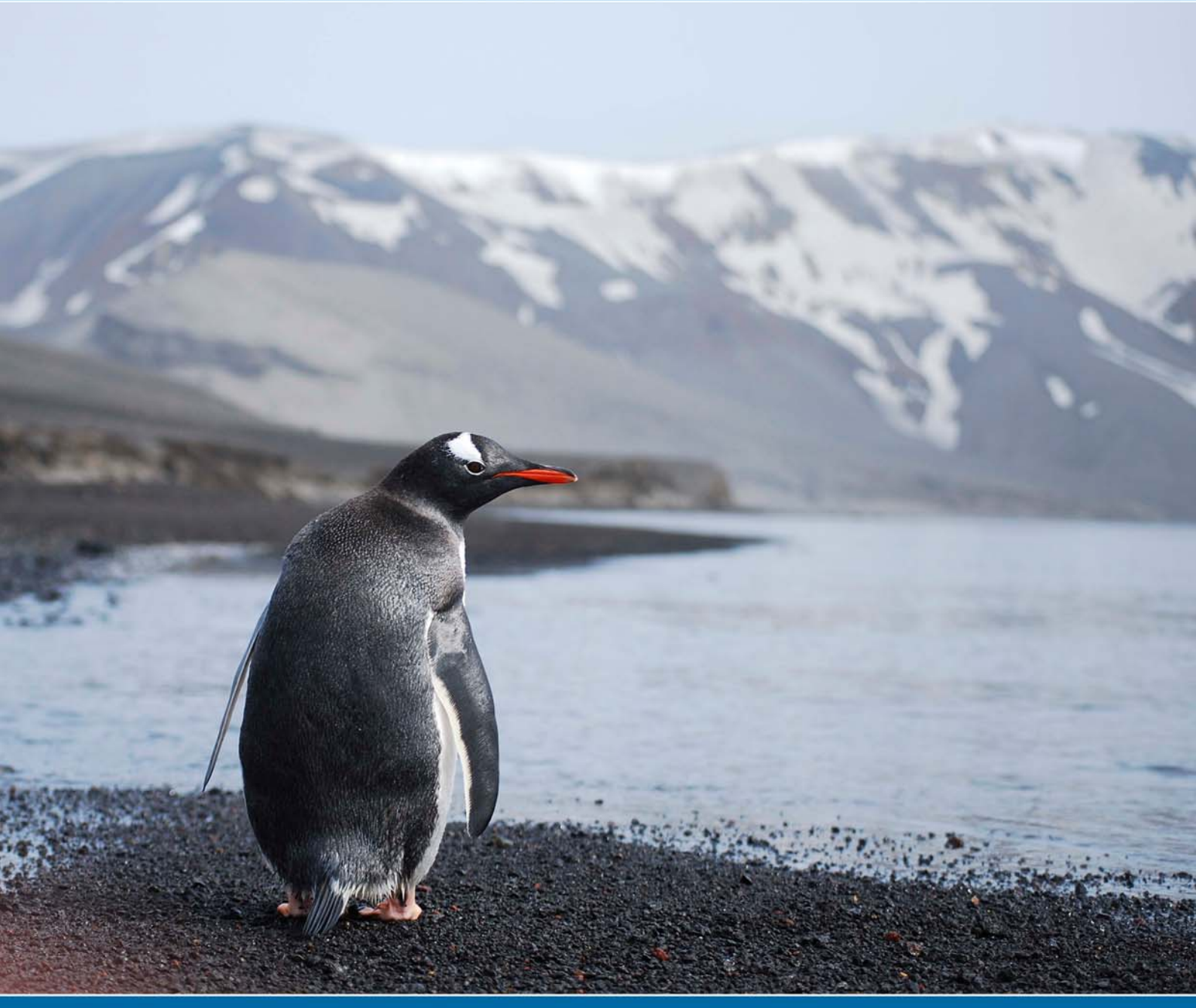

Photo by S. Taboada

General Introduction

The Southern Ocean invertebrate benthic fauna

Antarctica hosts a terrestrial and marine fauna unique on Earth. The shores of this continent are bathed by the Southern Ocean (SO), whose waters of about 35 million km^2 (the penultimate ocean in extension after the Arctic Ocean) have been subjected to the most extreme conditions over millions of years. Owing to its location in the southern pole, the SO is a markedly seasonal ocean. Its present-day uniqueness, though, is not only related to this extreme seasonality. As it happens everywhere around the world, fauna is shaped by a combination of long- and short-term evolutionary conditions as well as from ecological factors. On the longer time scale faunal assemblages reflect the influence of tectonics, climatic change, oceanographic changes, invasions, and radiation/extinction events (Arntz *et al*. 1994, Clarke & Johnston 2003). On the shorter time scale the organisms are subjected to ecological factors such as predation, competition, habitat characteristics, and food supply (Dayton *et al*. 1994, Arntz *et al*. 1994, Amsler *et al*. 2001a, Clarke & Johnston 2003, Barnes & Conlan 2007). All these factors have led to the current marine benthic invertebrate fauna, very well adapted to the harsh conditions that predominate in the SO (Brandt & Gutt 2011).

An ocean almost isolated

Some factors are assumed to participate in the physical isolation of the SO from the surrounding water masses. One of such factors is seawater temperature which is colder than anywhere else on Earth, having remained relatively constant through several million years (Zachos *et al*. 2001, Pörtner *et al*. 2007). The SO comprises all the waters south the Antarctic Polar Front or Antarctic Convergence (Figure 1), a well-defined belt that marks the northernmost extent of cold and dense surface water that is prevented to mix with the significantly warmer and less dense water masses of the surrounding oceans (Moore *et al*. 1999). Water temperature can range between the freezing point for seawater at -1.8ºC in the Weddell and Ross Seas, and +2.0ºC in West Antarctic waters (Brandt & Gutt 2011), though these values, for surface waters, can be higher in other areas (Barnes *et al*. 2006).

Despite the relatively constant and low water temperature over long time periods, it did not present an insuperable constraint for the evolution of a rich and specialized benthic fauna (Clarke 1988, Arntz *et al*. 1994). Actually, it has led to the development of a highly stenothermal marine invertebrate fauna, compared to species outside the SO (Pörtner *et al*. 2007). One of the consequences of Antarctic cooling for the SO marine shallow-water ecosystems was a dramatic shift in their biodiversity, including the loss (or migration out from the SO waters) of various major taxonomic groups within bivalves, teleosts fishes, and decapods owing to major physiological constraints (Clarke & Johnston 1996, Crame 2000, Aronson & Blake 2001, Thatje *et al*. 2005a). This triggered a gradual change in the shape of the structure of benthic shallow-water communities with dramatic and lasting ecological consequences. Thus, in the absence of durophagous (skeleton-breaking) predators such as fishes and decapods, other slow-moving organisms (predominantly echinoderms) occupied the predator ecological niche, causing a predation pressure that has demonstrated to be as intense as that reported in other geographic areas (Dearborn 1977, McClintock 1994). In summary, all these changes gave rise to shallow-water communities with a distinctly archaic (Paleozoic-like) deep-sea character, though species composition is not necessarily ancient or primitive, with a predominance of suspension feeding invertebrates (Aronson *et al*. 1997, Aronson & Blake 2001, Gili *et al*. 2006).

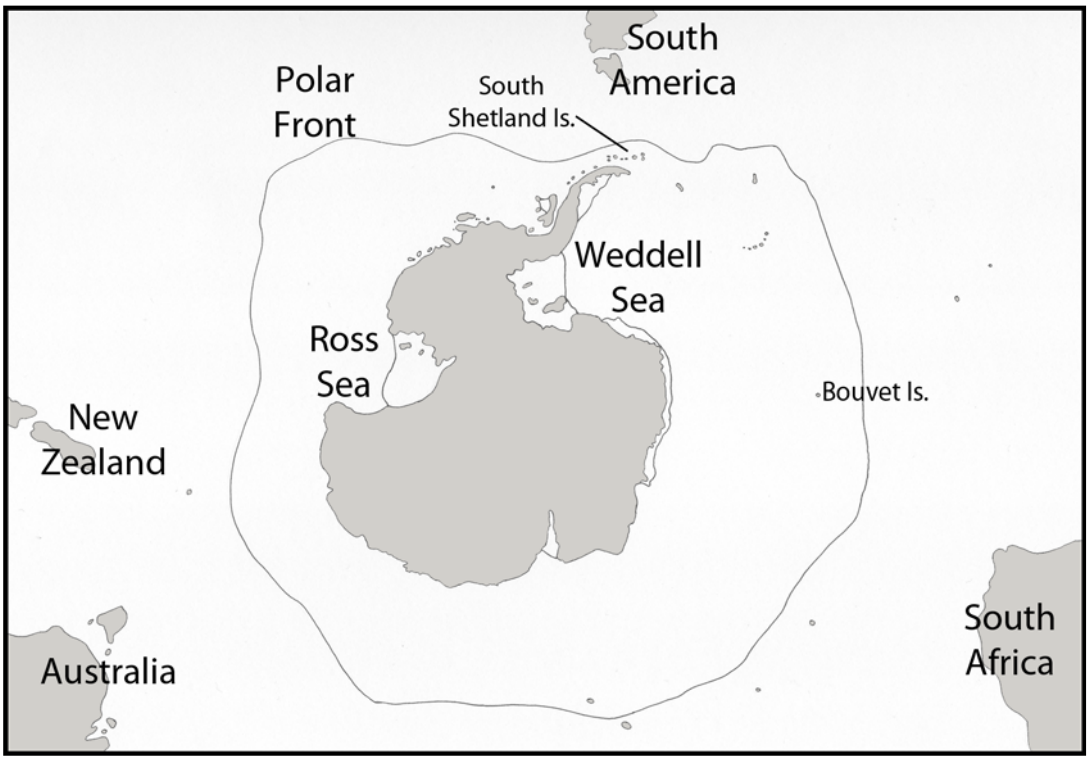

Figure 1. General map of Antarctica and the Southern Ocean

Much of the SO overlies deep sea floor. SO has a relatively little continental shelf, which in turn is unusually deep as a result of scouring from ice shelves and depression due to the huge ice loading on the continent. Continental shelves elsewhere in the world are typically 100–200 m deep and 75 km wide, while those around Antarctica are over 450 m deep (although in places they extend to over 1,000

m depth) and 125 km wide on average (see Clarke & Johnston 2003). These unusually deep and wide continental shelves appear to be zoogeographically well isolated from the adjacent seas owing to the effects of the Antarctic Circumpolar Current (ACC), crucial in the geological history of Antarctica as well as for the present-day SO marine fauna (Crame 1999). The period of the opening of the Drake Passage and the subsequent establishment of the ACC remains controversial but some recent estimates confirm it took place ~38–28 My or 29–22 My ago (Scher & Martin 2006, Lagabrielle *et al*. 2009), probably coinciding with the onset of the Antarctic glaciations and the sea water cooling (Barker & Thomas 2004, Katz *et al*. 2011). At present, this clockwise flowing marine current, mainly or entirely wind-driven, greatly contributes to the circumpolar distribution patterns observed in several benthic organisms (Arntz *et al*. 1997, Gutt *et al*. 2004). Apart from that, the ACC, considered the largest oceanic current system on Earth, is intimately related to the global climate through the Thermohaline Circulation, by exporting bottom waters (especially from the Weddell and Ross Seas) to the vast majority of deep waters in the rest of the world (Orsi *et al*. 1999). Thus, contrary to the SO shelf, the deep-sea fauna can freely migrate in and out of the SO abyssal plains making faunal connections between basins more likely (Brandt *et al*. 2007a,b, Brandt & Gutt 2011).

Benthic organisms are markedly eurybathic and endemic

Although there is a clear understanding of climate-induced long-term biodiversity changes through geological time, consequences of environmental changes caused by climatic oscillations on Milankovitch frequencies are still poorly understood (Clarke *et al*. 2004, Thatje *et al*. 2005b). Brey *et al*. (1996) showed that many of the benthic taxa examined (bivalves, gastropods, amphipods, and decapods, but also polychaetes, asteroids and ophiuroids) have a wider bathymetric range than relatives from a most surveyed area, such as Europe. Although the bathymetric ranges of several Antarctic species are likely to be underestimated due to the lack of comprehensive information for the species considered, the high levels of eurybathy seem to be explained by the palaeoclimatic history of Antarctica (Galéron *et al*. 1992, Clarke *et al*. 2004, Thatje *et al*. 2005b). During the Pleistocene, periods of large shelf ice extent and low sea water level (glacial period) alternated with periods of small shelf ice extent and high sea water level (interglacial period). It is hypothesized that these glacial-interglacial cycles may have driven an environmental force towards the evolutionary development of eurybathy in many Antarctic benthic invertebrates. During the extension of continental ice sheet, shelf fauna may have gone extinct or forced to go into deeper water refugia, while during the shelf ice retreats during the subsequent interglacial, the defaunated shelf could be re-colonized by slope fauna (Clarke *et al*. 2004). This hypothesis, however, has been challenged by Thatje *et al*. (2005b). In their work they suggest that slope was unlikely to become a refuge for fauna after the ice-sheet extension, and argue that survival of benthic communities was only possible in the deep sea or in shelters on the continental shelf, as a result of the diachronism in the maximum ice extent.

These glacial-interglacial alternations can be behind the high degree of endemism (60–90%) reported within marine benthic shelf fauna (Brandt & Gutt 2011), a fact that confirms the SO as a distinct evolutionary area (Linse *et al*. 2006). Endemicity values among different taxa may reflect environmental changes in the past and also, both duration and degree of isolation from other biogeographic zones. If marked environmental changes such as the advance and retreat of ice shelves coincided with isolation, allopatric speciation may have been favored causing adaptive radiation and endemisms (Arntz *et al*. 1997, Thatje *et al*. 2005b, Brandt & Gutt 2011). Documented radiation for groups such as pycnogonids, polychaetes, holothurians, and amphipods (accounting 17.5%, 12.2%, 9.2%, and 8.3% of global species, respectively) have led to a high taxonomic diversity in the respective groups. On the other hand, past ice sheet advance and retreat favoring speciation may have caused extinctions as in the case of decapods, cirripeds or bivalves (Clarke & Johnston 2003).

A particular food web under the ice

The presence of sea-ice, a common and obvious feature of the sea surface in both poles, varies dramatically in the SO through the year due to the highly seasonal light regime. During the winter maximum, 21 million km^2 of its area are covered by ice (an area larger than the Antarctic continent itself, 13 million km^2; Figure 2), while only about 4–7 million km^2 is covered at the summer minimum (Clarke & Johnston 2003, Brandt & Gutt 2011). This periodic advance and retreat of ice canopy creates one of the largest and most dynamic ecosystems on Earth (Brierley & Thomas 2002), which relies in the extraordinary primary production of bacteria and mainly algae (predominantly pinnate diatoms) that thrive in association within the pack ice. As the sea ice starts to melt and the irradiance increases during spring, phytoplankton blooms (several times more productive than open-water blooms) trigger a cascade response in the upper trophic levels. This way, a dramatic growth in both abundance and biomass of Antarctic krill (*Euphasia superba*) is promoted and this euphausiid becomes a vital food source for many large organisms such as fish, seabirds, and marine mammals. To complete the SO food web, water column-seabed interactions, the so called bentho-pelagic coupling, also need further explanation (reviewed by Smith *et al*. 2006). After the huge phytoplankton blooms during the spring-summer period in the photic zone, part of this organic matter is processed by the microbial community (bacteria, protozoa, and viruses) in the water column (Thompson *et al*. 2010), and the rest is exported to the Antarctic seabed. These intense pulses of dead algal cells, phytodetritus, and zooplankton fecal pellets directly affect the organisms inhabiting the benthos promoting the occurrence of a very rich and highly diverse suspension feeding invertebrate fauna. These inputs of organic matter, lagged both in space and time, are used as food by either shallow- and deep-water suspension feeders, which feed throughout the year thanks to resuspension and advection processes (Gili *et al*. 2001). Apart from these processes, the organic material deposited and accumulated in the marine sediment is mineralized through the microbial food web (Mincks *et al*. 2005). The final step in the SO food web comprises the upward processes connecting the benthic fauna with the pelagic compartment. Thanks to bottom currents micronutrients regenerated at the sea

floor arrive to the euphotic zone and are later incorporated again into the system by autotroph organisms (*e.g.* Sedwick *et al*. 2000).

Figure 2. Eastern Weddell Sea fragmented pack-ice during the ANTXV-3 expedition on board the R/V Polarstern in 1998 (photo by C. Avila)

State-of-the-art

A recent estimate of the number of benthic species inhabiting the SO gives a figure of more than 7,000 species (De Broyer *et al*. 2011), which represents a dramatic increase (nearly double) in the number of known species since one of the last reviews on marine benthic biodiversity (Clarke & Johnston 2003). This confirms that biodiversity in the SO benthos is higher than it was expected despite a large number of areas (*i.e.* deep-sea, under the floating ice shelves, intertidal areas) still remain poorly sampled or not sampled at all (Griffiths 2010). In this sense, the striking recent results reported for the deep-sea fauna from the Weddell and Scotia Seas (including a new hydrothermal-vent-endemic community) challenge the hypothesis of a depressed species richness in the deep SO (Brandt *et al*. 2007a,b, Rogers *et al*. 2012).

The accumulated knowledge over the years has confirmed that, as opposed to terrestrial fauna, SO benthic marine fauna does not show a latitudinal cline (Arntz & Gili 2001, Arntz *et al*. 2005). The "bell-shaped" latitudinal curve seems to be valid only for a few groups, whereas many others, such as pycnogonids or deep-water isopods, even increase their presence in the SO waters (Clarke & Johnston 2003, Brandt *et al*. 2007b); subsequently, the concept of asymmetric distribution of most taxa should be adopted instead (Arntz *et al*. 2005). Among the different groups occurring in the SO benthos, polychaetes appear to be one of the most represented taxa, although isopods and amphipods are also very speciose (Clarke & Johnston 2003, Brandt *et al*. 2007a,b). However, one of the most remarkable characteristics of the benthic fauna is that a rich and diverse sessile and sluggish suspension feeding fauna predominate in most of the SO environments. These communities are mainly favored on the Antarctic shelf, as a result of the combination of an adequate soft glacial-marine sediment and food supply originated by advective and resuspension processes after near-bottom currents (Clarke 1996, Gili *et al*. 2001, Gutt 2007). These suspension-feeding organisms usually conform tridimensional structures (Dayton *et al*. 1974, Clarke & Johnston 2003, Gili *et al*. 2006, Brandt *et al*. 2007a) with a large representation of epibiotic fauna that normally use large sponges, bryozoans, and cnidarians as substratum (Gutt & Schickan 1998) (Figure 3).

Structured suspension-feeding communities occur in the SO in part due to the highly predictable and relatively constant physical environment. Worth mentioning, these communities do not occur in most shallow-water and continental shelf areas since fauna here is greatly affected by ice scouring and anchor ice, two of the major natural agents of disturbance for Antarctic benthic fauna (Barnes & Conlan 2007). Thus, the suspension feeding communities occurring below the influence of disturbance agents appear to live under extremely constant environments, where biotic relationships seem to predominate and mechanisms such as predation or competition play a crucial role structuring benthic communities (Dayton *et al*. 1974, Arntz *et al*. 1994). All these suspension feeders have thrived in these ecosystems thanks to developing mechanisms against predation and competition, but also by having mechanisms that inhibit settling and fouling by other organisms (*e.g.* Dayton *et al*. 1974, Amsler *et al*. 2000b, Peters *et al*. 2009, Núñez-Pons *et al*. 2010, Koplovitz *et al*.

2011). Accordingly, to ensure survival, most of these species have developed, apart from structural and/or behavioral defenses, defensive secondary metabolites. The role that these natural products play in the SO ecological context is one of the main subjects of investigation in the present dissertation through a revision on the marine Antarctic chemical ecology (**Paper I**) and an experimental contribution in the antipredatory field using chemical extracts from benthic organisms **(Paper II**).

Apart from these two contributions in chemical ecology, a more applied study investigating the pharmacological potential of Antarctic and sub-Antarctic marine benthic invertebrates was conducted (**Paper III**). Both **Papers II** and **III** greatly contribute to increase the knowledge in the bioactivity of Antarctic benthic organisms.

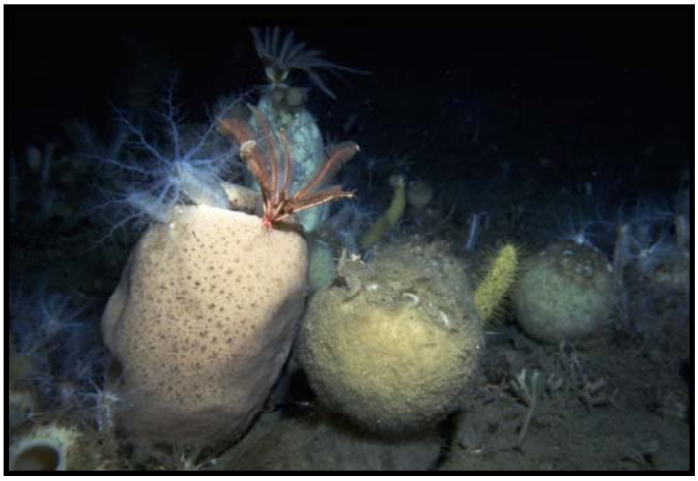

Figure 3. Seabed of the eastern Weddell Sea (photo by J. Gutt)

Chemical ecology of marine benthic organisms in Antarctic and sub-Antarctic waters

Marine organisms live under the pressure and constraints caused by the physical and biological intrinsic characteristics of the ecosystems they inhabit. To ensure survival, these organisms have developed during evolution different mechanisms including behavioral, physical, and/or chemical strategies. Over the last decades, several marine-derived chemicals have been described from a wide array of marine organisms, primarily from temperate and tropical waters (see Blunt *et al*. 2011 and previous reviews), leading to *ca.* 22,000 currently known compounds (MarinLit database 2011). However, despite this high and increasing number of described marine natural products, there is a significant lack of information about the ecological role that these chemicals play in the environment.

Comparatively, marine natural products from the SO have been scarcely studied in part due to the difficulties of surveying the harsh Antarctic waters but also by

former arguments predicting a low faunal biodiversity and a subsequent low chemical diversity (Lebar *et al*. 2007). Regardless of these difficulties and wrong arguments concerning the low chemodiversity (challenged by Amsler *et al*. 2000a), during the last years, the study of natural products in the SO has received a great deal of attention and this knowledge has been summarized in previous reviews (McClintock & Baker 1997a, Amsler *et al*. 2001a,b). Since a lot of work has been done after these preceding reviews, there was a need to update and integrate all the data related to the chemistry of Antarctic organisms. With this intention we conducted a review compiling all these information, up to May 2007, giving special emphasis on both the chemical features and the ecological roles of the described natural compounds (**Paper I**). Our comprehensive review was almost contemporary to a similar review done by Lebar *et al*. (2007) who included the marine natural products information from organisms occurring in both poles, and has recently been complemented by a review on chemical ecology aspects of the Western Antarctic Peninsula (McClintock *et al*. 2010).

As previously stated, most of the Antarctic seabed appears to be highly influenced by biotic relationships (Dayton *et al*. 1974, Arntz *et al*. 1994). As it happens for tropical and temperate areas (*e.g.* Scheuer 1990, Paul 1992, Pawlik 1993, Hay 1996), predator-prey interactions have attracted the greatest attention in Antarctic waters (see McClintock & Baker 1997a, Amsler *et al*. 2001a, Lebar *et al*. 2007, McClintock *et al*. 2010, **Paper I**). Unlike temperate and tropical regions, asteroids such as *Odontaster validus* have replaced fish as major potential predators in Antarctic communities, and the predation pressure caused by these organisms has demonstrated to be as intense as that reported in temperate and even tropical waters (Dearborn 1977, McClintock 1994). Thus, during the several million years that Antarctic ecosystems have remained environmentally stable and isolated, predatory pressure caused by these sympatric predators has acted as a selective force driving the development and acquisition of defensive secondary metabolites in many invertebrates (*e.g.* McClintock & Baker 1997a, Amsler *et al*. 2001a,b, **Paper I**). This is especially relevant when considering that suspension-feeding organisms predominate in the Antarctic benthos, since organisms of such a kind from other areas are known to have adopted chemical defensive strategies to ensure survival (Paul *et al*. 2011).

With the aim of expanding the knowledge on the antipredatory activity in the Antarctic and sub-Antarctic context, chemical extracts of several invertebrate species from different phyla were investigated against the common sympatric predator *O. validus* (**Paper II**). This circumpolar sea star has been used as a model organism to test predator-prey interactions in several previous works from other research groups (*e.g.* Slattery & McClintock 1995, McClintock & Baker 1997b, Peters *et al*. 2009) and also within our group (Avila *et al*. 2000, Iken *et al*. 2002, Núñez-Pons *et al*. 2010) (Figure 4). In this sense, **Paper II** represents a further step in the research of our group investigating ecologically relevant antipredatory relationships in marine benthic organisms, with a remarkable contribution for two main reasons: (i) it deals with organisms surveyed from two poorly known areas (eastern Weddell Sea and Bouvet Island) in terms of chemical ecology studies; and (ii) it focuses on deep-water organisms, hitherto scarcely investigated.

Figure 4. Feeding deterrence experiment using *Odontaster validus*

Bioactivity: Antitumoral potential in Antarctic and sub-Antarctic waters

Although terrestrial organisms have long been the traditional primary sources of new anticancer compounds, during the last decades marine pharmacology has become a very promising research field (Molinski *et al*. 2009). Actually, several of the future anticancer drugs currently in clinical and preclinical trials are originally marine-derived (Newman & Cragg 2004, Simmons *et al*. 2005, Mayer & Gustafson 2008), with some examples currently in the market such as the recently released Yondelis®. A few reasons may explain the interesting antitumoral/cytotoxic activity showed by several organisms inhabiting the seas. On the one hand, marine environments are the largest potential sources of biodiversity on Earth, with some ecosystems displaying higher diversity values than tropical rain forests (Haefner 2003). Moreover, marine habitats host a greater proportion of phyla (some of them are in fact exclusively marine) when compared to terrestrial habitats (Clarke & Johnston 2003), and this reality seems to be strongly correlated with the possibility of finding unique classes of chemical compounds with no comparable equivalent in terrestrial organisms (Devlin 1997, Munro *et al*. 1999). Finally, many marine organisms are sessile or sluggish, and need to defend themselves against possible predators and/or competitors, but also against settling and fouling by other organisms. The development of chemical defenses (some of which known to be useful in the fight against cancer) appears to be a widespread and effective mechanism for these organisms either on temperate and tropical environments as well as in Antarctic waters (*e.g.* Amsler *et al.* 2001a, Simmons *et al.* 2005, **Paper I**, **III**).

So far, temperate and tropical seas have had the greatest attention while prospecting for new natural products (see Blunt *et al*. 2011 and previous reviews). Compared to these seas, very few studies investigating the antitumoral/cytotoxic properties have been conducted in the SO, being shallow-water organisms the main

target (see discussion in **Paper III**). Nevertheless, the SO appears to be a very promising area in the search for new potential drugs since, as stated in the general introduction, it is a region that has remained almost isolated from the surrounding water masses for several million years, leading to a extremely high degree of endemicity (Brandt & Gutt 2011). Moreover, in the still poorly known but biodiversity-rich SO benthos, there is a predominance of sessile and sluggish organisms, which are known to provide the highest proportion of compounds with cytotoxic properties (Schmitz *et al*. 1993, Munro *et al*. 1999).

Taking advantage of two Antarctic cruises that surveyed three different areas (eastern Weddell Sea, South Shetland Islands, and Bouvet Island), a comprehensive study on the pharmacological potential of *ca.* 300 Antarctic and sub-Antarctic benthic species was performed (**Paper III**). The investigation, assaying the effects on three human tumor cell lines, was carried out in collaboration with the biopharmaceutical company PharmaMar SA, and the results obtained from these surveys comprise the largest pharmaceutical prospection conducted in Antarctic and sub-Antarctic waters ever.

Biodiversity: new polychaetes associated to whale bones

Whale-falls and the invertebrate and microbial marine communities they host, are currently one of the most extraordinary and poorly sampled habitats in the world. After the accidental discovery of these communities in a naturally implanted whale-carcass found in the eastern Pacific (Smith *et al*. 1989), several studies have followed describing the fauna that thrives in these specialized substrates, with the bulk of them mainly focusing on polychaetes, owing to the remarkable importance they play in both abundance and biodiversity (Baco & Smith 2003, Smith & Baco 2003, Smith 2006). These studies have investigated different aspects on the biology, ecology, taxonomy, and phylogeny of the invertebrate fauna associated to naturally implanted whale carcasses, but have also used experimentally implanted whale-falls in order to describe and characterize the fauna occurring in these substrates. So far, only the northern hemisphere (northeastern and northwestern Pacific, and north Atlantic), at depths between 30 to about 3,000 m has been investigated (*e.g.* Bennet *et al*. 1994, Rouse *et al*. 2004, Dahlgren *et al*. 2006, Fujiwara *et al*. 2007, Lundsten *et al*. 2010).

Owing to the global distribution of whales, however, communities associated to whale-falls are expected to naturally exist in any area of the planet, although chances to find this fauna should be higher in areas haunted by whales, where naturally sunken whale remains are more likely to occur. One of such areas is the Western Antarctic Peninsula (comprising the South Shetland Islands), where several cetacean species meet for breeding and feeding (Friedlander *et al*. 2006). Thus, to help filling the gap of knowledge for the SO, a pioneering experiment in Antarctic waters was conducted using whale bones as chemoattractive substrates to investigate the associated invertebrate fauna. The experiment consisted of three minke whale (*Balaenoptera*

acutorostrata) caudal vertebrae with no flesh implanted on the shallow-water seabed of Port Foster (Deception Island, South Shetland Islands) in January 2009. The vertebrae, firmly attached to a heavy metallic element by means of steel cables, were kept in the water using an acoustic release attached to a piece of ballast and an oceanographic buoy (Figure 5). After a year, only one out of the three bones was recovered. The other two bones were presumably lost after the attack of a leopard seal, since steel cables attaching the bones to the metallic element appeared to be bitten. Apart from this fresh bone, another whale bone (non-fresh, older) from unknown origin was also collected scuba-diving from a nearby shallow-water area in Port Foster. After retrieval and examination of both bones (January 2010) (Figure 6), it was concluded that polychaetes, as expected, were the most represented taxon while representatives of other groups, such as crustaceans, platyhelminthes, nemerteans, and oligochaetes were also present (unpublished results).

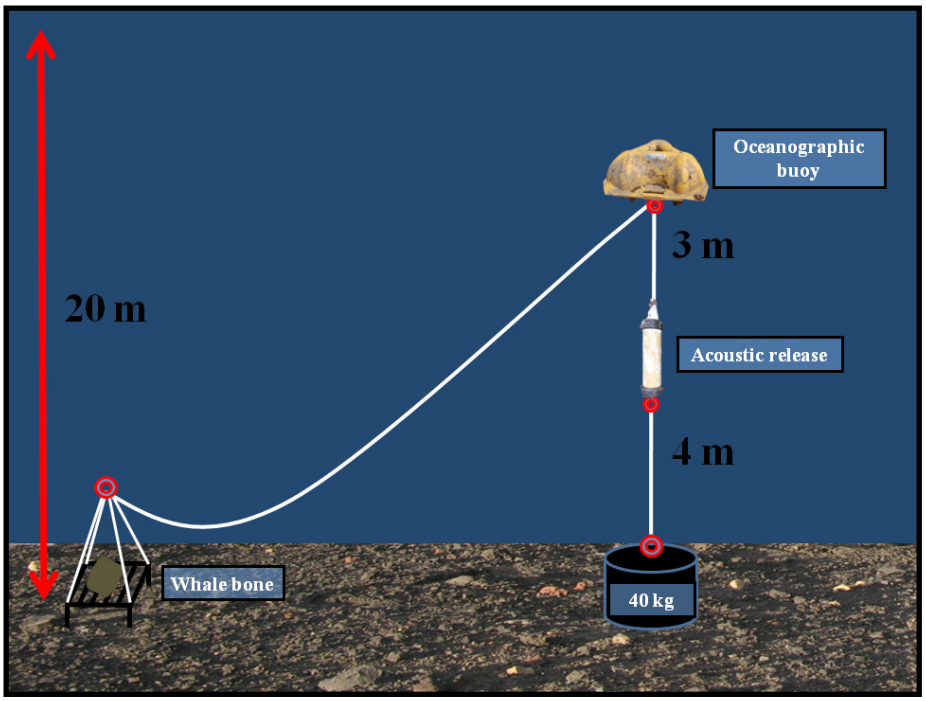

Figure 5. Schematic representation of the different elements composing the whale bone experiment conducted in Port Foster (Deception Island)

Remarkably, despite both bones were recovered from an area, Port Foster, with a very complete faunal background (see Barnes *et al*. 2008), they hosted at least five undescribed polychaete species from the families Terebellidae, Cirratulidae (**Paper IV**), Dorvilleidae (**Paper V**), and Siboglinidae (**Paper VI**).

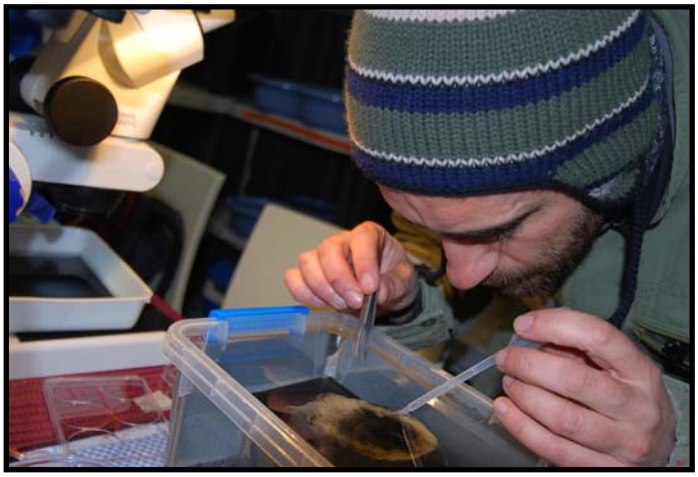

Figure 6. Examination of the whale bone from Deception Island at the "Gabriel de Castilla" Antarctic Spanish Base (photo by J. Cristobo)

A new cirratulid described from a shallow-water whale bone

Cirratulids are traditionally divided into two main groups: bitentaculates and multitentaculates (Blake 1996). Among multitentaculates, the genus *Cirratulus* is the most speciose, consisting of more than 50 currently accepted species, six of them described or recorded from the SO or adjacent waters. Opportunistic cirratulids have been reported in the literature associated with organic-enriched and polluted areas in temperate regions (*e.g.* Pearson & Rosenberg 1978, Elías *et al*. 2006), as well as in organically rich and ice-scouring disturbed areas in Antarctica (Lenihan *et al*. 1995, Conlan *et al*. 2004, 2010). Although cirratulids are not a common group of organisms occurring in whale-falls, some studies have documented its presence in whale remains in association with other polychaetes (Bennet *et al*. 1994, Smith *et al*. 2002, Fujiwara *et al.* 2007).

In **Paper IV**, we formally describe the first cirratulid to be originally described from whale bone remains. The cytochrome *c* oxidase I (COI) sequence is presented, as well as some remarks about its feeding preferences and ecology.

Two new Antarctic *Ophryotrocha* described from shallow-water whale bones

Members of the genus *Ophryotrocha* are small opportunistic benthic worms that chiefly inhabit nutrient-rich environments ranging from shallow-waters to deep-sea sediments (Thornhill *et al*. 2009). *Ophryotrocha* is one of the largest genera within the family Dorvilleidae, comprising approximately 50 described species with just two species formally described from the SO waters: *O. notialis* (Ehlers, 1908) and *O. claparedei* Studer, 1878. Among the opportunistic polychaetes occurring in whale-falls, *Ophryotrocha* is one of the most represented clades. Actually, so far, nine new species

have recently been reported from shallow- and deep-water whale remains off the Swedish and Californian coasts (Wiklund *et al*. 2009a,b). In the phylogeny context of the genus, previous molecular analyses using 16S and COI sequences agree on two main clades, the 'hartmanni' clade and the 'labronica' clade (Dahlgren *et al*. 2001, Heggøy *et al*. 2007). A third clade was suggested by Paxton (2009), the 'lobifera' clade, containing some species that were formerly described in the genus *Palpiphitime*.

In **Paper V** we formally describe two new species of *Ophryotrocha*, *O.* **sp. nov.** 1 and *O.* **sp. nov.** 2, and give some remarks about their feeding preferences and ecology. Phylogenetic information, after the analysis of three genes (H3, COI, and 16S), is also provided.

First *Osedax* described from Antarctic waters

Members of the genus *Osedax* (Fam. Siboglinidae), commonly known as 'bone-eating worms', are unusual sessile annelids lacking mouth and gut. They display a marked sexual dimorphism with paedomorphic dwarf males hosted within the lumen of the female's tube (Rouse *et al*. 2004). Females of these organisms live anchored to bones thanks to a ramified root system, and obtain nutrition via a symbiosis with heterotrophic bacteria that degrade organic compounds sequestered in the bone (Goffredi *et al*. 2005). So far, the 25 *Osedax* extant taxonomic members (operational taxonomic units), occur only in the northern hemisphere (Pacific and North Atlantic). Although they cover a very wide bathymetric range (30 to 2,891 m), the bulk of *Osedax* members have been described from deep waters. Interestingly, these organisms can thrive not only in whale remains, where they have mostly been reported, but also in the bones of other mammals, as well as in bones from birds and fish (Jones *et al.* 2008, Kiel *et al.* 2010, Rouse *et al.* 2011).

Although it has been postulated that *Osedax* members live world-wide (Glover *et al*. 2005), no record of its occurrence in Antarctic waters has been published to date. In **Paper VI** we report the existence of the first Antarctic *Osedax.* This new species is the shallowest *Osedax* described so far. We provide a morphological description as well as a discussion of its phylogenetic position in the frame of its clade.

Objectives of this Thesis

The present PhD dissertation covers a wide range of topics related to Antarctic marine benthic invertebrates. According to the general subjects treated here the work can be divided into three main parts: Part I, chemical ecology part, including two papers. **Paper I** comprises a comprehensive revision of the natural products described in Antarctic waters, whereas **Paper II** is an original contribution investigating the predator-prey interactions in different marine benthic invertebrates from Antarctic and sub-Antarctic waters; Part II, antitumoral activity part, including **Paper III**, where we discuss the results obtained after the largest pharmacological study ever carried out in Antarctic and sub-Antarctic waters; and Part III, biodiversity part, including three papers (**Papers IV-VI**), where we formally describe four different polychaete species reported from whale bones in the SO shallow-waters.

The specific objectives for every publication are summarized below.

Part I. Chemical ecology of marine benthic organisms in Antarctic and sub-Antarctic waters

Paper I. *Antarctic marine chemical ecology: what is next?*

The main objective within this paper is to review the existing information on the chemical ecology of SO marine organisms, providing an overview on what is known up to May 2007. The compiled information is integrated and discussed for every taxonomical group and a general future perspective for the Antarctic chemical ecology is given.

Paper II. *Feeding repellence of Antarctic and sub-Antarctic benthic invertebrates against the omnivorous sea star Odontaster validus*

With the background established after the revision in **Paper I**, our intention was to deepen in the chemically-based predator-prey interactions in a wide array of marine benthic invertebrates. In **Paper II** we describe these interactions using a common sympatric predator, the sea star *O. validus*, as a model in the feeding deterrence experiments. We also: (i) analyze and compare our results, studying deep-water organisms from two poorly surveyed areas (eastern Weddell Sea and Bouvet Island), compared to previous studies mostly investigating shallow-waters; and (ii) test the Optimal Defense Theory (ODT; Rhoades 1979) which, under the hypothetic predation pressure of *O. validus*, predicts the allocation of defensive metabolites in the most exposed tissues.

Part II. Bioactivity: Antitumoral potential in Antarctic and sub-Antarctic waters

Paper III. *Antitumoral activity in Antarctic and sub-Antarctic benthic organisms*

Antitumoral activity has been scarcely investigated in Antarctic and sub-Antarctic waters (see **Paper I**). Our main objective in **Paper III** is to establish the antitumoral activity of 290 different species (from a total of 770 benthic invertebrate samples) against three human tumor cell lines (colorectal adenocarcinoma, lung carcinoma, and breast adenocarcinoma). With this study we test the pharmacological potential of benthic invertebrates from three different areas: the eastern Weddell Sea, the South Shetland Islands, and the Bouvet Island.

Part III. Biodiversity: new polychaetes associated to whale bones

Despite whale remains being very common in the SO benthos, whale-falls have systematically been overlooked in Antarctic waters. The main objective in this part is to describe some of the most common polychaetes associated to shallow-water whale remains in Deception Island (South Shetland Islands).

Paper IV. *The first Cirratulidae (Annelida: Polychaeta) described from a shallow-water whale bone in Antarctica*

In this paper we formally describe the first cirratulid originally described from a whale bone. The COI sequence is also provided in order to facilitate future studies addressed to clarify the phylogenetic relationships among cirratulids.

Paper V. *Two new Antarctic Ophryotrocha (Annelida: Dorvilleidae) described from shallow-water whale bones*

Ophryotrocha members have been barely investigated in Antarctic waters. The objectives for this paper are to formally describe two new species in the genus *Ophryotrocha* occurring in whale remains and place these species in their phylogenetic context.

Paper VI. *First Osedax described from the Southern Ocean*

Polychaetes within the genus *Osedax* have never been investigated before in the SO waters. In this paper we formally describe the first *Osedax* occurring in the SO and discuss its position in its phylogenetic context.

Listado de artículos de esta Tesis publicados, enviados o en preparación

Capítulo 1

Avila C[1], **Taboada S[1]**, Núñez-Pons L[1] (2008) Antarctic marine chemical ecology: what is next? *Marine Ecology* 29: 1–71. Impact Factor: 1.272

Capítulo 2

Taboada S[1], Núñez-Pons L[1], Avila C[1] (*submitted*) Feeding repellence of Antarctic and sub-Antarctic benthic invertebrates against the omnivorous sea star *Odontaster validus. Polar Biology*. Impact Factor: 1.445

Capítulo 3

Taboada S[1], García-Fernández LF[2], Bueno S[2], Vázquez J[1], Cuevas C[2], Avila C[1] (2010) Antitumoral activity in Antarctic and sub-Antarctic benthic organisms. *Antarctic Science* 22(5): 494–507. Impact Factor: 1.328

Capítulo 4

Taboada S[1], Doner S[3], Blake JA[3], Avila C[1] (*in press.*) A new species of *Cirratulus* (Annelida: Polychaeta) described from a shallow-water whale bone in Antarctica. *Zootaxa*. Impact Factor: 0.853

Capítulo 5

Taboada S[1], Wiklund H[4], Glover AG[4], Dahlgren TG[5], Cristobo J[6], Avila C[1] (*in prep.*) Two new Antarctic *Ophryotrocha* (Annelida: Dorvilleidae) described from shallow-water whale bones. *Polar Biology*. Impact Factor: 1.445

Capítulo 6

Taboada S[1], Wiklund H[4], Glover AG[4], Dahlgren TG[5], Cristobo J[6], Avila C[1] (*in prep.*) The first *Osedax* (Annelida: Siboglinidae) described from the Southern Ocean.

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Otros artículos del autor publicados o en preparación relacionados (directa o indirectamente) con esta Tesis

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Informe de la directora de Tesis

Barcelona, 23 d'Abril de 2012

Com a directora de la present Tesi Doctoral, la sota-signant, Conxita Avila Escartín, certifico que el treball que s'inclou en aquesta Tesi és el resultat de la feina del Doctorand, Sergi Taboada Moreno. En Sergi ha participat en els articles que s'inclouen en la Tesi a tots els nivells, des de la seva gestació fins a la publicació, passant pel disseny experimental, la recollida de mostres i dades, la realització de les tasques de laboratori i de camp, l'anàlisi de dades i mostres, i la redacció i elaboració de les publicacions. Els articles de la Tesi han sigut fets en col·laboració amb altres autors, i en particular els dos primers són compartits amb la Doctoranda Laura Núñez-Pons. La resta d'articles no formen part de cap altra Tesi.

Aprofito l'avinentesa per destacar la tasca excel·lent feta per en Sergi, no només en aquests articles si no també en d'altres que no s'han inclòs a la Tesi. La seva maduresa científica al llarg del desenvolupament de la Tesi, la seva professionalitat, la seva disponibilitat i força de voluntat han fet que aquesta Tesi sigui avui finalitzada i és mèrit seu que el resultat sigui brillant.

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Chapter 1

Antarctic marine chemical ecology: what is next?

Photos by C. Avila & J. Gutt

Chapter 1

Antarctic marine chemical ecology: what's next?

Abstract. Antarctic ecosystems are exposed to unique environmental characteristics resulting in communities being structured both by biotic interactions such as predation and competition, as well as abiotic factors such as seasonality and ice scouring. It is important to understand how ecological factors may trigger chemical mechanisms in marine Antarctic organisms as a response for survival. However, very little is known yet about the evolution of chemical compounds in Antarctic organisms. Chemical ecology investigations have demonstrated over the last years that defensive metabolites have evolved in numerous representative Antarctic species. This contradicts early theories concerning biogeographic variation in predation and chemical defenses. As reviewed here, a number of interesting natural products have been isolated from Antarctic organisms. However, we believe many more are still to be discovered. Currently, many groups such as microorganisms, planktonic organisms and deep-sea fauna remain almost totally unknown regarding their natural products. Furthermore, for many described compounds, ecological roles have yet to be evaluated. In fact, much of the research carried out to date has been conducted in the laboratory, and only in a few cases in an ecologically relevant context. Therefore, there is a need to extend experiments to the field, as done in tropical and temperate marine ecosystems, or at least, to test the activity of the chemicals in natural conditions and ecologically meaningful interactions. Defense against predators is always one of the main topics when talking about natural products roles in species interactions, but many other interesting aspects, such as competition, chemoattraction, fouling avoidance and UV-protection, also deserve further attention. In our opinion, challenging future developments are to be expected for Antarctic marine chemical ecology in the years to come.

Introduction

Chemical ecology is considered a multidisciplinary field including both, chemical and biological research (Paul 1992). Natural products (also called secondary metabolites) are chemicals produced by the organisms, which regulate the biology, co-existence, and co-evolution of the species without participating directly in their primary metabolism (Torssel 1983). They are characterized by a restricted distribution, occurring only in some groups or species, and by their wide heterogeneity (*e.g.* Luckner 1984, Avila 1995, Cimino *et al.* 1999, 2001, Pietra 2002). In contrast to terrestrial studies, much less is known about the biological function of natural products in the marine environment. In fact, terrestrial chemical ecology, which has focused on animal-plant interactions, has served as a model for many of the studies in marine chemical ecology (Paul 1992, Pietra 2002). Historically, the research on marine toxins began in the 1960s, when also an important development in the taxonomy of marine animals took place. Over the 1970–80s, the field expanded towards the search for new compounds and new skeletons. Soon after, the activity-driven research of secondary metabolites was a priority, since a great potential biomedical interest of new natural products was expected. It was not until all these aspects were developed that marine chemical ecology appeared as an interesting field to explore by the end of the 1980s and the beginnings of the 1990s. Currently, with more than 18,000 compounds described (MarinLit database 2007), the field of marine natural products has grown and developed, and actually many compounds are under clinical trials to be used as drugs (*e.g.* Newman & Cragg 2004, Salomon *et al*. 2004, Chin *et al*. 2006). Still, chemical ecology is developing slowly, with many chemical and ecological key aspects yet to be studied and understood, and especially in geographic areas where the access to the organisms is difficult and/or expensive.

Marine organisms are under constant intense pressure for space, light and food. Thus it is not surprising that they developed, during evolution, a range of defense mechanisms including behavioral, physical and chemical strategies to ensure survival. Ecological roles for marine natural products include anti-predation, mediation of spatial competition, prevention of fouling, facilitation of reproduction, protection from ultraviolet radiation, and others (Sammarco & Coll 1992, McClintock & Baker 2001, Rittschof 2001). The most studied activity is the ability of some of these metabolites to deter predators (Paul 1992, Pawlik 1993, Avila 1995, Hay 1996, McClintock & Baker 1997a, Amsler *et al.* 2001a). Even if there are thousands of published studies describing the natural products present in marine organisms (see Blunt *et al.* 2007 and previous reviews), much less studies provide ecological information about the functional significance of these compounds (*e.g.* Paul 1992, Avila 1995, 2006, Hay 1996, McClintock & Baker 1997a, 2001). In many cases, biological activity has been evaluated as the ability of a compound to cause cell lysis or inhibit growth of a non-marine microbe in laboratory assays. This is very useful for pharmaceutical considerations and possible practical applications; however, it is not representative of the ecological effects of the natural products. More realistic assays are needed to prove the ecologically relevant activities of marine secondary metabolites on natural predators, competitors and fouling organisms (Munro *et al.* 1987, Scheuer 1990, Hay & Fenical 1996). Also, natural products may have multiple defensive functions, and many

marine organisms may produce a variety of these substances which affect different species of predators and/or pathogens (Paul 1992). Field experiments are necessary for examining deterrent activities and other ecological roles of these compounds.

Marine natural products have been isolated primarily from sponges, cnidarians, molluscs and ascidians, and in to a lesser extent from other invertebrate groups and seaweeds (Baker 1996, Faulkner 1996, McClintock & Baker 1997a, Pietra 2002). By 1993, nearly 7,000 different chemical structures for marine natural products had been documented; these included terpenes, alkaloids, polyketides, peptides, and shikimate-derived metabolites, as well as compounds of mixed biogenesis (McClintock & Baker 2001, Pietra 2002). However, most of the research on marine invertebrate chemical ecology was focused on tropical and temperate environments (Bakus 1964, Bakus *et al.* 1986, Paul 1992, Avila 1995, Pietra 2002). Geographical comparisons on early chemical ecology studies led to a latitudinal hypothesis, suggesting an inverse correlation between latitude and chemical defense strategies in marine invertebrates (Bakus 1974; see also McClintock *et al.* 1990 and Amsler *et al*. 2000a). According to this latitudinal gradient, chemical defense is mainly driven by predation pressure, which was thought to be proportionally higher in the tropics than in polar zones. Chemical defensive compounds employed by marine invertebrates were then expected to be more frequent at low latitudes than at the poles. However, the incidence of bioactivity detected in recent feeding deterrence and toxicity bioassays conducted with sessile or sluggish Antarctic marine organisms were shown to be commensurable with temperate, and perhaps even tropical, marine environments (McClintock 1989, McClintock *et al.* 1990, Baker *et al*. 1993, Amsler *et al.* 2000a, McClintock & Baker 2001, Avila 2006). Predation intensity, mainly due to fish, is considered to be greatest in the tropics, particularly in the Indo-Pacific region, and plays an important role structuring tropical and temperate benthic communities (Bakus 1964, 1969, Vermeij 1978, 1987, Bertness *et al.* 1981, Gaines & Lubchenco 1982, Steneck 1986, Paul 1992). The Antarctic benthos is also exposed to a high incidence of predation, although the main difference would then be that fish predators that browse on sessile marine invertebrates are rare in high latitudes (Eastman 1993), being substituted in Antarctica by a very high incidence of predation by mobile macroinvertebrates, particularly echinoderms, such as large sea stars. In this case, physical devices like structural skeletal elements, such as spicules from sponges or sclerites from cnidarians may not have the same relevance than in tropical sessile organisms subject to intense fish grazing, since sea stars often feed by extruding their cardiac stomachs over their prey (Hyman 1955). Thus, it is reasonable to predict that natural selection would favor the evolution of chemical defenses against sea stars in Antarctic organisms (Amsler *et al.* 2000a). The latitudinal hypothesis was based only on data from the Northern hemisphere, and the high predation pressure produced by sea stars in Antarctic communities was not widely recognized at that time (Dearborn 1977, McClintock & Baker 1997a, Amsler *et al.* 2000a).

The Antarctic marine benthic fauna evolved during the Cretaceous break up of Gondwana and the relative movement and separation of the forming continents, including the Antarctic continent (Clarke & Crame 1989, Crame 1992, Dayton *et al.* 1994, Gili *et al*. 2006). The climate remained temperate to sub-tropical until 22 million years ago when the establishment of a circumpolar current led to a hydrographical

isolation of the continent, which promoted a high proportion of endemism (Dayton *et al.* 1994, Crame 1999, Gili *et al.* 2000). Antarctic biota are therefore derived from a relict autochthonous fauna, plus an eurybathic fauna from deeper waters, and also some cool-temperate species, mostly arrived from South America (Brey *et al.* 1996, McClintock & Baker 1997a, Gili *et al.* 2006, Brandt *et al.* 2007). The Antarctic communities inhabiting the shallow continental shelf waters are very diverse (Burton 1932, Koltun 1970, Dayton *et al.* 1974, Dayton 1979, 1989, Blunt *et al.* 1990, Gambi *et al*. 1994, Arntz *et al.* 1997). In some areas, there is a dominant sponge community accompanied by many other invertebrate groups. Below the zone of ice scour, the physical environment of Antarctic marine community is very stable. Such stability has, in part, led to the conclusion that the Antarctic benthic community is structured mainly by biological factors (biologically accommodated), such as predation and competition (Dayton *et al.* 1974, McClintock & Baker 2001). Thus, Antarctic benthos, like tropical benthic systems, is dominated by biological interactions, and it is expected that many marine invertebrates use chemicals as means of defense from predators, inhibiting settling and fouling organisms and preventing overgrowth (McClintock & Baker 2001). As we will see in this study, recent laboratory experiments using sympatric bioassay species have demonstrated that natural products are involved in mediating ecological relationships in many different groups of Antarctic organisms, including macroalgae, poriferans, cnidarians, nemerteans, molluscs, echinoderms, brachiopods, and tunicates, and we will review these data here.

Currently, there are around 170,000 natural products known from around the world (Laatsch *et al*. 2007), and from these only about 18,000 are compounds from marine sources (MarinLit database). To date, as we will see here, there are only about 300 natural products (excluding fatty acids and sterols) described from Antarctic marine organisms, many of which are not found in congeners from temperate and tropical regions. These natural compounds from Antarctic marine organisms are reviewed here from the perspective of their ecological functions, emphasizing the ecological studies done up to date, as well as the chemistry of the natural products, considering what a marine chemical ecologist may need to know when starting to work in this field. The vast majority of the studies on chemical ecology in Antarctica have been conducted in McMurdo Sound, although other areas, such as the Weddell Sea, Antarctic Peninsula, and some Subantarctic Islands, are starting to be investigated in recent years (McClintock & Baker 1997a, Avila *et al.* 2000, Iken *et al.* 2002, Davies-Coleman, 2006). In fact, some reviews on the chemical ecology of Antarctic marine invertebrates, mainly from McMurdo, were published in the past years (McClintock & Baker 1997a, 2001, Amsler *et al.* 2001a). Since then, a lot of work has been done in Antarctica. The aim of this study is to provide an overview of what it is known to date on the chemical ecology of Antarctic marine organisms. Thus, in this review we include information on the chemical structure of the natural products described, location in the body, origin, bioactivity, and, when known, ecological role(s). We evaluate the work done to date for each taxonomic group and we outline further developments of the field in the near future, considering the current status of the information available as well as the challenging opportunities for the next years.

Material and Methods

An extensive bibliographic research has been carried out to obtain the information needed for this review. The results of the review are displayed in the format of a table (Table 1), including all the details about the natural products and chemical ecology of Antarctic marine organisms described up to May 2007. MarinLit, as well as other searchable databases, have been a useful tool in preparing the table. The formulae and chemical details of every compound are not included here, since it is outside the scope of this review, although they can easily be found in the references quoted in the table. Only a few chemical structures are shown in Figures 1–3, as examples of interesting compounds described in Antarctic organisms.

The general scheme and nomenclature codes for the table have been chosen in a similar way to previous reviews (Avila 1995). World Porifera Database, Algae Base and other databases have been used to check current names for all the species. Species names which have changed after the referenced study was published are corrected, with the changed name included in brackets. Abbreviated codes and long chemical names are numbered and reported at the end of Table 1.

Unless otherwise specified, the data in the table refer to the whole body extracts of the organisms studied or the compounds when described. Many algal studies have been done in different laboratory conditions of light, and thus may provide different compounds and/or activities in these conditions (*e.g*. Riegger & Robinson 1997, Hannach & Sigleo 1998, Laturnus *et al*. 1998b, Hoyer *et al*. 2001); details on these aspects should be confirmed directly in the papers reported.

When activity or origin is suspected but unproven, we include a question mark in the table to indicate it is only a suggestion by the authors of that particular study. Activities are usually reported for a single species tested, and thus may or may not be the same if tested for other species. Contradicting results may occasionally be obtained in different studies, which is reflected in the table. As for the origin, most algal compounds are suggested to be biosynthesized although this has not been proven and therefore it is not included in Table 1.

For each species, the first study is named first on the reference column; after that they are organized by groups of compounds. Within the groups, they are in chronological order. In order to simplify the table, references that are mentioned for one species are not repeated for the different compounds, even if they do contain data for more than one compound, origin or activity.

Results and Discussion

We review here all the natural products described to date (May 2007) from Antarctic marine organisms, their chemical structure, location in the body, origin, as well as bioactivity (if reported), and their ecological role when known (Table 1). There are only about 300 natural products, plus many fatty acids and sterols, described from 263 Antarctic marine organisms (94 algae, 166 invertebrates and 3 fishes). Results are analyzed by taxonomical groups, with general remarks and conclusions at the final part. For each taxonomical group, some general comments are provided, and selected examples of chemically mediated ecological interactions are reported.

Algae

Macroalgae dominate shallow marine communities on hard substrates along the Antarctic continent and are the most studied organisms regarding chemical ecology in Antarctica. About 120 species of macroalgae have been described up to now (Clarke & Johnston 2003), and from them, a total of 94 species have been chemically studied so far (Table 1). In general, macroalgae are known to defend themselves against herbivory by both physical and chemical mechanisms. A number of Antarctic marine organisms can be potential consumers of macroalgae, however there is little evidence of significant macroalgal grazing in the field. With the exception of amphipods, one fish, and two gastropods, macroalgae have only rarely been reported in the guts of potential herbivores (Iken *et al.* 1997, 1999, Iken 1999, McClintock & Baker 2001). Diatoms, other microalgae and green algae possess mainly UV protectants and volatile halogenated compunds. Brown macroalgae (class Phaeophyceae) elaborate prenylated terpenes, hydrocarbons, and phlorotannins and appear to be the major sources of volatile halogenated organic compounds (VHOC) with ozone-depleting properties. Phlorotannins (polyphenols) are known to have antifeedant effects in temperate and tropical phaeophytes. However, the ecological role of these compounds still remains to be determined in Antarctic brown algae, which have been scarcely studied so far (McClintock & Baker 2001, Iken *et al.* 2001, 2007, Fairhead *et al.* 2005a, Amsler & Fairhead 2006). Antarctic red macroalgae (class Rhodophyceae), like their temperate and tropical congeners, produce a variety of halogenated terpenes and halogenated alkanes, the latter with ozone-depleting properties. To date, more than 50 compounds have been reported from Antarctic red macroalgae, thus proving them a rich source of natural compounds, although many uncertainities remain about their ecological roles.

Many species of macroalgae possess UV-protectant compounds, such as mycosporine-like amino acids (Table 1). Macroalgal UV-absorbing compounds may vary with development, body part, depth or species (Hoyer *et al.* 2001, 2003) and also with laboratory conditions (Laturnus *et al.* 1998b, 2000, Hoyer *et al.* 2002). They are mainly present in red algae, and only in some green algae, while are scarce in brown algae (Karentz *et al.* 1991, Karentz 1994, Hoyer *et al.* 2001, Rautenberger & Bischof 2006). Also, UVA and UVB-absorbing compounds have been described in Antarctic microalgae, such as *Nitzschia* sp., *Dunaliella* sp., *Geminifera cryophila*, *Pyramimonas gelidicola* and *Phaeocystis pouchetti* (Karentz *et al.* 1991, Marchant *et al.* 1991,

Helbling *et al.* 1996, Riegger & Robinson 1997, Jeffrey *et al.* 1999). Some Antarctic diatoms such as *Nitzschia stellata* and *Porosira pseudodenticulata*, contain bromoalkanes which produce the photolysis of bromoform, which is suggested to be the cause of surface ozone losses (Sturges *et al.* 1993).

Interestingly, crude extracts of two Antarctic red macroalgae, *Iridaea cordata* and *Phyllophora antarctica* have been found to display antiherbivore effects against the sea urchin *Sterechinus neumayeri* in a phagostimulation assay (Amsler *et al.* 1998). Also, Amsler *et al.* (1999) discovered a unique trophic interaction involving defensive interactions of these two species of macroalgae, the sea urchin *Sterechinus neumayeri*, and the voracious opportunistic sea anemone, *Isotealia antarctica*. *Iridaea cordata* and *Phyllophora antarctica* are chemically defended against herbivory by *Sterechinus neumayeri*, and the sea urchin covers itself with these macroalgae. This algal cover significantly increases the likelihood of escape from *Isotealia antarctica*, and thus protects the sea urchin from predation by the sea anemone. It is a mutualistic relationship in which the macroalgae also benefit from this behavior because fertile drift plants are retained in the photic zone where they continue to contribute to the gene pool (Amsler *et al.* 1999).

Other interesting studies reported bioassays with different species of Antarctic macroalgae. Grazing experiments using the littorinid gastropod *Laevilacunaria antarctica* were conducted using intact algae, homogenates and solidified algae in agar, but no chemical defence was detected against this gastropod. The results showed that the five studied macroalgae (*Ascoseira mirabilis, Phaeurus antarcticus, Himantothallus grandifolius, Palmaria decipiens* and *Curdiea racovitzae*) presented physical defenses against mollusc grazing, since all the algae homogenates were eaten by the gastropod. However, none of the intact algae were consumed, showing no chemical implication in this feeding deterrence (Iken 1999). Another study evaluated the palatability and chemical defenses of 35 species of subtidal macroalgae from the Antarctic Peninsula and found out that most species had feeding deterrent activity against the sea star *Odontaster validus*, the rockfish *Notothenia coriiceps* and the amphipod *Gondogeneia antarctica*, and from these data concluded that Antarctic macroalgae are commonly unpalatable to sympatric herbivores due to their chemical composition (Amsler *et al.* 2005a). Bioassays to test potential defenses against diatom fouling also showed that antifouling properties are prominent among Antarctic macroalgae (Amsler *et al.* 2005b).

Pantoneura plocamioides has been found to contain a wide variety of terpenoid derivate compounds (Figure 1), such as several pantofuranoids (Cueto & Darias 1996), pantoneurotriols (which are proposed as biogenic precursors of pantofuranoids; Cueto *et al.* 1998c), pantoneurines (Cueto *et al.* 1998b, Argandoña *et al.* 2002), pantopyranoids and pantoisofuranoids (Cueto *et al.* 1998a). Pantoneurines A and B showed antifeedant properties against *Leptinotarsa decemlineata,* an allopatric chrysomelid insect (Argandoña *et al.* 2002).

Halogenated lactones (fimbrolides, acetoxyfimbrolides and hydroxyfimbrolides) with antimicrobial activity against allopatric bacteria and fungi were described from *Delisea fimbriata* (also called *Delisea pulchra*) (Pettus *et al.* 1977, Cueto *et al.* 1991, 1997, Ankisetty *et al.* 2004b). *Plocamium cartilagineum* is known to contain

monoterpenes with antibacterial activity (Rovirosa *et al.* 1990, Cueto *et al.* 1991), as well as two terpenoid compounds, *epi*-plocamene D and anverene (Figure 1), the latter presenting modest antimicrobial activity, and both of them showing feeding deterrence against the herbivorous amphipod *Gondogeneia antarctica* (Ankisetty *et al.* 2004b). Also, halogenated monoterpenes from this red alga (plocamene D and *epi*-plocamene D) possess antifungal activity (Cueto *et al.* 1991).

The brown macroalga *Desmarestia menziesii* produces plastoquinones, which have been suggested to present cytotoxic activity against leukemia cells, toxicity to fish, and are thought to inhibit mitosis of fertilized sea urchin eggs (Rivera 1996). *Desmarestia menziesii* and *Desmarestia anceps* are amongst the few species that have been studied in terms of the variation in the chemical and physical defenses in different parts of the algal thallus (Fairhead *et al.* 2005a,b, 2006). UV-induction experiments showing an increase in phlorotannin concentrations and feeding preference experiments against the amphipod *Gondogeneia antarctica* have also been conducted with these two Antarctic brown macroalgae (Fairhead *et al.* 2005a, 2006). Huang *et al.* (2006) studied 3 species of macroalgae of the genus *Desmarestia* (*D. anceps, D. antarctica* and *D. menziesii*) and found that all of them had feedant deterrent properties against Antarctic sympatric gammarid amphipods.

Halogenated compounds have been found to be very common in Antarctic macroalgae. Laturnus *et al*. (1997, 2000) conducted some experiments measuring the release of volatile halogenated organic compounds (organobromine, organoiodine and organochlorine derivatives), and their halogenating activity. Giese *et al.* (1999) measured the release of volatile iodinated C-1-C-4 hydrocarbons in 16 algal species. Twenty-eight species of Antarctic macroalgae were found to be the source of halogenated volatiles and these compounds were suggested to act as chemical defenses against microorganisms or herbivores (Laturnus *et al.* 1996). Later, methyl halides were found in 22 species of Antarctic macroalgae, including methyl bromide, methyl iodide, methyl chloride, and bromoform (Laturnus *et al.* 1998a,b).

Novel Antarctic algal compounds not previously described from any other organism include several monoterpenes from *Pantoneura plocamioides* (Cueto & Darias 1996, Cueto *et al.* 1998c), *Plocamium* sp. and *Plocamium cartilagineum* (Stierle & Sims 1979, Stierle *et al.* 1979, Darias *et al.* 1987, Rovirosa *et al.* 1990, Cueto *et al.* 1991, Ankisetty *et al.* 2004b), as well as several halogenated compounds and quinones from other species (Laturnus *et al.* 1996, Cueto *et al.* 1997, Ankisetty *et al.* 2004a). Matsuhiro & Urzua (1996a,b) reported some interesting polysaccharides from *Palmaria decipiens*.

UV-protecting molecules, mainly mycosporine-like amino acids, are very common in Antarctic marine algae. They have been detected in a large number of species and are thought to be synthesized by the algae and then transferred through the trophic chain by their consumption. This has been proposed to be an adaptation to ozone depletion (Karentz *et al.* 1991, Kattner *et al.* 1994, McClintock & Karentz 1997, Hoyer *et al.* 2001, 2002, 2003). Some other chemical compounds found to act as natural radiation protectants include some UV-absorbing pigments from *Palmaria decipiens* and *Enteromorpha bulbosa* (Post & Larkum 1993) and some carotenoid

pigments from *Leptosomia simplex* which may have a role in protecting from UV and X radiations (Karentz & Bosch 2001).

Although ecological information on some macroalgal natural products is already available (Amsler *et al.* 2001b, 2005a,b, Iken *et al*. 2001) many other natural compounds have been described from different species (Table 1) for which their ecological role remains unknown. Since macroalgae are an important component of shallow-water communities, a lot of questions about chemically-mediated interactions with other organisms remain unanswered, thus providing a good field to develop in the future. Furthermore, regarding their chemical ecology, microalgae remain mostly unknown in Antarctic waters, thus providing a potential source of interesting bioactive natural products.

Poriferans

Sponges are the dominant macroinvertebrate organisms in many Antarctic benthic communities and play a central position in the ecology of these ecosystems (Burton 1932, Koltun 1970, Dayton *et al.* 1974). They are one of the major targets of chemical investigations in Antarctica and elsewhere because of their high biomass and the well documented ability of this group to possess interesting natural products. Dayton *et al.* (1974) were among the first to suggest that Antarctic sponges could harbor chemical defenses in their bodies, having observed no predation on the sponges *Leucetta leptoraphis*, *Dendrilla membranosa* and *Isodictya erinacea*. Today, from the *ca*. 280 species described in Antarctica (Clarke & Johnston 2003), only 55 Antarctic sponge species have been chemically studied, producing terpenes, halogenated compounds, alkaloids and mycosporine-like amino acids (Table 1). The first studies evaluating chemical bioactivity used crude extracts of different sponges to test ichthyotoxicity against the goldfish *Carassius auratus* (McClintock 1987) and inhibition of growth in allopatric microorganisms (McClintock & Gauthier 1992). Also, some antiviral activity was reported by Blunt *et al.* (1990) in several Antarctic and Subantarctic sponges. In addition, the ability of some sponges from McMurdo Sound (*Cynachyra antarctica*, *Latrunculia* sp., *Polymastia* sp.) to reject tissues from congeners producing defensive chemicals was discovered by Battershill (1990) in immunological assays. These data supported the occurrence of a variety of active natural compounds in Antarctic sponges and provided information which could be useful for pharmacological and agrochemical applications. Nonetheless, these results gave little information on the ecological significance of these natural products.

McClintock *et al*. (1990) used 18 species of Antarctic sponges to carry out three types of ecologically relevant bioassays: cytotoxicity to *Sterechinus neumayeri* gametes, rightening response in *Odontaster validus*, and tube-foot retraction in *Odontaster validus*, *Odontaster meridionalis*, *Diplasterias brucei*, *Acodontaster conspicuus* and *Perknaster fuscus*. Out of the 18 species, 9 (50%) showed positive activities to all three tests, 6 (33%) were negative to all the tests, and 3 species (17%) showed positive response only to the seastar tube-foot retraction test. Subsequent investigations conducted by McClintock's group (McClintock *et al.* 1993a, 1994b, 2000) focused on the feeding deterrence activity of hexane, chloroform and methanol (non-polar to polar) extracts of some Antarctic sponges. They designed tube-foot assay employing an ecologically relevant predator, the common Antarctic spongivorous sea

star *Perknaster fuscus*. When the chemosensory tube-feet were presented sponge extracts applied to a glass rod, responses were either non-deterrent when tube-feet attached to the glass rod, or deterrent when there was a retraction of the tube-feet for up to 60s. Significant tube-foot retraction activity was detected in the chloroform and methanol extracts of 75% of the 35 species tested. These results were comparable to those obtained in anti-predation experiments conducted with reef fish and feeding pellets containing extracts of Caribbean sponges (Pawlik *et al.* 1995). Other defensive activities of sponge extracts have been assessed recently. Amsler *et al.* (2000b) detected chemical defenses against diatom fouling in 7 out of the 8 Antarctic sponges tested. Furthermore, protection against UV radiation was found in methanol extracts of 14 species of Antarctic sponges, likely due to the presence of a variety of mycosporine-like amino acids, most of them derived from algae (McClintock & Karentz 1997). Among these compounds it is remarkable the presence of mycosporine-glycine:valine, found in some Antarctic sponges and also present in many other invertebrate groups. This compound is absent in algae and it has been suggested to be either *de novo* biosynthesized by the organisms or being chemically modified from another mycosporine-like amino acid.

Over the years, a wide range of secondary metabolites has been isolated from Antarctic sponges, most of them with some bioactive characteristics, but, as already said, not always ecologically significant (Baker *et al.* 1993, Baker & Yoshida 1994, McClintock & Baker 1997a, Amsler *et al.* 2001a). *Suberites* sp. has been found to produce suberitenones and suberiphenol (Shin *et al.* 1995, Lee *et al.* 2004). From these, suberitenones A (Figure 1) and B produced tube-foot retraction in *Perknaster fuscus,* and they also showed a modest antibacterial activity against sympatric microbes isolated from the hydroid *Halecium arboreum* and the sea star *Acodontaster conspicuous* (Baker *et al.* 1997). Related new compounds were recently described from *Suberites caminatus* (Díaz-Marrero *et al.* 2003, 2004a) although their activity has not yet been tested. From *Dendrilla membranosa*, 7-methyladenine and picolinic acid produced sea star tube-foot retraction, while the yellow pigment 4,5,8-trihydroxyquilonine-2-carboxylic acid showed antibacterial activity, and membranolides C (Figure 1) and D displayed antibacterial and antifungal activity (Molinski & Faulkner 1987, 1988, Ankisetty *et al.* 2004a). *Kirkpatrickia variolosa* produces the bioactive stilbene derivative, resveratrol triacetate (Figure 1), as well as several variolins, a group of alkaloids, some of which have antitumor and antiviral activity (Perry *et al.* 1994, Trimurtulu *et al.* 1994, Jayatilake *et al.* 1995). Moreover, an uncharacterized pigment of *Kirkpatrickia variolosa* caused tube-foot retraction in *Perknaster fuscus* (Baker & Yoshida 1994).

Latrunculia apicalis and other species of the genus *Latrunculia* contain a variety of discorhabdin pigments (Figure 1) which are cytotoxic (Perry *et al.* 1988a,b, Blunt *et al.* 1990, Baker & Yoshida 1994, Yang *et al.* 1995, Ford & Capon 2000) and cause sea star tube-foot retraction (Furrow *et al.* 2003). Several compounds were isolated from *Isodictya erinacea* (Table 1) but only *p*-hydroxybenzaldehyde produced tube-foot retraction in *Perknaster fuscus* (Baker & Yoshida 1994, Moon *et al.* 1998). Body extracts from *Leucetta leptoraphis* showed antibacterial activity to allopatric microorganisms and antifouling properties against sympatric species. However, the methanolic extract was the only one that caused strong sea star foot tube retraction

and ichthyotoxicity against allopatric fish (McClintock 1987, McClintock *et al.* 1993a, 1994b, Amsler *et al.* 2000b). Taurine and rhapsamine have also been isolated from the methanolic extract of this sponge. Rhapsamine promotes cytotoxicity in fertilized sea urchin assay and cytotoxicity against different cell lines (Jayatilake *et al.* 1997). *Lissodendoryx flabellata* possesses 2 new cembranes, flabellatene A (Figure 1) and B, the first one with antitumoral properties (Fontana *et al.* 1999).

Cadmium and zinc are present in *Tedania charcoti* and they are included here, even though inorganic elements, because they seem to inhibit the growth of some species of allopatric bacteria (*Staphylococcus aureus*, *Micrococcus* sp., *Serratia* sp. and *Escherichia coli*) as well as to modulate protein phosphorylation in chicken forebrain (Capon *et al.* 1993). Guella *et al*. (1988) found sterones (*e.g.* ergosta-4,24(28)dien-3-one) in a group of unidentified Subantarctic shallow-water sponges. In fact, several Antarctic sponges possess steroidal derivates as secondary metabolites, as in the case of *Artemisina apollinis* (Seldes *et al.* 1990b), *Homaxinella balfourensis* (Seldes *et al.* 1986), *Xestospongia* sp. and *Cinachyra barbata* (Seldes *et al.* 1990a, Cueto *et al.* 1991).

Vetter & Janussen (2005) studied 5 species of Antarctic sponges: *Kirkpatrickia variolosa*, *Halichondria* sp., *Artemisina apollinis*, *Phorbas glaberrima* and *Leucetta antarctica* and obtained halogenated natural products from their tissues. Finally, bioactive metabolites have also been isolated from bacteria associated with the studied sponges. Diketopiperazines (DKP) and phenazine alkaloids are synthesized by *Pseudomonas aeruginosa* which is associated with *Isodictya setifera* (Jayatilake *et al.* 1996). Symbiotic microorganisms seem to be involved in the production of natural products of many marine invertebrates from tropical and temperate waters (König *et al*. 2006). The relationship between natural products from Antarctic sponges and their symbiotic microorganisms is an important open question which has not yet been studied in depth and therefore is expected to provide interesting results in the future (Webster *et al.* 2004).

Novel natural products described in Antarctic Porifera include many interesting compounds such as alkaloids (Butler *et al.* 1992, Baker *et al.* 1997, Moon *et al.* 1998, Ford & Capon 2000), sterols (Seldes *et al.* 1990a, Díaz-Marrero *et al.* 2004a), and diterpenes (Molinski & Faulkner 1987, Baker *et al.* 1993, Fontana *et al.* 1999, Díaz-Marrero *et al.* 2004b).

The spongivorous sea star *Perknaster fuscus* is a specialist feeder whose diet is almost exclusively based on the fast-growing and potentially space-dominating sponge *Mycale acerata* (Amsler *et al.* 2000a). This predation prevents competitive exclusion of slow-growing sponge species. This brings up the hypothesis that there might be a correlation between growth rate and production of chemical defenses in Antarctic sponges suggesting that slow-growing species are more likely to possess chemical defenses, although this has yet to be tested (Amsler *et al.* 2000a). In fact, very few data exist on this topic even in other areas of the world.

The primary predators of Antarctic sponges are described to be sea stars (McClintock 1994), which are able to chemically orientate towards their prey (Sloan 1980), but are not visually oriented. Thus, it is unlikely that Antarctic sponges use

warning colorations or aposematism to avoid being predated by them, while instead a wide range of chemical and physical strategies may increase their survival. Nevertheless some pigments have demonstrated to play a role as defensive metabolites, such as erebusinone (Figure 1) from *Isodictya erinacea* which causes molt inhibition (Moon *et al.* 2000) and a purple uncharacterized pigment from *Kirkpatrickia variolosa* producing foot tube retraction on sympatric sea stars (Jayatilake *et al.* 1995). As mentioned above, however, only a few studies really demonstrate the activity of their described natural compounds against sympatric species. Therefore, a lot of work still needs to be done regarding field or ecologically meaningful testing.

Cnidarians

Cnidarians also are an ecologically important group in Antarctic benthic communities and they possess a variety of natural products with interesting bioactivities. There are 272 species on Antarctic Cnidaria described (Clarke & Johnston 2003); however, only 8 species have been chemically studied so far (Table 1). The most studied Antarctic cnidarians belong to the group of the soft corals (O. Alcyonacea) and include *Clavularia frankliniana*, *Alcyonium paessleri* and *Gersemia antarctica*. These three species are chemically defended (McClintock & Baker 1997a). Experiments showed that extracted tissues are not ichthyodeterrent compared to non-extracted tissues, suggesting that sclerites have no apparent effect in deterring potential predatory fish. This indicates that chemical compounds, removed during the organic extraction process, are responsible for predator deterrence. Organic extracts of *Alcyonium paessleri* and *Gersemia antarctica* have also been found to possess antifouling and antimicrobial activities and both are toxic to larvae of the Antarctic sea urchin *Sterechinus neumayeri.* Moreover, *Perknaster fuscus* and *Odontaster validus*, two potential soft coral predators, showed tube-foot retraction to organic and aqueous extracts of all three soft coral species (Slattery & McClintock 1995, 1997, Slattery *et al.* 1995).

Clavularia frankliniana has been shown to produce chimyl alcohol, which was suggested to deter predation by the omnivorous sea star *Odontaster validus* (McClintock & Baker 2001). Homarine and trigonelline (Figure 1), two water-borne metabolites which cause growth inhibition in Antarctic microbes such as *Alteromonas* sp., *Moraxella* sp. and *Psychrobacter* sp. have been extracted from *Gersemia antarctica* (Slattery *et al.* 1997a). Other water-borne sterol compounds (like cholesterol, 22-dehydrocholesterol, 24-methylenecholesterol and 22-dehydro-7β-hydroxy-cholesterol) have been isolated from *Alcyonium paessleri* and all of them except 24-methylenecholesterol promote sea star tube-foot retraction. A strong chemo-avoidance in the Y-maze experiments of water-borne cholesterol from *Alcyonium paessleri* was also observed for 3 Antarctic echinoderms and the nemertean *Parborlasia corrugatus* (Slattery *et al.* 1997a). Some other metabolites have been identified in *Alcyonium paessleri*, such as paesslerins (Rodríguez-Brasco *et al.* 2001) and alcyopterosins (Palermo *et al.* 2000) (Figure 1), but no ecological activity has been reported so far. Slattery *et al.* (1997b) studied the steroid metabolism in the two soft corals *Clavularia frankliniana* and *Alcyonium paessleri* reporting the presence of steroid metabolic enzymes with the capacity to metabolize precursors like progesterone and androstenedione into other steroid products; this ability has no ecological role described at the moment.

Novel compounds described in Antarctic alcyonarians are mainly terpenes and steroids from *Alcyonium paessleri* (Palermo *et al.* 2000, Rodríguez-Brasco *et al.* 2001) and *Dasystenella acanthina* (Gavagnin *et al.* 2003c, Mellado *et al.* 2004). Crude extracts from *Ainigmaptilon antarcticus* possess feeding deterrent activity against *Odontaster validus*, and two sesquiterpenes, ainigmaptilones A and B (Figure 1), have been isolated from this species. Ainigmaptilone A shows sympatric antimicrobial activity, antifouling activity against sympatric diatoms, and feeding deterrence against *Odontaster validus* (Iken & Baker 2003). The Antarctic gorgonia *Dasystenella acanthina*, has also been found to contain sesquiterpenes: *trans*-*β*-farnesene, furanoeudesmane and isofuranodiene (Figure 1), the two latter being ichthyotoxic against allopatric fish (Gavagnin *et al.* 2003c). At least 8 other polyoxygenated steroids with cytotoxic activities against human tumor cell lines have been obtained from this octocoral (Mellado *et al.* 2004). *Anthomastus bathyproctus*, another Antarctic octocoral, is responsible for the production of a variety of steroids, some of them with a slight cytotoxicity against human tumor cell lines (Mellado *et al.* 2005).

Furthermore, mycosporine-like amino acids providing UV radiation protection were found in the soft coral *Alcyonium paessleri,* in the sea anemone *Isotealia antarctica,* and in another unidentified Antarctic sea anemone (Karentz *et al.* 1991, McClintock & Karentz 1997).

Further studies on the chemical ecology of cnidarian natural products are strongly needed. Other cnidarian groups in Antarctica remain totally unexplored in chemical ecology studies.

Molluscs

The diversity of Antarctic molluscs has triggered a lot of interest in studying their biology and ecology, even if only 17 species, out of *ca*. 700 (Clarke & Johnston 2003) have been chemically analyzed to date (Table 1). Most of them have only been analyzed for the presence of UV-protectant compounds, mycosporine-like amino acids (Table 1). Chemical defense has been studied in several circumpolar molluscan species. For some species, it has been observed that their chemical defensive systems are similar across a wide geographic range, while for others, geographical variations seem to exist. McClintock's group, studying the nudibranchs *Austrodoris kerguelenensis* and *Tritoniella belli*, and the prosobranch *Marseniopsis mollis,* found that their mantle tissues were rejected by two species of sympatric fish, and their aqueous extracts caused sea star tube-foot retraction, arm retraction, and had cytotoxic activity against *Sterechinus neumayeri* sperm cells (McClintock *et al.* 1992a). The sea slug *Austrodoris kerguelenensis* produces a series of bioactive acid glycerides, terpenoid acylglycerols such as austrodorins (Figure 2), and 2 nor-sesquiterpene compounds called austrodoral (Figure 2) and austrodoric acid (Davies-Coleman & Faulkner 1991, Gavagnin *et al.* 1995, 1999a,b, 2003a,b). Diterpene acylglycerols from *Austrodoris kerguelenensis* have been found to deter potential predators such as the sea star *Odontaster validus* in ecologically significant experiments. This species has been suggested to biosynthesize their own defensive compounds (Iken *et al.* 2002), and we recently tried to prove this by doing biosynthetic experiments with labeled precursors (*e.g*. Cimino *et al*. 2004, Fontana 2006). In fact, *de novo* biosynthesis does occur in *A. kerguelenensis*, although the produced compounds

show a large variability between individuals, even from the same population (Avila *et al*. 2007). To our knowledge, this is the first demonstration of *de novo* biosynthesis in an Antarctic organism.

Tritoniella belli contains chimyl alcohol which apparently is derived from its main diet the soft coral *Clavularia frankliniana*, and was shown to be a feeding deterrent against *Odontaster validus* (McClintock *et al.* 1994c,d). Also, the mantle mucus of *Tritoniella belli* generates tube-foot retraction in *Odontaster validus* and *Perknaster fuscus* and feeding deterrence in the sympatric fish *Pseudotrematomus bernacchii* (Bryan *et al.* 1998). Moreover, egg masses of this nudibranch seem to be chemically defended and deter the sympatric predator *Odontaster validus* but neither the amphipod *Paramoera walkeri* or the sea anemone *Isotealia antarctica* (McClintock & Baker 1997b).

Mantle tissues and aqueous extracts of the prosobranch *Marseniopsis mollis* are rejected by Antarctic fish and omnivorous sea stars and homarine (Figure 1) has been isolated from the mantle, foot and viscera (McClintock *et al.* 1992a, 1994a,d). Homarine has also been isolated from the dense assemblage of epizooites fouling the tunic of the ascidian *Cnemidocarpa verrucosa*, the presumed primary prey of this gastropod. A dietary origin from fouling organisms (basically bryozoans and hydroids) could explain the presence of homarine in the viscera of *Marseniopsis mollis* (McClintock *et al.* 1992a, 1994a). Homarine is a very common chemical substance in marine invertebrates and it is a feeding deterrent against *Odontaster validus* (McClintock *et al.* 1994a,d).

Bathydoris hodgsoni is another dorid nudibranch, which has been found to possess a sesquiterpene, hodgsonal (Figure 2), which is accumulated in the mantle and papillae and causes feeding deterrence to the sea star *Odontaster validus* (Iken *et al.* 1998, Avila *et al.* 2000, Gavagnin *et al.* 2000). *De novo* biosynthesis has also been suggested for this species (Iken *et al.* 1998, Avila *et al.* 2000), although our experiments to prove this have been not successful so far (C. Avila & A. Fontana, unpublished observations).

The common pelagic pteropod *Clione antarctica* is a very exciting example in marine chemical defensive strategies. Living individuals of these sea butterflies and whole body homogenates are consistently rejected by the Antarctic zooplanktivorous fish *Pagothenia borchgrevinki* (Foster *et al.* 1987) indicating the presence of chemical defenses (McClintock & Janssen 1990). The nature of the compound responsible for the chemical deterrence is linear hydroxyketone, named pteroenone (Figure 2) (Bryan *et al.* 1995, Yoshida *et al.* 1995). This is one of the first defensive compounds isolated from a planktonic macroinvertebrate. Interestingly, the hyperiid amphipod *Hyperiella dilatata* abducts and carries a single individual of *Clione antarctica* on its back thus providing itself with chemical defenses against fish predators (McClintock & Janssen 1990). *Clione antarctica* seems to feed mainly on *Limacina helicina*, another pteropod. Both have been chemically studied and found to possess exceptional lipophilic secondary metabolites and fatty acids (Phleger *et al.* 1997, Kattner *et al.* 1998). Among the compounds isolated from *Clione antarctica* are triacylglycerols and 1-O-alkyldiacylglycerol ethers (not reported in Table 1). These compounds seem to be derived from its main diet, *Limacina helicina*. All these fatty acids and lipophilic

compounds are thought to have a buoyancy function in these pelagic pteropods. *Limacina helicina* also contains triacylglycerols, phospholipids, sterols, fatty acids and wax esters, and the triacylglycerols are apparently obtained from its phytoplankton diet. The same kind of chemical products were found in the pteropod *Spongiobranchaea australis* (Phleger *et al.* 1997) (not reported in table 1).

Novel natural products in Antarctic molluscs include those mentioned for the nudibranchs *Austrodoris kerguelenensis* (Davies-Coleman & Faulkner 1991, Gavagnin *et al.* 1995, 1999a, 1999b, 2003b) and *Bathydoris hodgsoni* (Iken *et al.* 1998) as well as the pteroenone from *Clione antarctica* (Yoshida *et al.* 1995). Although both dietary and *de novo* biosynthesized compounds have been found in Antarctic molluscs, it is remarkable that chemically-established prey-predator relationships as those reported for molluscs from other latitudes (Cimino & Sodano 1994, Avila 1995) have not been reported in Antarctica yet, for example dietary compounds from predation upon poriferans and tunicates.

Several studies have identified mycosporine-like amino acids in Polyplacophora, Prosobranchia, Opistobranchia and Bivalvia (Karentz *et al.* 1991, 1992, McClintock & Karentz 1997, Whitehead *et al.* 2001).

Even though some Antarctic molluscs have been studied in greater detail, many species still remain to be further investigated. In addition, more accurate investigations should be conducted in terms of histological localization of these chemical defensive compounds as it has been done in Mollusca from other latitudes (Wägele *et al.* 2006).

Bryzoans

Antarctic bryozoans are very abundant and diverse, and they are amongst the dominant members of some benthic communities. As an example, in the Ross Sea the described bryofauna alone comprises around 250 species, and the total Antarctic fauna consists of at least 322 species (Clarke & Johnston, 2003). However, there are very few studies that investigate their chemical ecology and only 10 species have been chemically studied (Table 1). Colon-Urban *et al.* (1985) tested the antibiotic activity of crude extracts of 6 species, finding a strong inhibition of growth for *Staphylococcus aureus* when exposed to extracts of *Himantozoum antarcticum* and *Cyclicopora polaris* and a moderate inhibition with extracts from *Caberea darwini*, *Nematoflustra flagellata* and *Flustra thysanica*. Another bioassay examining the haemolytic activity against various mammalian erythrocytes was carried out using extracts of 5 species of Antarctic bryozoans collected from the Antarctic Peninsula. These studies showed that the extracts of *Carbasea curva* caused significant lysis of mammalian cells, showing a trace presence of bioactive natural products (Winston & Bernheimer 1986). However, the nature of these secondary metabolites and their ecological significance are still unknown to date. The signs of toxic substances being used for chemical defense by *Carbasea curva* would explain the success of its weakly calcified body plan, considering that this is one of the most abundant bryozoans in benthic samples from the Antarctic Peninsula and the Ross Sea (Winston & Bernheimer 1986). Furthermore, McClintock & Karentz (1997) found mycosporine-like amino acids providing UV-radiation protection in an unidentified Antarctic bryozoan and other species are similarly protected as well (Table 1).

This group remains largely ignored and the recent advances in their taxonomy (Gordon 2000, Taylor 2000, Todd 2000) should provide a good basis for further development of their promising chemical ecology.

Echinoderms

The research conducted with echinoderms suggests that bioactive metabolites are very common in a large number of species, particularly saponin-related compounds. Saponins are a group of water-soluble isoprenoid glycosides and sulphated glycosides generally regarded as toxins, and are isolated especially from sea cucumbers and sea stars. In asteroids these saponins are primarily steroidal glycosides, whereas in ophiuroids they are basically polyhydroxysteroids and their sulphates (Paul 1992, McClintock & Baker 2001). Chemical studies have been done for 35 species of Antarctic echinoderms [out of more than 400 existing species (Clarke & Johnston 2003)]: one crinoid, 19 sea stars, five ophiuroids, four sea urchins and six sea cucumbers (Table 1).

McClintock (1989) examined the toxicity of the body wall of 23 species of shallow-water Antarctic echinoderms to the allopatric mosquito fish *Gambusia affinis*, finding that 39% of the total species were toxic. The highest levels of toxicity causing fish mortality occurred in the body tissues of holothurians and asteroids. The first saponine isolated from an Antarctic sea star was santiagoside (Figure 2), extracted from *Neosmilaster georgianus* (Vázquez *et al.* 1992). Crude extracts from this species induced avoidance behavior to the limpet *Nacella concinna* (Mahon *et al.* 2000). Feeding deterrence against *Odontaster validus* was observed when presented to intact animals, extracts, mucus or intact embryos or juveniles of *Neosmilaster georgianus* (McClintock *et al.* 2003, 2006). Intact animals and body wall crude extracts of the sea star *Granaster nutrix* showed feeding deterrence activity against *Odontaster validus* as well (McClintock *et al.* 2006). Crude homogenates extracted from the body wall of *Perknaster fuscus* caused significant tube-foot retractions in sympatric sea stars, inhibition in the rightening response of *Odontaster validus*, and have toxic properties against the sperm of the sea urchin *Sterechinus neumayeri* (McClintock *et al.* 1992b). The bioactive tetrahydroisoquinoline alkaloid fuscusine (Figure 2) has been isolated from the body wall tissues of *Perknaster fuscus* (Kong *et al.* 1992) and is thought to be responsible for these diverse reactions (McClintock *et al.* 1992b). Fuscusine has not been detected in the sea star's main diet, the sponge *Mycale acerata*, therefore this compound is supposed to be *de novo* synthesized by *Perknaster fuscus*. It is remarkable that *Perknaster fuscus* has never been observed as a prey item while a number of other Antarctic sea stars are commonly included in the diets of many other echinoderms and anemones (Dearborn 1977). This might be attributable to its previously mentioned chemical activities.

The saponins marthasterone (Figure 2) and dihydromarthasterone were isolated from *Diplasterias brucei* and shown to possess haemolytic activity against sheep blood cells when assayed as a mixture (Mackie *et al.* 1977). Their ecological significance has not been studied yet. De Marino *et al.* (1997b) found sulphated polyhydroxylated sterols, asterasterols A-C (Figure 2), in an unidentified echinoderm pertaining to the Asteriidae family. Similarly, the sea star *Acodontaster conspicuous* and the ophiuroids *Ophionotus victoriae* and *Ophiosparte gigas* were found to possess

steroidal glycosides and/or polyhydroxylated steroids (D'Auria *et al.* 1993, 1995, De Marino *et al.* 1997a, Duque *et al.* 1997) while asterosaponins (Figure 2), halityloside 1 and acodontasterosides were isolated from *Acodontaster conspicuous*. Most of these compounds promote growth inhibition in 3 species of Antarctic bacteria isolated from the surfaces of Antarctic sponges and echinoderms (De Marino *et al.* 1997a). Moreover, *Acodontaster conspicuous* contains polyhydroxylated steroids and some acodontasterosides, the majority of which have antimicrobial activity (De Marino *et al.* 1997a). These results suggest a possible ecological role for these compounds related to the prevention of microbial fouling. The sea star *Labidiaster annulatus* has been found to possess two novel sulfated pentaglycosides (saponins), labidiasteroside A (Figure 3) and ovarian asterosaponin 1, with still unknown chemical activities (Díaz de Vivar *et al.* 2000).

The ophiuroids *Astrotoma agassizii* and *Gorgonocephalus chilensis* also possess sulphated polyhydroxysteroids in their tissues. Some of the compounds found in *Astrotoma agassizii* have also been described in *Ophiosparte gigas* (Roccatagliata *et al.* 1998, Comin *et al.* 1999, Maier *et al.* 2000). More polyhydroxylated steroids, antarcticosides, and other asterosaponins such as brasiliensoside, 24S-methylbrasiliensoside, pectinoside A and 24S-methylpectinoside (Figure 3) were found in a sea star of the family Echinasteridae, probably of the genus *Henricia* (De Marino *et al.* 1996, Iorizzi *et al.* 1996). Steroidal diglycosides, asteriidosides, have been obtained from an unknown sea star (Fam. Asteriidae). Bioassays indicate that most of these compounds have cytotoxic activity against human carcinoma cells (De Marino *et al.* 1998) but no ecological activity is known so far. Similarly, the sea cucumber *Staurocucumis liouvillei* contains trisulphated triterpene glycosides, liouvillosides A (Figure 3) and B, which have been shown to possess antiviral activity against *Herpes simplex* virus type 1 (HSV-1) (Maier *et al.* 2001), but no ecological information is available.

Some studies focused on chemical defenses in early life stages. McClintock & Vernon (1990) examined the ichthyotoxic characteristics of the eggs and embryos of 15 species of Antarctic echinoderms, using the allopatric killifish *Fundulus grandis*. Feeding deterrent chemical compounds were detected in eggs and embryos of the sea stars *Diplasterias brucei*, *Perknaster fuscus, Notasterias armata* and *Porania antarctica*, all of which produce large yolky lecithotrophic eggs. Other authors found that whole embryos, juveniles and their extracts from *Lysasterias perrieri* showed feeding deterrence to *Odontaster validus* (McClintock *et al.* 2003). Also, lecithotrophic eggs, embryos and larvae of three species of Antarctic echinoderms were found unpalatable or chemically defended against ecologically relevant predators such as the sea star *Odontaster validus*, the sea anemone *Isotealia antarctica* and the amphipod *Paramoera walkeri* in further studies; however, the sea urchin *Sterechinus neumayeri* and the sea star *Odontaster validus,* both possessing planktotrophic development, lacked chemical defenses in their eggs or larvae (McClintock & Baker 1997b). This may indicate that lecitotrophic embryos and larvae are more likely to be defended, similarly to what is reported for tropical marine invertebrates (Lindquist & Hay 1996), and it is consistent with the 'Optimal Defense Theory' (Rhoades 1979). In early life stages of Antarctic organisms, this fact may be especially relevant since developmental times are usually much longer (Pearse *et al.* 1991).

Many Antarctic echinoderms have been found to contain mycosporine-like amino acids, which have protectant activity against UV radiation. Some examples include *Promachocrinus kerguelensis*, *Sterechinus neumayeri*, *Diplasterias brucei*, *Odontaster validus*, *Cucumaria ferrari, Granaster nutrix, Amphioplus affinis* and *Ekmocucumis steineri* (Karentz *et al.* 1991, 1997, McClintock & Karentz 1997). Eggs and embryos of the sea star *Psilaster charcotti* contain carotenoids, which also have been suggested to protect them against UV radiation in their early life stages (Karentz & Bosch 2001).

Novel natural products in Antarctic echinoderms include saponins and steroids in several sea star species such as *Acodontaster conspicuous* (De Marino *et al.* 1997a), *Labidiaster annulatus* (Díaz de Vivar *et al.* 2000), *Neosmilaster georgianus* (Vázquez *et al.* 1992), *Perknaster fuscus* (Kong *et al.* 1992) and two unidentified species (De Marino *et al.* 1996, 1997b) as well as from the ophiuroid *Astrotoma agassizii* (Roccatagliata *et al.* 1998) and the sea cucumber *Staurocucumis liouvillei* (Maier *et al.* 2001).

Although echinoderms seem to be more studied than other groups, relevant ecological experiments are lacking in most cases and the taxonomical difficulties for some of them are an important handicap in the development of further studies.

Tunicates

Many ascidians have been identified in the Antarctic benthos and they are both abundant and diverse. Clarke & Johnston (2003) mentioned a total of 118 species; however, only 7 species have been chemically investigated to date (Table 1). The common solitary ascidian *Cnemidocarpa verrucosa*, which has a circumpolar distribution, was studied by McClintock's group. They conducted an analysis of the palatability and chemical defense of the tunic, ovitestes, branchial basket, body wall, endocarps and intestines. The results showed that the tunic was deterrent to sympatric pelagic and benthic fishes in addition to an allopatric fish (McClintock *et al.* 1991a,b). Their tunic surface is heavily fouled by hydroids and bryozoans, which indicates that there are no effective antifouling chemicals. Mature ovitestes are rejected by the Antarctic fish *Pagothenia borthgrevinki*, and alginate krill pellets containing lipophilic extracts of ovitestes deter predation by the sea star *Odontaster validus*, indicating that eggs and larvae may possess chemical defenses (McClintock & Baker 1997a).

Feeding deterrence against *Odontaster validus* was also detected in the whole tissue extract and the lipophilic extract of *Distaplia cylindrica*, and antifouling activity against chain-forming pennate diatoms was detected in both its lipophilic and hydrophilic extracts (McClintock *et al.* 2004).

Synoicum adareanum produces palmerolide A (Figure 2), which has been found to be cytotoxic against melanoma cells (Diyabalanage *et al*. 2006, Jiang *et al*. 2007). Furthermore, *Cnemidocarpa verrucosa*, *Molgula enodis,* and another unidentified Antarctic ascidian contain mycosporine-like amino acids which provide protection against UV radiation. Among these compounds the presence of mycosporine-glycine:valine in *Molgula enodis* is noteworthy; this compound is also present in other invertebrate groups (as mentioned for Porifera) and has been suggested to be either

de novo biosynthesized or chemically modified from related compounds (Karentz *et al.* 1991, McClintock & Karentz 1997).

Salps are an important component of the Southern Ocean food webs. Several polyunsaturated acids with haemolytic activity have been isolated from individuals of *Salpa thompsoni* (Mimura *et al.* 1986). Also, a complex sterol mixture containing brassicasterol has been obtained from another tunicate salp, *Ihlea racovitzai* (Schor & Seldes 1989). The ecological roles of these compounds are still unknown.

Many abundant, large synascidians are observed when sampling the Antarctic benthos (personal observations from the authors) which are not obviously overgrown by any other organisms or predated upon by any omnivorous species; however they remain largely unexplored so far regarding their chemical ecology. This, therefore, is a very interesting unexplored group, expected to provide not only ecologically active compounds but perhaps potential pharmacologically useful products too, as found in their tropical and temperate congeners.

Other groups

Nichols *et al*. (1993, 1997) isolated polyunsaturated fatty acids (PUFA), eicosapentaenoic acid and arachinoic acid from different strains of the Antarctic bacteria *Pseudoalteromonas* sp. Although outside the scope of this review, it has to be mentioned that many other Antarctic bacteria have been studied for their fatty acid composition (Nichols 1999). Some exopolysaccharides have been suggested to play a role as cryoprotectants and to participate in iron sequestration (Nichols *et al.* 2005), while some fatty acids seem to modulate fluidity in response to temperature within cellular membranes (Nichols *et al.* 1997).

The following remaining groups have been only occasionally studied to date: protozoans (3 spp), ctenophores (2 spp), platyhelminthes (2 spp), nemerteans (3 spp), annelids (8 spp), crustaceans (12 spp), pycnogonids (2 spp), brachiopods (1sp), chaetognaths (1 sp) and fishes (3 spp) (Table 1). Hemichordata and other minor groups have not been studied at all.

The diterpenes epoxyfocardin and focardin, both with cytotoxic activity, have been isolated from the ciliate *Euplotes focardii* (Guella *et al.* 1996). Focardin is suggested to be the precursor of epoxyfocardin. Another ciliate *Euplotes nobilii* (Strain AC-1) produces nitrogenated compounds that act as pheromones, named pheromone En-1 and pheromone En-2, which cause mating induction between cells of complementary strains (Felici *et al.* 1999).

Two species of ctenophores have been analyzed for UV-protectants but none has been found so far (Karentz *et al.* 1991). In the same study, 2 platyhelminthes and 3 nemerteans were found to possess mycosporine-glycine:valine for UV protection (Table 1). The nemertean worm *Parborlasia corrugatus* is a very abundant invertebrate in the Antarctic benthos. It has been observed that these organisms are rarely preyed upon, despite their lack of skeletal protection and rich energy content (Dayton *et al.* 1974, Heine *et al.* 1991), which suggests the presence of chemical defenses. Bioassays indicate that homogenates of whole body tissues of this nemertean cause mortality in gametes of the Antarctic sea urchin *Sterechinus neumayeri*, feeding

deterrence in two species of Antarctic fish *Dissostichus mawsoni* and *Trematomus bernacchii* (Heine *et al.* 1991, McClintock *et al.* 1991b) and haemolytic activity against bovine erythrocytes (Berne *et al.* 2003). These defensive properties, the citotoxicity and the feeding-deterrence may be due to the production of a copious acidic mucus (pH=3.5). Furthermore, *Parborlasia corrugatus* possesses in its mucus a potent toxic neuropeptide, parbolysin, with haemolytic activity against mammalian erythrocytes (Berne *et al.* 2003). This compound could also be involved in ecologically relevant interactions.

A novel bromophenolic compound (Table 1) was described in 2 Antarctic polychaete species of the genus *Thelepus*. Both terebellid species have been found to contain some of their bromophenols in the distal regions of the worm, suggesting a role as antibiotics in fouling and infection control (Goerke *et al.* 1991). The rest of annelid species studied has only been analyzed for the presence of UV-protectants, with the presence of mycosporine-glycine:valine in *Neanthes kerguelensis, Trachelobdella australis* and an unidentified polychaeta species (Table 1). Considering that there are more than 600 species of Antarctic polychaetes (Clarke & Johnston 2003) it is obvious that very little is known so far for this group.

Four species of copepods have been chemically studied: *Calanoides acutus*, *Calanus propinquus* (Hagen *et al.* 1993), *Rhincalanus gigas* and *Metridia gerlachei* (Graeve *et al.* 1994), and all of them have been found to contain wax esters and/or triacylglycerols stored in their tissues, sometimes in lipidic oil sacs. Their ecological role is still unknown, although a buoyancy function similar to that described for pteropods and krill may be suggested. In fact, lipids and wax esters have been proposed to have a role in buoyancy in polar zooplankton, especially in cold deep waters (Lee *et al*. 2006). These data are not reflected on Table 1 since they are outside the scope of this review.

Antarctic krill contains high levels of prostaglandins, even higher than in mammalian tissues (Mezykowski & Ignatowska-Switalska 1981, Pawlowicz 1989). High levels of prostanoids in the tropical soft coral *Plexaura homomalla* are known to deter fish predation (Weinheimer & Spraggins 1969, Gerhart 1984), which rises the question whether they play a similar role in Antarctic krill (McClintock & Baker 2001). Three species of Antarctic krill, *Euphasia superba*, *E. crystallorophias* and *Thysanoessa macrura*, have been found to accumulate phospholipids and phosphotidylcholine, which they use to achieve neutral buoyancy in the water column (Hagen *et al.* 1996). Data on these cumulative lipid compounds are not shown on Table 1.

Intact juvenile individuals of the isopod *Glyptonotus antarcticus* and body extracts cause feeding deterrence of the sea star *Odontaster validus* (McClintock *et al.* 2003). Other isopods and amphipods have only been tested for the presence of mycosporin-like amino acids (Table 1).

Liothyrella uva is an Antarctic brachiopod and a common component of the benthic system in the Southern Ocean. Crude extracts of whole brachiopod soft tissues caused significant retraction of sensory tube-feet in six species of sympatric sea stars, and also significant feeding deterrence in the allopatric fish *Cyprinidon variegatus* (McClintock *et al.* 1993b). More detailed investigations with different anatomic parts of

the brachiopod reported that the peduncle was rejected by the sympatric fish *Notothenia coriiceps* and the sea star *Odontaster validus*. This is consistent with the 'Optimal Defense Theory' (Rhoades, 1979) since the peduncle is the most exposed and unprotected part of the animal. Antimicrobial activity against psycotrophic marine bacteria was detected in the lophophore, stomach-intestine, and female reproductive tissues (Mahon *et al.* 2003).

Mycosporine-like amino acids with UV radiation protectant activity have been isolated from all the studied species of crustaceans and pycnogonids. Also other organisms such as the nemertine *Parborlasia corrugatus* and some fish have been found to possess UV-protectants (Table 1) (Nakamura & Kobayashi 1982, Karentz *et al.* 1991, McClintock & Karentz 1997, Newman *et al.* 2000). All the UV protecting compounds mentioned in the different groups may play an important role in Antarctica (Bandaranayake 1998, Karentz & Bosch 2001) due to the high levels of radiation in the area, and in fact they seem to be quite widespread among different groups of Antarctic organisms.

General Remarks

The Antarctic marine ecosystems have classically been classified as old and stable, and for this reason, the interactions between organisms play an essential role in the communities structure (Dayton *et al.* 1974). However, there also are some variability and perturbations due to the marked seasonality in light regime, variations in ice cover, erosion caused by icebergs and seasonal and interannual variations in currents pattern (Arntz & Gallardo 1994, Gili *et al.* 2000, 2006, Gutt 2000, Orejas *et al.* 2000). The erosive action of the icebergs produces devastating effects on the platform sea floor that are followed by a long and slow process of recolonization. The available substrate after a perturbation will be initially colonized by mobile, invasive species, and pioneer sessile species (Gutt 2000). Both in their adult and their larval phases and in the settlement after a perturbation produced by an iceberg, the community interactions may be regulated by chemical products. The study of these interactions between the organisms and the environment, and between organisms at intra- and interspecific level mediated by natural products, gives us information about the ecology and biology of the involved species, the functioning and the structure of the community, and, simultaneously, new compounds that may be useful to man from a pharmacological point of view (*e.g*. Avila 1995, 2006, Bhakuni 1998, Munro *et al.* 1999, Faulkner 2000, Cimino & Gavagnin 2006).

Marine chemical ecology is several decades behind terrestrial chemical ecology, even though in the last two decades great advances have been made due to the new technologies for collecting and studying marine samples and in the identification of small amounts of molecules (Faulkner 2000, Paul *et al*. 2006). Marine organisms are currently providing larger percentages of bioactive natural products than terrestrial organisms (Munro *et al.* 1999). Temperate and tropical organisms have been the most studied so far, while polar organisms have received proportionally less attention (Paul 1992, Blunt 2003, Blunt *et al.* 2007 and previous reviews). The review

provided here, however, shows that Antarctic benthic organisms are a rich and diverse source of natural products, with great interest from both ecological and pharmacological viewpoints. From the 263 studied organisms from the Southern Oceans, *ca.* 300 compounds have been described; in some cases, a defensive role has been demonstrated. This contradicts early theories concerning biogeographic variation in predation and in chemical defenses (see also Amsler *et al.* 2000a). A number of interesting natural products have been isolated from Antarctic invertebrates and macroalgae; however, we believe many more are still to be discovered. Also, further evaluations of the ecological functional roles of known compounds need to be undertaken. Much of the research done to date on chemical ecology has been conducted only in the laboratory, occasionally using ecologically relevant predators. There is a need to extend experiments to the field, as has been done in tropical marine environments (Paul 1992, Pawlik 1993, Hay 1996). More realistic assays need to be developed to test the real effects of marine secondary metabolites on sympatric predators, competitors and fouling organisms (Munro *et al.* 1987, Scheuer 1990, Hay & Fenical 1996) and complemented with field experiments, even if difficult, since they are most useful for examining ecological activities. Defense from predation has been the most studied ecological role for Antarctic secondary metabolites, however other functional roles including fouling control and alellochemical interactions are also important and need to be understood.

Another interesting feature in Antarctic chemical investigations is how secondary metabolic pathways of Antarctic organisms compare with those in organisms from Northern latitudes in terms of evolution. For example, few investigations have evaluated the defensive metabolites in Antarctic macroalgae although it is of particular interest to understand biogeographic patterns of herbivory. Brown algae are known to produce polyphenolic compounds, which could be responsible for the apparently low levels of herbivory, as it happens to their temperate and tropical congeners; nonetheless these experiments are still to be conducted. On the other hand, the fact that many Antarctic organisms (which are generally considered to be old) do possess chemical defenses may actually be an indication that chemical mechanisms evolved very early in the evolution of different taxa, but more data are needed in the different groups to support this hypothesis.

Several groups, as already mentioned, remain almost ignored. Little is known about defensive chemistry employed by Antarctic microorganisms and if some of the metabolites observed in macroinvertebrates may actually have their source in microorganisms. This has been hypothesized to occur in other geographic areas (*e.g*. König *et al*. 2006), but only recently Antarctic organisms, in this case sponges, have been searched for microbial symbionts providing very interesting results, which include the presence of diatoms, archaea, bacteria and dinoflagellates (Cerrano *et al*. 2000, Bavestrello *et al*. 2000, Webster *et al*. 2004). In planktonic systems, more information is needed on how secondary metabolites mediate patterns of predation on the pelagic embryos and larvae of macroinvertebrates, as well as on cyanobacteria, dinoflagellates, diatoms, protozoans, and other organisms. The Antarctic deep sea, which is proving to be very interesting (Brandt *et al.* 2007) remains unknown from the chemical ecology side. In general, we believe it is important to understand how

ecological factors may trigger chemical mechanisms in marine Antarctic organisms as a response for survival.

Since many important aspects of the reproduction of Antarctic organisms remain poorly understood, it seems that the significance of chemical ecology along the reproductive cycle and in the different developmental phases is difficult to evaluate. The few known studies have been mentioned throughout the previous sections (*e.g.* echinoderms) but further data are needed to correlate both fields. Recently, Palma *et al.* (2007) showed that Antarctic broadcaster echinoderms are predominant in ice-disturbed areas, while brooders only occurred in less ice-disturbed areas. Whether reproduction and development patterns correlate with natural products and chemical ecology largely remains to be evaluated.

An important topic in chemical ecology is the possible antifouling activity displayed by some organisms. This may act at different levels: initial stages (primary colonizers such as bacteria and diatoms), secondary stages (such as macroalgal spores or protozoans), and later stages, when larvae of macrofouling organisms arrive and settle. At these different levels, natural products may have different effects, but very few data are available for recruitment and colonization in Antarctic organisms so far (Webster *et al*. 2006). Effects may include inhibition of settlement, attachment and/or germination of spores and zygotes, growth inhibition for bacteria, fungi, protozoa and/or larvae. Further research is needed to understand these mechanisms in the benthic communities of Antarctica.

MAAs (mycosporine-like aminoacid compounds) seem to be an important, common trend in many Antarctic organisms, related to the acquisition of UV-protection, which is considered a more primitive way than that of terrestrial organisms (Karentz *et al.* 1991). Changes in global climate and the ozone layer may have, therefore, important effects in Antarctic marine communities (Karentz & Bosch 2001, Poppe *et al.* 2002, Rautenberger & Bischof 2006). Furthermore, ice melting due to climate change is showing new unexplored communities (*e.g.* Larssen areas) and how these new areas could be colonized by the surrounding organisms, although the same climate change may block the further development of these Antarctic communities (Odling-Smee 2007). These changes may have a terrible effect on Antarctic organisms, their biology and their chemical ecology, with enormous potential losses both in biological and chemical diversity.

Faulkner (2000) stated that chemical defense mechanisms cannot be directly equated with potential biomedical activity, but that it was remarkable how well the two correlate in reality. Possible applications of marine natural products, including those from the Antarctic, are enormous for obtaining pharmaceutical drugs, such as antitumor, antiviral (including HIV), antibacterial, antifungal, antituberculosis, antiparasites (against malaria, leishmaniasis, trypanosomiasis, etc.), antiinflammation, antiobesity, for use against Alzheimer, Parkinson and other neural diseases, against cystic fibrosis or against osteoporosis, as inhibitors of insuline-like growth factors, for producing or regulating apoptosis, etc. But they may also be useful for UV protection, antiaging and skin protecting, as well as for agrochemistry and other industrial applications (*e.g.* Blunt *et al.* 2007 and previous reviews). The search for active compounds is currently ongoing in areas considered the last frontiers of marine natural

products chemistry, such as unexplored polar areas, the deep sea and microbial communities (natural or cultured). Therefore, this is a field presently under strong developmental pressure, and chemical ecology should greatly benefit from this interest in natural products. Once the field expands to cover all the possibilities reviewed here, it will be very interesting to see how Antarctic organisms compare to similar species from other latitudes and whether any biogeographical patterns can be observed.

Fenical (2007) mentioned six areas with most potential future interest in marine chemical ecology to be undertaken from a multidisciplinary perspective. These areas included (i) studying small marine organisms (such as fungi, bacteria, radiolarians, ciliates, foraminifera, and others, including their culturing conditions); (ii) studying "difficult" organisms (difficult due to collection, taxonomy, culture, chemistry, etc.); (iii) focusing on symbiotic relationships between microbes and invertebrates (exo- and endosymbionts); (iv) investigating unexplained chemical phenomena (*e.g.* translocation of metabolites); (v) answering "old" problems that have not yet been solved (origins of many toxins, etc.); and (vi) integrating molecular approaches and marine genomics. Although for Antarctic chemical ecology we are still far from the basic knowledge which would allow us to pursue these objectives, we agree these could be very interesting future research lines. However, to achieve good results in these areas, we still need much basic information on Antarctic species, their natural products and their biology and ecology. Natural history and even taxonomy in some Antarctic groups is still poorly known and therefore, future research should provide useful information to develop all these challenging research lines. We should not forget our main aim: to know how, what for and why the species do possess these natural compounds, before they (both species and natural products) disappear.

Conclusions

In the future development of marine chemical ecology, an effort has to be dedicated to underexplored areas such as Antarctica. Randomly collecting material is not a satisfying methodology anymore, but focusing on biologically interesting species or groups and collecting these selectively should improve our chances to understand their ecology and evolution. The recent developments in natural products chemistry and associated technologies do provide high chances of detecting compounds in small amounts, thus making the ecological work easier. Also, collaboration with marine natural products chemists is a must for all marine chemical ecology studies to be done well. And finally, we should not forget the new developments in the fields of molecular genetics and genomics, which are opening new areas connected to chemical ecology, which will surely lead to challenging new approaches. In any of the related fields (collection, location, growth, activity, culture, chemistry, synthesis, etc.), technical advances are improving, and will continue to improve, our chances to get chemical ecology questions answered, even in the cold, remote, serendipitous waters of Antarctica.

Table 1. Antarctic natural products described up to May 2007: taxonomic group, species, location in the body (if provided), natural products, chemical structure, origin, activity and references

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
"ALGAE"				
Unidentified Sea Ice Algae				
?porphyra-334	MA	−	UV?	Ryan *et al*. (2002)
CL. CRYPTOPHYCEAE				
Geminigera cryophila				
UVA and UVB absorbing compounds	−	−	UV	Jeffrey *et al*. (1999)
CL. DINOPHYCEAE				
Amphidinium carterae				
mycosporine-like amino acid	MA	−	−	Hannach & Sigleo (1998)
CL. PRASYNOPHYCEAE (PHYTOFLAGELLATE)				
Pyramimonas gelidicola				
UVA and UVB absorbing compounds	−	−	UV	Jeffrey *et al*. (1999)
Pyramimonas parkeae				
mycosporine-like amino acid	MA	−	−	Hannach & Sigleo (1998)
CL. PRYMNESIOPHYCEAE				
Isochrysis sp.				
mycosporine-like amino acid	MA	−	−	Hannach & Sigleo (1998)
Pavlova gyrans				
3 mycosporine-like amino acids	MA	−	−	Hannach & Sigleo (1998)
Phaeocystis antarctica				
mycosporinee-like amino acid	MA	−	UV	Riegger & Robinson (1997)
Phaeocystis pouchetii				
UVA and -B absorbing compounds	−	−	UV	Marchant *et al*. (1991); Jeffrey *et al*. (1999)
CL. CHRYSOPHYCEAE				
Antarctosaccion applanatum				
dibromomethane	VH	−	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
CL. BACILLARIOPHYCEAE (DIATOMS)				
Chaetoceros sp. 1 and C. sp. 2				
porphyra-334	MA	−	UV	Riegger & Robinson (1997)
shinorine	MA	−	UV	
Coretron cryophilum				
porphyra-334	MA	−	UV	Helbling *et al*. (1996)
shinorine	MA	−	UV	
Coscinodiscus centralis				
porphyra-334	MA	−	UV	Riegger & Robinson (1997)
shinorine	MA	−	UV	
Fragilariopsis cylindrus				
porphyra-334	MA	−	UV	Helbling *et al*. (1996); Riegger & Robinson (1997)
shinorine	MA	−	UV	
mycosporine-glycine:valine	MA	−	UV	
Fragilariopsis linearis				
porphyra-334	MA	−	UV	Riegger & Robinson (1997)
shinorine	MA	−	UV	
Navicula sp.				
dibromomethane	VH	−	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
Nitzschia stellata				
bromoform	VH	−	−	Sturges et al. (1993)
dibromomethane	VH	−	−	
bromomethane	VH	−	−	
mixed bromochloromethanes	VH	−	−	
Nitzschia sp.				
UVA and UVB absorbing compounds	−	−	UV	Jeffrey *et al*. (1999)
Porosira glacialis				
porphyra-334	MA	−	UV	Riegger & Robinson (1997)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
shinorine	MA	−	UV	
Porosira pseudodenticulata				
bromoform	VH	−	−	Sturges *et al*. (1993)
dibromomethane	VH	−	−	
bromomethane	VH	−	−	
mixed bromochloromethanes	VH	−	−	
porphyra-334	MA	−	UV	Riegger & Robinson (1997)
mycosporine-glycine	MA	−	UV	
shinorine	MA	−	UV	
Proboscia inermis				
porphyra-334	MA	−	UV	Riegger & Robinson (1997)
shinorine	MA	−	UV	
Pseudonitzschia sp.				
porphyra-334	MA	−	UV	Helbling *et al*. (1996)
Stellarima microtrias				
porphyra-334	MA	−	UV	Riegger & Robinson (1997)
shinorine	MA	−	UV	
Thalassiosira antarctica				
porphyra-334	MA	−	UV	Riegger & Robinson (1997)
shinorine	MA	−	UV	
Thalassiosira tumida				
porphyra-334	MA	−	UV	Riegger & Robinson (1997)
shinorine	MA	−	UV	
Thalassiosira weissflogii				
mycosporine-like amino acid	MA	−	−	Hannach & Sigleo (1998)
Thalassiosira sp.				
porphyra-334	MA	−	UV	Helbling *et al*. (1996)
shinorine	MA	−	UV	
Diatom mat (mixture of *Achnantes* sp., *Licmophora* sp., *Navicula* sp.)				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
CL. CHLOROPHYCEAE (GREEN ALGAE)				
Dunaliella tertiolecta				
mycosporine-like amino acid	MA	−	−	Hannach & Sigleo (1998)
Dunaliella sp. (Ace Lake) and *Dunaliella* sp. (Burton Lake)				
UVA and UVB absorbing compounds	−	−	UV	Jeffrey *et al*. (1999)
Enteromorpha bulbosa				
UV-absorbing pigments	−	−	UV	Post & Larkum (1993)
porphyra-334	MA	−	UV	Hoyer *et al*. (2001)
dibromomethane	VH	−	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
Enteromorpha compressa				
bromomethane	VH	−	−, UV	Laturnus *et al*. (1998a,b)
bromoform	VH	−	−, UV	
dibromomethane	VH	−	UV	
bromochloromethane	VH	−	UV	
bromodichloromethane	VH	−	UV	
bromoethane	VH	−	UV	
dibromoethane	VH	−	UV	
chloromethane	VH	−	UV	
iodomethane	VH	−	−, UV	Giese *et al*. (1999)
iodoethane	VH	−	UV, −	
chloroiodomethane	VH	−	UV, −	
diiodomethane	VH	−	UV, −	
1-iodopropane	VH	−	−	
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	
2-iodobutane	VH	−	−	
Lambia antarctica				
unspecified brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified iodating activity	−	−	−	
bromomethane	VH	−	−	Laturnus *et al*. (1998a)
bromoform	VH	−	−	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
iodomethane	VH	−	−	
iodoethane	VH	−	−	Giese *et al*. (1999)
1-iodopropane	VH	−	−	
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	
2-iodobutane	VH	−	−	
diiodomethane	VH	−	−	
chloroiodomethane	VH	−	−	
thallus	−	−	D_{SS}, no D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	no D_{SS}, no D_{SC}	
hydrophilic extract (methanol:water)	−	−	no D_{SS}, no D_{SC}	
Monostroma hariotii				
dibromomethane	VH	−	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
shinorine	MA	−	UV	Hoyer *et al*. (2001)
lipophilic extract (CH_2Cl_2:methanol)	−	−	FO_S	Amsler *et al*. (2005b)
Prasiola crispa ssp. *antarctica*				
mycosporine-glycine	MA	−	UV	Hoyer *et al*. (2001, 2003)
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	−	UV	
mycosporine-like amino acid	−	−	UV	
Green algal mat (mixture of *Ulothrix* cf. *australis, Urospora* cf. *penicilliformis*)				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
asterina-330	MA	−	UV	
CL. PHAEOPHYCEAE (BROWN ALGAE)				
Adenocystis utricularis				
dibromomethane	VH	−	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
no mycosporine-like amino acids	−	−	−	Hoyer *et al*. (2001)
thallus	−	−	D_{SS}, D_{SF}	Amsler *et al*. (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	−	−	D_{SS}, no D_{SF}, no D_{SC}, FO_S	
hydrophilic extract (methanol:water)	−	−	no D_{SS}, no D_{SF}, D_{SC}, FO_S	
phlorotannin	PT	−	−	Iken *et al*. (2007)
Ascoseira mirabilis				
bromomethane	VH	−	−	Laturnus (1995); Laturnus *et al*. (1998a)
dibromomethane	VH	−	−, B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	−, B_S? or D_S?	
bromoethane	VH	−	−	
1,2-dibromoethane	VH	−	−, B_S? or D_S?	
bromochloromethane	VH	−	−	
bromodichloromethane	VH	−	−, B_S? or D_S?	
dibromochloromethane	VH	−	−, B_S? or D_S?	
diiodomethane	VH	−	−, B_S? or D_S?	
iodoethane	VH	−	−	
chloroiodomethane	VH	−	−, B_S? or D_S?	
chloromethane	VH	−	−	
iodomethane	VH	−	−	
unspecified no brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified no iodating activity	−	−	−	
homogenated algae	−	−	no G_{SM}	Iken (1999)
intact tissue	−	−	G_{SM}	
no mycosporine-like amino acid	−	−	−	Hoyer *et al*. (2001)
thallus	−	−	no D_{SS}, D_{SF}	Amsler *et al*. (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	−	−	no D_{SS}, noD_{SF},	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
			no D_{SC}, FO_S	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no $D_{SC,}$ FO_S	
phlorotannin	PT	–	–	Iken *et al*. (2007)
Chordaria linearis				
thallus	–	–	D_{SS}	Amsler *et al*. (2005a)
phlorotannin	PT	–	–	Iken *et al*. (2007)
Cystosphaera jacquinotii				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
cystosphaerol	TS	–	–	Ankisetty *et al*. (2004b)
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, noD_{SC}	
hydrophilic extract (methanol:water)	–	–	D_{SS}, D_{SC}	
phlorotannin	PT	–	G_S?	Iken *et al*. (2007)
Desmarestia anceps				
bromomethane	VH	–	–	Laturnus (1995)
dibromomethane	VH	–	–, B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	–	–, B_S? or D_S?	
bromoethane	VH	–	–	
1,2-dibromoethane	VH	–	–, B_S? or D_S?	
bromodichloromethane	VH	–	–, B_S? or D_S?	
dibromochloromethane	VH	–	–, B_S? or D_S?	
diiodomethane	VH	–	–. B_S? or D_S?	
iodoethane	VH	–	–	
chloroiodomethane	VH	–	–, B_S? or D_S?	
thallus	–	–	D_{SS}, $D_{SF,}$ D_{SC}	Amsler *et al*. (2005a,b); Huang *et al*. (2006)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SF}, no D_{SC}, FO_S	
hydrophilic extract (methanol:water)	–	–	D_{SS}, D_{SF}, D_{SC}, FO_S	
extracts of different parts of thallus	–	–	D_{SC}	Fairhead *et al*. (2005a)
phlorotannin	PT	–	–	Fairhead *et al*. (2005b, 2006); Iken *et al*. (2007)
Desmarestia antarctica				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
thallus	–	–	D_{SC}	Huang *et al*. (2006)
Desmarestia antartica (1st year)				
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al*. (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, no D_{SF}, no D_{SC}, FO_S	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SC}, FO_S	
Desmarestia antarctica (2nd year)				
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SC}, FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	–	–	D_{SS}, D_{SC}	
phlorotannin	PT	–	–	Iken *et al*. (2007)
Desmarestia menziesii				
bromoform	VH	–	B_S? or D_S?, –	Laturnus *et al*. (1996, 1998a)
bromomethane	VH	–	–	
dibromomethane	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
iodomethane	VH	–	–	
plastoquinones	QN	–	S?, I?, L?	Rivera *et al*. (1990)
benzoquinones [1,2]	QN	–	S?, I?, L?	Rivera (1996)
hydroquinone	QN	–	–	
menzoquinone	QN	–	–	Ankisetty *et al*. (2004b)
sargadiol-I	CR	–	–	
sargadiol	CR	–	–	
palythene	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
mycosporine-glycine	MA	–	UV	
unspecified no brominating activity	–	–	–	Laturnus *et al*. (1997)
unspecified iodating activity	–	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al*. (2001)
thallus	–	–	D_{SS}, D_{SF}, D_{SC}	Amsler *et al*. (2005a,b); Huang *et al*. (2006)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, D_{SF}, D_{SC}, FO_S	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SF}, no D_{SC} , FO_S	
extracts of different parts of thallus	–	–	D_{SC}	Fairhead *et al*. (2005a)
phlorotannin	PT	–	–, no D_{SC}	Fairhead *et al*. (2005b, 2006); Iken *et al*. (2007)
Geminocarpus geminatus				
thallus	–	–	no D_{SS}	Amsler *et al*. (2005a)
Halopteris obovata				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
thallus	–	–	no D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SC}	
hydrophilic extract (methanol:water)	–	–	no D_{SC}	
Himantothallus grandifolius				
bromomethane	VH	–	–	Laturnus (1995)
dibromomethane	VH	–	–, B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	–	–, B_S? or D_S?	
bromoethane	VH	–	–	
1,2-dibromoethane	VH	–	–, B_S? or D_S?	
bromochloromethane	VH	–	–	
bromodichloromethane	VH	–	–, B_S? or D_S?	
dibromochloromethane	VH	–	–, B_S? or D_S?	
diiodomethane	VH	–	–, B_S? or D_S?	
iodoethane	VH	–	–	
chloroiodomethane	VH	–	–, B_S? or D_S?	
homogenated algae	–	–	no G_{SM}	Iken (1999)
intact tissue	–	–	G_{SM}	
porphyra-334	MA	–	UV	Hoyer *et al*. (2001)
palythine	MA	–	UV	
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al*. (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, no D_{SF}, D_{SC}, no FO_S	
hydrophilic extract (methanol:water)	–	–	D_{SS}, D_{SF}, D_{SC}, FO_S	
phlorotannin	PT	–	G_S?	Iken *et al*. (2007)
Phaeurus antarcticus				
dibromomethane	VH	–	–, B_S? or D_S?	Laturnus (1995);
bromoform	VH	–	–, B_S? or D_S?	Laturnus *et al*. (1996)
bromoethane	VH	–	–	
1,2-dibromoethane	VH	–	–, B_S? or D_S?	
bromochloromethane	VH	–	–	
bromomethane	VH	–	–	
bromodichloromethane	VH	–	–, B_S? or D_S?	
dibromochloromethane	VH	–	–, B_S? or D_S?	
diiodomethane	VH	–	–, B_S? or D_S?	
iodoethane	VH	–	–	
chloroiodomethane	VH	–	–, B_S? or D_S?	
homogenated algae	–	–	no G_{SM}	Iken (1999)
intact tissue	–	–	G_{SM}	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
no mycosporine-like amino acids	–	–	–	Hoyer *et al*. (2001)
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SC}	
hydrophilic extract (methanol:water)	–	–	D_{SC}	
phlorotannin	PT	–	G_S?	Iken *et al*. (2007)
CL. RODOPHYCEAE (RED ALGAE)				
Antarcticothamnion polysporum				
bromomethane	VH	–	–	Laturnus *et al*. (1998a)
iodomethane	VH	–	–	
bromoform	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al*. (2001, 2002)
Audouinella purpurea				
no mycosporine-like amino acids	–	–	–	Hoyer *et al*. (2001, 2002)
Ballia callitricha				
unspecified brominating activity	–	–	–	Laturnus *et al*. (1997)
bromomethane	VH	–	–	Laturnus *et al*. (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	
iodoethane	VH	–	–	Giese *et al*. (1999)
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al*. (2001, 2002)
Bangia atropurpurea				
porphyra-334	MA	–	UV	Hoyer *et al*. (2001)
palythinol	MA	–	UV	
Callophyllis atrosanguinea				
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SC}	
hydrophilic extract (methanol:water)	–	–	D_{SS}, no D_{SF}, no D_{SC}	
Curdiea racovitzae				
palythine	MA	–	UV	Karentz *et al* (1991);
shinorine	MA	–	UV	Hoyer *et al*. (2001)
mycosporine-glycine	MA	–	UV	
palythene	MA	–	UV	
palythinol	MA	–	UV	
porphyra-334	MA	–	UV	
asterina-330	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 324nm)	MA	–	UV	Hoyer *et al*. (2003)
unknown mycosporine-like amino acid (max. absorb. 357nm)	MA	–	UV	
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
homogenated algae	–	–	no G_{SM}	Iken (1999)
intact tissue	–	–	G_{SM}	
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, no D_{SC}, FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	–	–	D_{SS}, no D_{SC}, FO_S	
Delesseria lancifolia				
bromoform	VH	–	B_S? or D_S?	Laturnus *et al*. (1996,1998a)
bromomethane	VH	–	–	
1,2-dibromoethane	VH	–	B_S? or D_S?	
dibromomethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?, –	Giese *et al*. (1999)
chloroiodomethane	VH	–	B_S? or D_S?, –	
iodomethane	VH	–	–	
iodoethane	VH	–	–	
1-iodopropane	VH	–	–	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	
2-iodobutane	VH	−	−	
unspecified no brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified no iodating activity	−	−	−	
no mycosporine-like amino acids	−	−	−	Hoyer *et al*. (2001, 2002)
thallus	−	−	no D_{SS}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	no D_{SS}, no D_{SC}	
hydrophilic extract (methanol:water)	−	−	no D_{SS}, D_{SC}	
Delesseria salicifolia				
thallus	−	−	D_{SS}, D_{SF}	Amsler *et al*. (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	−	−	no D_{SS}, D_{SF}, D_{SC}	
hydrophilic extract (methanol:water)	−	−	D_{SS}, no D_{SF}, D_{SC}, no FO_S	
Delisea fimbriata (= *Delisea pulchra)*				
acetoxyfimbrolides A, B, C, D, E, and F	HP	−	B_A	Pettus *et al*. (1977)
2 acetoxyfimbrolides	HP	−	−	Cueto *et al*. (1991)
2 acetyl derivatives	HP	−	−	Cueto *et al*. (1997)
4 fimbrolides	HP	−	−	
fimbrolide	HP	−	B_A, F	Ankisetty *et al*. (2004b)
acetoxyfimbrolide	HP	−	B_A, F	
hydroxyfimbrolide	HP	−	B_A, F	
pulchralides A, B and C	HP	−	−	
2 polyhalogenated unsaturated ketones	HP	−	−	
thallus	−	−	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	D_{SS}, D_{SC}	
hydrophilic extract (methanol:water)	−	−	no D_{SS}, no D_{SC}	
Georgiella confluens				
dibromomethane	VH	−	B_S? or D_S?, UV	Laturnus *et al*. (1996, 1998b)
bromoform	VH	−	B_S? or D_S?, UV, −	Laturnus *et al*. (1998a)
bromomethane	VH	−	−, UV	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?, UV	
dibromochloromethane	VH	−	B_S? or D_S?	
bromoethane	VH	−	UV	
bromochloromethane	VH	−	UV	
dibromoethane	VH	−	UV	
chloroiodomethane	VH	−	B_S? or D_S?, UV, −	Giese *et al*. (1999)
chloromethane	VH	−	−, UV	
diiodomethane	VH	−	B_S? or D_S?, UV, −	
iodomethane	VH	−	−, UV	
iodoethane	VH	−	UV, −	
1-iodopropane	VH	−	−	
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	
2-iodobutane	VH	−	−	
unspecified no brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified no iodating activity	−	−	−	
shinorine	MA	−	UV	Hoyer *et al*. (2001)
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	Hoyer *et al*. (2003)
thallus	−	−	no D_{SS}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	FO_S	
Gigartina papillosa				
dibromomethane	VH	−	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
Gigartina skottsbergii				
unspecified brominating activity	−	−	−	Laturnus *et al*. (1997)
chloromethane	VH	−	−	Laturnus *et al*. (1998a)
bromomethane	VH	−	−	
iodomethane	VH	−	−	
bromoform	VH	−	−	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
iodoethane	VH	−	−	Giese *et al*. (1999)
1-iodopropane	VH	−	−	
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	
2-iodobutane	VH	−	−	
diiodomethane	VH	−	−	
chloroiodomethane	VH	−	−	
shinorine	MA	−	UV	Hoyer *et al*. (2001)
palythine	MA	−	UV	
asterina-330	MA	−	UV	
porphyra-334	MA	−	UV	
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	−	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	Hoyer *et al*. (2003)
thallus	−	−	no D_{SS}, no D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	−	−	no FO_S	
Gymnogongrus antarcticus				
dibromomethane	VH	−	B_S? or D_S?, UV	Laturnus *et al*. (1996, 1998b)
bromoform	VH	−	B_S? or D_S?, −, UV	Laturnus *et al*. (1998a, 2000)
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromomethane	VH	−	−, UV	
bromochloromethane	VH	−	UV	
bromoethane	VH	−	UV	
dibromoethane	VH	−	UV	
bromodichloromethane	VH	−	B_S? or D_S?, UV	
dibromochloromethane	VH	−	B_S? or D_S?, UV, −	Giese *et al*. (1999)
chloroiodomethane	VH	−	B_S? or D_S?, UV, −	
chloromethane	VH	−	−, UV	
iodomethane	VH	−	−, UV	
iodoethane	VH	−	UV, −	
1-iodopropane	VH	−	−, UV	
2-iodopropane	VH	−	−, UV	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−, UV	
2-iodobutane	VH	−	−, UV	
iodoethane	VH	−	UV	
unspecified brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified iodating activity	−	−	−	
shinorine	MA	−	UV	Hoyer *et al*. (2001, 2002)
palythine	MA	−	UV	
asterina-330	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	Hoyer *et al*. (2003)
thallus	−	−	no D_{SS}, D_{SF}	Amsler *et al*. (2005a)
hydrophilic extract (methanol:water)	−	−	no D_{SC}	
lipophilic extract (CH_2Cl_2:methanol)	−	−	no D_{SC}, FO_S	Amsler *et al*. (2005b)
Gymnogongrus turquetii				
mycosporine-glycine	MA	−	UV	Hoyer *et al*. (2001)
shinorine	MA	−	UV	Hoyer *et al*. (2002, 2003)
porphyra-334	MA	−	UV	
thallus	−	−	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	no D_{SS}, D_{SF}, D_{SC}, FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	−	−	D_{SS}, no D_{SF}, D_{SC}, FO_S	
Hymenocladiopsis crustigena				
dibromomethane	VH	−	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
no mycosporine-like amino acids	−	−	−	Hoyer *et al*. (2001, 2002, 2003)
Iridaea cordata				
palythine	MA	−	UV	Karentz *et al.* (1991); McClintock & Karentz (1997);

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
shinorine	MA	−	UV	Hoyer *et al*. (2001)
mycosporine-glycine	MA	−	UV	
palythene	MA	−	UV	
asterina-330	MA	−	UV	
palythinol	MA	−	UV	
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	−	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	Hoyer *et al*. (2003)
bromomethane	VH	−	−	Laturnus (1995); Laturnus *et al*. (1998a)
dibromomethane	VH	−	−, B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	−, B_S? or D_S?, −	
bromoethane	VH	−	−	
1,2-dibromoethane	VH	−	−, B_S? or D_S?	
bromochloromethane	VH	−	−	
bromodichloromethane	VH	−	−, B_S? or D_S?	
dibromochloromethane	VH	−	−, B_S? or D_S?	
iodomethane	VH	−	−	
diiodomethane	VH	−	−, B_S? or D_S?	Giese *et al*. (1999)
iodoethane	VH	−	−	
chloroiodomethane	VH	−	−, B_S? or D_S?	
1-iodopropane	VH	−	−	
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	
2-iodobutane	VH	−	−	
unspecified no brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified no iodating activity	−	−	−	
thallus	−	−	P_{SU}, D_{SS}, no D_{SF}	McClintock & Baker (1995)
thallus on *S. neumayeri*	−	−	PP_S	Amsler *et al*. (1998, 2005a)
thallus without chemicals on *S. neumayeri*	−	−	PP_S	Amsler *et al*. (1999)
lipophilic extract (CH_2Cl_2:methanol)	−	−	P_{SU}, no D_{SS}, no D_{SC}, FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	−	−	P_{SU}, D_{SS}, D_{SC}, FO_S	
Kallymenia antarctica				
bromoform	VH	−	B_S? or D_S?, −	Laturnus *et al*. (1996, 1998a)
bromomethane	VH	−	−	
dibromomethane	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
iodomethane	VH	−	−	
unspecified no brominating activity	−	−	−	Laturnus *et al*. (1997)
mycosporine-glycine	MA	−	UV	Hoyer *et al*. (2001)
shinorine	MA	−	UV	Hoyer *et al*. (2002, 2003)
palythine	MA	−	UV	
asterina-330	MA	−	UV	
palythinol	MA	−	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	−	UV	
mycosporine-glycine	MA	−	UV	
porphyra-334	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	
Leptosomia simplex				
carotenoids	CA	−	UV?, X?	Karentz & Bosch (2001)
Lithothamnion cf. *antarcticum*				
porphyra-334	MA	−	UV	Karentz *et al.* (1991)
shinorine	MA	−	UV	
Myriogramme manginii				
bromoform	VH	−	B_S? or D_S?, −	Laturnus *et al*. (1996, 1998a)
bromomethane	VH	−	−	
dibromomethane	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
chloroiodomethane	VH	−	B_S? or D_S?	
iodomethane	VH	−	−	
unspecified brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified iodating activity	−	−	−	
shinorine	MA	−	UV	Hoyer *et al*. (2001)
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
asterina-330	MA	−	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	Hoyer *et al*. (2003)
thallus	−	−	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	D_{SS}, no D_{SC}, FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	−	−	no D_{SS}, no D_{SC}, FO_S	
Myriogramme smithii				
no mycosporine-like amino acids	−	−	−	Hoyer *et al*. (2001, 2002, 2003)
p-hydroxybenzaldehyde	AA	−	−	Ankisetty *et al*. (2004b)
p-methoxyphenol	QN	−	−	
thallus	−	−	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	D_{SS}, D_{SF}, no D_{SC}, FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	−	−	D_{SS}, no D_{SF}, no D_{SC} , no FO_S	
Nereoginkgo adiantifolia				
thallus	−	−	no D_{SS}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	FO_S	Amsler *et al*. (2005b)
Neuroglossum ligulatum				
iodoethane	VH	−	−	Giese *et al*. (1999)
1-iodopropane	VH	−	−	
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	
2-iodobutane	VH	−	−	
diiodomethane	VH	−	−	
chloroiodomethane	VH	−	−	
shinorine	MA	−	UV	Hoyer *et al*. (2001, 2002, 2003)
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	
Notophycus fimbriatus				
mycosporine-glycine	MA	−	UV	Hoyer *et al*. (2001)
shinorine	MA	−	UV	
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
asterina-330	MA	−	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	Hoyer *et al*. (2003)
Pachymenia orbicularis				
mycosporine-glycine	MA	−	UV	Hoyer *et al*. (2001)
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	Hoyer *et al*. (2003)
thallus	−	−	D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	no D_{SS}, no D_{SC}, FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	−	−	no D_{SS}, no D_{SC}	
Palmaria decipiens				
palythine	MA	−	UV	Karentz *et al.* (1991);
shinorine	MA	−	UV	Hoyer *et al*. (2001, 2002)
porphyra-334	MA	−	UV	Hoyer *et al*. (2003)
mycosporine-glycine	MA	−	UV	
palythene	MA	−	UV	
asterina-330	MA	−	UV	
palythinol	MA	−	UV	
usujirene	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
UV-absorbing pigments	−	−	UV	Post & Larkum (1993)
bromomethane	VH	−	−	Laturnus (1995)
bromomethane	VH	−	−	Laturnus *et al*. (1998a)
dibromomethane	VH	−	−, B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	−, B_S? or D_S?	
bromoethane	VH	−	−	
1,2-dibromoethane	VH	−	−, B_S? or D_S?	
bromochloromethane	VH	−	−	
bromodichloromethane	VH	−	−, B_S? or D_S?	
dibromochloromethane	VH	−	−, B_S? or D_S?	
diiodomethane	VH	−	−, B_S? or D_S?	
iodoethane	VH	−	−	
chloroiodomethane	VH	−	−, B_S? or D_S?	
chloromethane	VH	−	−	
iodomethane	VH	−	−	
unspecified brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified no iodating activity	−	−	−	
homogenated algae	−	−	no G_{SM}	Iken (1999)
intact tissue	−	−	G_{SM}	
thallus	−	−	no D_{SS}, no D_{SF}	Amsler *et al*. (2005a)
Pantoneura plocamioides				
bromoform	VH	−	B_S? or D_S?, −	Laturnus *et al*. (1996, 1998a)
bromomethane	VH	−	−	
dibromomethane	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
iodomethane	VH	−	−	
diiodomethane	VH	−	B_S? or D_S?, −	Giese *et al*. (1999)
chloroiodomethane	VH	−	B_S? or D_S?, −	
iodoethane	VH	−	−	
1-iodopropane	VH	−	−	
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	
2-iodobutane	VH	−	−	
unspecified brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified no iodating activity	−	−	−	
pantofuranoids A, B, C, D, E and F	MT	−	−	Cueto & Darias (1996)
pantoneurotriol 1a and 2a	MT	−	−	Cueto *et al*. (1998c)
2 epimeric alcohols	−	−	−	
pantoneurines A and B	MT	−	−, D_{AI}	Cueto *et al*. (1998b); Argandoña *et al*. (2002)
pantopyranoids A, B and C	MT	−	−	Cueto *et al*. (1998a)
pantoisofuranoids A, B and C	MT	−	−	
no mycosporine-like amino acids	−	−	−	Hoyer *et al*. (2001, 2002)
thallus	−	−	no D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	no D_{SF}, no D_{SC}, FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	−	−	no D_{SF}, no D_{SC}, no FO_S	
Picconiella plumosa				
bromoform	VH	−	B_S? or D_S?, −	Laturnus *et al*. (1996, 1998a)
bromomethane	VH	−	−	
dibromomethane	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
iodomethane	VH	−	−	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
chloromethane	VH	−	−	
unspecified brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified no iodating activity	−	−	−	
no mycosporine-like amino acids	−	−	−	Hoyer *et al*. (2001, 2003)
thallus	−	−	no D_{SS}, D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	no D_{SS}, no D_{SC}	
hydrophilic extract (methanol:water)	−	−	D_{SC}, FO_S	Amsler *et al*. (2005b)
Phycodrys austrogeorgica				
unspecified no brominating activity	−	−	−	Laturnus *et al*. (1997)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
unspecified no iodating activity	–	–	–	
bromomethane	VH	–	–	Laturnus *et al*. (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al*. (2001, 2002, 2003)
thallus	–	–	no D_{SS}	Amsler *et al*. (2005a)
Phycodrys quercifolia				
bromomethane	VH	–	–, UV	Laturnus *et al*. (1998a,b)
bromoform	VH	–	–, UV	
dibromomethane	VH	–	UV	
bromochloromethane	VH	–	UV	
bromodichloromethane	VH	–	UV	
bromoethane	VH	–	UV, –	Giese *et al*. (1999)
chloromethane	VH	–	–, UV	
chloroiodomethane	VH	–	UV, –	
iodomethane	VH	–	–, UV	
iodoethane	VH	–	UV	
diiodomethane	VH	–	UV, –	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al*. (2001, 2002)
Phyllophora ahnfeltioides				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?, –	Giese *et al*. (1999)
chloroiodomethane	VH	–	B_S? or D_S?, –	
iodoethane	VH	–	–	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al*. (2001, 2002)
Phyllophora antarctica				
shinorine	MA	–	UV	McClintock & Baker (1995)
palythine	MA	–	UV	McClintock & Karentz (1997)
bromomethane	VH	–	–	Laturnus *et al*. (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	
thallus	–	–	P_{SU}	Amsler *et al*. (1998)
polar extract	–	–	P_{SU}	
non polar extract	–	–	P_{SU}	
thallus on *S. neumayeri*	–	–	PP_S	Amsler *et al*. (1999)
thallus without chemicals on *S. neumayeri*	–	–	PP_S	
lipophilic extract (CH_2Cl_2:methanol)	–	–	FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	–	–	FO_S	
Phyllophora appendiculata				
palythine	MA	–	UV	Karentz *et al*. (1991)
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
iodoethane	VH	–	–	Giese *et al*. (1999)
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
Plocamium cartilagineum				
mixture of compounds (TLC)	–	–	F_T	Stierle & Sims (1979)
cyclohexanes [3, 4, 5, 6]	MT	–	F_T	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
plocamene D	MT	−	−, B_A, Y	Darias *et al*. (1987); Cueto *et al*. (1991)
epi-plocamene D	MT	−	−, B_A, no Y, Y, D_{SC}, no D_{SS}	Rovirosa *et al*. (1990); Ankisetty *et al*. (2004b)
acyclic halogenated monoterpene	MT	−	−	
monoterpene 7	MT	−	B_A, Y	
monoterpene 8	MT	−	−	
monoterpene 9 and 11	MT	−	B_A, no Y	
monoterpene 10	MT	−	B_A, no Y, Y, IN,	
anverene	MT	−	B_A, no Y, $D_{SC,}$ no D_{SS}	
pyranoid	MT	−	no B_A, Y, no D_{SC}, no D_{SS}	
unspecified brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified iodating activity	−	−	−	
bromomethane	VH	−	−	Laturnus *et al*. (1998a)
bromoform	VH	−	−	
iodomethane	VH	−	−	
iodoethane	VH	−	−	Giese *et al*. (1999)
1-iodopropane	VH	−	−	
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	
2-iodobutane	VH	−	−	
diiodomethane	VH	−	−	
chloroiodomethane	VH	−	−	
shinorine	MA	−	UV	Hoyer *et al*. (2001, 2002)
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
asterina-330	MA	−	UV	
palythinol	MA	−	UV	
mycosporine-like amino acid	MA	−	UV	Hoyer *et al*. (2003)
thallus	−	−	no D_{SS}, no D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	D_{SS}, D_{SF}, D_{SC}, FO_S	Amsler *et al*. (2005b)
hydrophilic extract (methanol:water)	−	−	D_{SS}, no D_{SF}, D_{SC}, FO_S	
Plocamium coccineum				
dibromomethane	VH	−	B_S? or D_S?	Laturnus *et al*. (1996)
bromoform	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?	
chloroiodomethane	VH	−	B_S? or D_S?	
Plocamium sp.				
mixture compounds in TLC	−	−	F_T	Stierle *et al*. (1979)
4 monoterpenes	MT	−	F_T	
Plumariopsis peninsularis				
thallus	−	−	no D_{SS}, no D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	−	−	D_{SS}, no D_{SF}, no D_{SC}	
hydrophilic extract (methanol:water)	−	−	no D_{SS}, D_{SC}	
Porphyra endiviifolium				
unspecified brominating activity	−	−	−	Laturnus *et al*. (1997)
unspecified no iodating activity	−	−	−	
bromoform	VH	−	B_S? or D_S?, −	Laturnus *et al*. (1996,1998a)
bromomethane	VH	−	−	
dibromomethane	VH	−	B_S? or D_S?	
1,2-dibromoethane	VH	−	B_S? or D_S?	
bromodichloromethane	VH	−	B_S? or D_S?	
dibromochloromethane	VH	−	B_S? or D_S?	
diiodomethane	VH	−	B_S? or D_S?, −	Giese *et al*. (1999)
chloromethane	VH	−	−	
chloroiodomethane	VH	−	B_S? or D_S?, −	
iodomethane	VH	−	−	
iodoethane	VH	−	−	
1-iodopropane	VH	−	−	
2-iodopropane	VH	−	−	
1-iodo-2-methylpropane	VH	−	−	
1-iodobutane	VH	−	−	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
2-iodobutane	VH	–	–	
mycosporine-glycine	MA	–	UV	Hoyer *et al*. (2001)
shinorine	MA	–	UV	Hoyer *et al*. (2002)
porphyra-334	MA	–	UV	Hoyer *et al*. (2003)
palythine	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	
Porphyra plocamiestris				
shinorine	MA	–	UV	Hoyer *et al*. (2002)
porphyra-334	MA	–	UV	
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al*. (2005a)
Rhodymenia subantarctica				
bromomethane	VH	–	–	Laturnus *et al*. (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	
iodoethane	VH	–	–	Giese *et al*. (1999)
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
porphyra-334	MA	–	UV	Hoyer *et al*. (2001)
Sarcothalia papillosa				
shinorine	MA	–	UV	Hoyer *et al*. (2001)
palythine	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al*. (2003)
Trematocarpus antarcticus				
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al*. (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SF}, no D_{SC}, FO_S	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SF}, no D_{SC}	
Undescribed species, probably *Pugetia* sp. (Kallymeniaceae)				
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al*. (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, D_{SF}, no D_{SC}	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SF}, D_{SC}	
PH. CILIATA				
Euplotes focardii				
epoxyfocardin	DT	–	C_S, C_A	Guella *et al*. (1996)
focardin	DT	–	C_S, C_A	
Euplotes nobilii (strain AC-1)				
pheromone En-1	NC	–	MI	Felici *et al*. (1999)
pheromone En-2	NC	–	MI	
PH. SARCOMASTIGOPHORA				
Gromia oviformis				
no mycosporine-like amino acids	–	–	–	Karentz *et al*. (1991)
PH. PORIFERA				
Unidentified species (#1)				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
palythinol	MA	–	UV	
Unidentified species (#3)				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
Unidentified species (#5)				

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
Unidentified species (#6)				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Unidentified species				
sesquiterpene alcohol	SQ	−	B_A	Urban *et al*. (1995)
Unidentified species (#6)				
hydrophilic extract	−	−	no T_S	McClintock *et al*. (2000)
lipohilic extract	−	−	T_S	
Unidentified species (#20)				
hydrophilic extract	−	−	no T_S	McClintock *et al*. (2000)
lipohilic extract	−	−	T_S	
Unidentified species (#21)				
hydrophilic extract	−	−	no T_S	McClintock *et al*. (2000)
lipohilic extract	−	−	no T_S	
Unidentified species (#23)				
hydrophilic extract	−	−	no T_S	McClintock *et al*. (2000)
lipohilic extract	−	−	T_S	
Unidentified species (#29)				
hydrophilic extract	−	−	no T_S	McClintock *et al*. (2000)
lipohilic extract	−	−	T_S	
CL. CALCAREA, O. CALCINEA				
Leucetta antarctica				
bromochlorophenol	HP	−	−	Vetter & Janussen (2005)
2,4-dibromophenol	HP	−	−	
2,6-dibromophenol	HP	−	−	
bromochloroanisole	HP	−	−	
bromodichlorophenol	HP	−	−	
dibromoanisole	HP	−	−	
dibromochlorophenol	HP	−	−	
2,4,6-tribromoanisole	HP	−	−	
tribromooctenone	HP	−	−	
2,4,6-tribromophenol	HP	−	−	
mixed halogenated compounds (MHC-1)	HP	−	−	
Leucetta leptoraphis				
methanolic extract	−	−	I_A, B_A, T_S, no Y	McClintock (1987); McClintock *et al*. (1993a, 1994b)
methanolic extract fraction 1 (taurine)	−	−	−	Baker *et al*. (1993)
methanolic extract fraction 2	−	−	C	
methanolic extract fraction 3	−	−	C	
methanolic/dichloromethanolic extract	−	−	L_A	Jayatilake *et al*. (1997)
methanol-toluenic extract	−	−	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	−	−	C_S, R_S, T_S	McClintock *et al*. (1990)
hexane extract	−	−	B_A, no T_S, no Y	
chloroform extract	−	−	B_A, no T_S, no Y	
rhapsamine	NC	−	L_A, S	
non polar extract	−	−	FO_S	Amsler *et al*. (2000b)
polar extract	−	−	FO_S	
CL. HEXACTINELLIDA, O. LYSSACINOSA				
Unidentified species				
ergosta-4,24(28)-dien-3-one	TS	−	−	Guella *et al*. (1988)
Rossella nuda				
methanolic extract	−	−	no I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al*. (1993a, 1994b)
hexane extract	−	−	no B_A, no T_S, no Y	
chloroform extract	−	−	no B_A, T_S, no Y	
palythine	MA	−	UV	McClintock & Karentz (1997)
Rossella racovitzae				
methanolic extract	−	−	no I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al*. (1993a, 1994b)
aqueous extract	−	−	no C_S, no R_S,	McClintock *et al*. (1990)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
			no T_S	
hexane extract	–	–	no B_A, T_S, no Y	
chloroform extract	–	–	B_A, no T_S, no Y	
mycosporine-glycine	MA	–	UV	McClintock & Karentz (1997)
palythine	MA	–	UV	
Scolimastra joubini				
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al*. (1990)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
hydrophilic extract	–	–	T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	T_S	
CL. DEMOSPONGIAE, O. POECILOSCLERIDA				
Artemisina apollinis				
12 sterols	TS	–	–	Seldes *et al*. (1990b)
mixture steroidal ketones	TS	–	–	
bromochlorophenol	HP	–	–	Vetter & Janussen (2005)
2,4-dibromophenol	HP	–	–	
2,6-dibromophenol	HP	–	–	
dibromoanisole	HP	–	–	
dibromochlorophenol	HP	–	–	
2,4,6-tribromoanisole	HP	–	–	
tribromooctenone	HP	–	–	
2,4,6-tribromophenol	HP	–	–	
mixed halogenated compound (MHC-1)	HP	–	–	
Ectyodoryx ramilobosa (= *Lissodendoryx (Ectyodoryx) ramilobosa*)				
hydrophilic extract	–	–	no T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	T_S	
Inflatella belli				
methanolic extract	–	–	I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al*. (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al*. (1990)
hexane extract	–	–	no B_A, T_S, no Y	
chloroform extract	–	–	no B_A, T_S, no Y	
palythine	MA	–	UV	McClintock & Karentz (1997)
Isodictya erinacea				
methanolic extract	–	–	no I_A, T_S, no B_A, T_S, no Y	McClintock (1987); Moon *et al*. (1998); McClintock *et al*. (1993a, 1994b); Baker & Yoshida (1994)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al*. (1990)
chloroform extract	–	–	T_S, B_A, no Y	Baker *et al*. (1993)
hexane extract	–	–	B_A, no T_S, no Y	
erinacean	NC	–	B_A, S, no T_S	
inosine	NC	–	no T_S	
uridine	NC	–	no T_S	
2'-deoxycytidine	NC	–	no T_S	
1,9-demethylguanine	NC	–	no T_S	
7-methyladenine	NC	–	no T_S	
p-hydroxybenzaldehyde	AA	–	T_S	
erebusinone (erebusphenone)	NC	–	no T_S, M_S	Moon *et al*. (2000)
palythine	MA	–	UV	McClintock & Karentz (1997)
palythinol	MA	–	UV	
Isodictya setifera				
methanolic extract	–	–	no I_A, B_A, no T_S, no Y	McClintock (1987); McClintock *et al*. (1993a)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	B_A, no T_S, no Y	
whole body sponge	(no DK, no PA)	–	–	Jayatilake *et al*. (1996)
eggs	–	–	D_{SS}, D_{SA}, D_{SC}	McClintock & Baker (1997b)
associated bacteria (*Pseudomonas aeruginosa*)				
cyclo-(L-Pro-L-Met)	DK	–	no C_A, no B_A	Jayatilake *et al*. (1996)
cyclo-(L-Pro-L-Val)	DK	–	no C_A, no B_A	
cyclo-(L-Pro-L-Leu)	DK	–	no C_A, no B_A	
cyclo-(L-Pro-L-Ile)	DK	–	no C_A, no B_A	
cyclo-(L-Pro-L-Phe)	DK	–	no C_A, no B_A	
cyclo-(L-Pro-L-Tyr)	DK	–	no C_A, no B_A	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
phenazine-1-carboxylic acid	PA	–	B_A	
phenazine-1-carboxamide	PA	–	B_A	
Isodictya spinigera				
hydrophilic extract	–	–	no T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	T_S	
Kirkpatrickia variolosa				
methanolic extract	–	–	I_A, B_A, no T_S, no Y, T_S	McClintock (1987); McClintock *et al*. (1993a, 1994b); Baker & Yoshida (1994)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	no C_S, no R_S, T_S	McClintock *et al*. (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, T_S, no Y	
crude extract	–	–	no B_A	Trimurtulu *et al*. (1994)
variolin A	PY	–	S, no T_S	
variolin B	PY	–	A, S	Perry *et al*. (1994)
variolin D	PY	–	no A, no S	
N(3')-methyl tetrahydrovariolin B	PY	–	F, S	
resveratrol triacetate	SF	–	–	Jayatilake *et al*. (1995)
purple uncharacterized pigment	–	–	T_S	
shinorine	MA	–	UV	McClintock & Karentz (1997)
mycosporine-glycine-valine	MA	–	UV	
palythine	MA	–	UV	
non polar extract	–	–	FO_S	Amsler *et al*. (2000b)
polar extract	–	–	FO_S	
2,4-dibromophenol	HP	–	–	Vetter & Janussen (2005)
2,6-dibromophenol	HP	–	–	
bromochloroanisole	HP	–	–	
bromodichlorophenol	HP	–	–	
dibromoanisole	HP	–	–	
dibromochlorophenol	HP	–	–	
2,4,6-tribromoanisole	HP	–	–	
tribromooctenone	HP	–	–	
2,4,6-tribromophenol	HP	–	–	
mixed halogenated compounds (MHC-1)	HP	–	–	
Latrunculia apicalis (=*Latrunculia* (*Latrunculia*) *apicalis*)				
methanolic extract	–	–	I_A, B_A, T_S, no Y	McClintock (1987); McClintock *et al*. (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al*. (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	B_A, no Y	
discorhabdin C	DA	–	T_S, B_S, B_A	Baker & Yoshida (1994); Yang *et al*. (1995)
discorhabdin G	DA	–	D_{SS}, B_A, B_S	Furrow *et al*. (2003)
shinorine	MA	–	UV	McClintock & Karentz (1997)
porphyra-334	MA	–	UV	
mycosporine-glycine-valine	MA	–	UV	
palythine	MA	–	UV	
Latrunculia sp.				
discorhabdins B and R	DA	–	B_A	Ford & Capon (2000)
Lissodendoryx flabellata (= *Lissodendoryx (Lissodendoryx) flabellata*)				
flabellatene A	DT	–	S	Fontana *et al*. (1999)
flabellatene B	DT	–	–	
Mycale acerata (= *Mycale (Oxymycale) acerata*)				
methanolic extract	–	–	I_A, no B_A, no T_S, no Y	McClintock (1987) McClintock *et al*. (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al*. (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, no T_S, no Y	
non polar extract	–	–	FO_S	Amsler *et al*. (2000b)
polar extract	–	–	no FO_S	
palythine	MA	–	UV	McClintock & Karentz (1997)
Myxodoryx hanitschi				
hydrophilic extract	–	–	no T_S	McClintock *et al*. (2000)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
lipohilic extract	–	–	no T_S	
Phorbas areolatus				
hydrophilic extract	–	–	no T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	T_S	
Phorbas glaberrimus				
bromochlorophenol	HP	–	–	Vetter & Janussen (2005)
2,4-dibromophenol	HP	–	–	
2,6-dibromophenol	HP	–	–	
bromochloroanisole	HP	–	–	
bromodichlorophenol	HP	–	–	
dibromoanisole	HP	–	–	
dibromochlorophenol	HP	–	–	
2,4,6-tribromoanisole	HP	–	–	
1,1,2-tribromooct-1-en-3-one	HP	A?	–	
2,4,6-tribromophenol	HP	–	–	
mixed halogenated compound (MHC-1)	HP	–	–	
Psammopemma sp. (= *Psammoclema* sp.)				
psammopemmins A, B and C	BA	–	–	Butler *et al*. (1992)
Tedania charcoti (= *Tedania* (*Tedaniopsis*) *charcoti*)				
Cd	IC	S	B_A	Capon *et al*. (1993)
Zn	IC	S	B_A	
O. HAPLOSCLERIDA				
Calyx arcuaria				
aqueous extract	–	–	no C_S, no R_S, T_S	McClintock *et al*. (1990)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
hexane extract	–	–	no B_A, T_S, no Y	McClintock *et al*. (1993a, 1994b)
chloroform extract	–	–	no B_A, T_S, no Y	
methanolic extract	–	–	no B_A, T_S, no Y	
non polar extract	–	–	no FO_S	Amsler *et al*. (2000b)
polar extract	–	–	no FO_S	
Clathria nidificata (= *Clathria* (*Axosuberites*) *nidificata*)				
hydrophilic extract	–	–	T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	no T_S	
Gellius benedeni (=*Haliclona* (*Gellius*) *benedeni*)				
methanolic extract	–	–	no I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al*. (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al*. (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, T_S, no Y	
mycosporine-glicine	MA	–	UV	McClintock & Karentz (1997)
shinorine	MA	–	UV	
palythine	MA	–	UV	
Gellius tenella (= *Haliclona* (*Gellius*) *tenella*)				
methanolic extract	–	–	no I_A, B_A, no Y	McClintock (1987); McClintock *et al*. (1993a)
aqueous extract	–	–	no C_S, no R_S, T_S	McClintock *et al*. (1990)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
hexane extract	–	–	no B_A, no Y	
chloroform extract	–	–	B_A, no Y	
Haliclona dancoi (=*Haliclona* (*Rhizoniera*) *dancoi*)				
methanolic extract	–	–	I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al*. (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al*. (1990)
hexane extract	–	–	B_A, T_S, no Y	
chloroform extract	–	–	B_A, no T_S, no Y	
non polar extract	–	–	FO_S	Amsler *et al*. (2000b)
polar extract	–	–	FO_S	
Haliclona scotti				
hydrophilic extract	–	–	no T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	no T_S	
Haliclona sp.				
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
hexane extract	–	–	no B_A, T_S, no Y	McClintock *et al*. (1993a, 1994b)
chloroform extract	–	–	no B_A, T_S, no Y	
methanolic extract	–	–	no B_A, T_S, no Y	
mycosporine-glicine	MA	–	UV	McClintock & Karentz (1997)
palythine	MA	–	UV	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
Hemigellius fimbriatus				
hydrophilic extract	–	–	no T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	no T_S	
Microxina charcoti				
hydrophilic extract	–	–	no T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	no T_S	
Xestospongia sp.				
(22E)-24-norcolesta-5,22-dien-3β-ol	TS	–	–	Seldes *et al*. (1990a)
(22E)-27-nor-24-metilcolesta-5,22-dien-3β-ol	TS	–	–	
(22E)-colesta-5,22-dien-3β-ol	TS	–	–	
colest-5-en-3β-ol	TS	–	–	
5α-colestan-3β-ol	TS	–	–	
(22E,24ε)-24-metilcolesta-5,22-dien-3β-ol	TS	–	–	
(24ε)-24-metilcolesta-5-en-3β-ol	TS	–	–	
24-metilcolesta-5,24(28)-dien-3β-ol	TS	–	–	
(22E,24E)-24-etilcolesta-5,22-dien-3β-ol	TS	–	–	
24-etilcolesta-5,24(28)-dien-3β-ol	TS	–	–	
24E-etilcolest-5-en-3β-ol	TS	–	–	
24-propilcolesta-5,24(28)-dien-3β-ol	TS	–	–	
Xestospongia sp.				
11 steroids	TS	P?	–	Cueto *et al*. (1991)
Xestospongia sp.				
hydrophilic extract	–	–	no T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	T_S	
O. ASTROPHORIDA				
Cinachyra antarctica				
methanolic extract	–	–	no I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al*. (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al*. (1990)
hexane extract	–	–	no B_A, T_S, no Y	
chloroform extract	–	–	B_A, T_S, no Y	
polar extract	–	–	FO_S	Amsler *et al*. (2000b)
Cinachyra antarctica (white phenotip)				
hydrophilic extract	–	–	no T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	T_S	
Cinachyra antarctica (yellow phenotip)				
shinorine	MA	–	UV	McClintock & Karentz (1997)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
hydrophilic extract	–	–	T_S	McClintock *et al*. (2000)
lipohilic extract	–	–	T_S	
Cinachyra barbata				
(22E)-24-norcholesta-5,22-dien-3β-ol	TS	–	–	Seldes *et al*. (1990a)
(22E)-27-nor-24-methylcholesta-5,22-dien-3β-ol	TS	–	–	
(22E)-cholesta-5,22-dien-3β-ol	TS	–	–	
cholest-5-en-3β-ol	TS	–	–	
5α-cholestan-3β-ol	TS	–	–	
(22E,24ε)-24-methylcholesta-5,22-dien-3β-ol	TS	–	–	
(24ε)-24-methylcholesta-5-en-3β-ol	TS	–	–	
24-methylcholesta-5,24(28)-dien-3β-ol	TS	–	–	
(22E,24E)-24-ethylcholesta-5,22-dien-3β-ol	TS	–	–	
24-ethylcholesta-5,24(28)-dien-3β-ol	TS	–	–	
24E-ethylcholest-5-en-3β-ol	TS	–	–	
24-propylcholesta-5,24(28)-dien-3β-ol	TS	–	–	
11 steroids	TS	P?	–	Cueto *et al*. (1991)
Tetilla leptoderma				
methanolic extract	–	–	I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al*. (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al*. (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, Y	
shinorine	MA	–	UV	McClintock & Karentz (1997)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
O. AXINELLIDA				

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
Homaxinella balfourensis				
cholest-5-en-3β-ol	TS	−	−	Seldes *et al*. (1986)
cholestan-3β-ol	TS	−	−	
22-trans-24ξ-methyl-5α-cholest-22-en-3β-ol	TS	−	−	
24ξ-methyl-5α-cholestan-3β-ol	TS	−	−	
24-methyl-5α-cholest-24(28)-en-3β-ol	TS	−	−	
22-trans-24ξ-ethyl-5α-cholest-22-en-3β-ol	TS	−	−	
24ξ-ethyl-5α-cholestan-3β-ol	TS	−	−	
aqueous extract	−	−	no C_S, no R_S, no T_S	McClintock *et al*. (1990)
methanol-toluenic extract	−	−	B_A, Y, F	McClintock & Gauthier (1992)
methanolic extract	−	−	no B_A, no T_S, no Y	McClintock *et al*. (1993a, 1994b)
hexane extract	−	−	no B_A, no T_S, no Y	
chloroform extract	−	−	no B_A, T_S, no Y	
non polar extract	−	−	FO_S	Amsler *et al*. (2000b)
polar extract	−	−	FO_S	
shinorine	MA	−	UV	McClintock & Karentz (1997)
porphyra-334	MA	−	UV	
mycosporine-glycine-valine	MA	−	UV	
palythine	MA	−	UV	
Homaxinella sp.				
methanolic extract	−	−	I_A	McClintock (1987)
O. HADROMERIDA				
Polymastia invaginata				
aqueous extract	−	−	C_S, R_S, T_S	McClintock *et al*. (1990)
methanol-toluenic extract	−	−	B_A, Y, F	McClintock & Gauthier (1992)
methanolic extract	−	−	no B_A, T_S, no Y	McClintock *et al*. (1993a, 1994b)
hexane extract	−	−	B_A, T_S, no Y	
chloroform extract	−	−	B_A, no Y	
Sphaerotylus antarcticus				
hexane extract	−	−	no B_A, no T_S, no Y	McClintock *et al*. (1993a, 1994b)
chloroform extract	−	−	B_A, T_S, no Y	
methanolic extract	−	−	B_A, no T_S, no Y	
shinorine	MA	−	UV	McClintock & Karentz (1997)
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
Suberites caminatus				
caminatal	TS	−	−	Díaz-Marrero *et al*. (2003)
oxaspirosuberitenone	ST	−	−	Díaz-Marrero *et al*. (2004a)
19-episuberitenone	ST	−	−	
suberitenone B	ST	−	−	
Suberites sp.				
suberitenone A	ST	−	no C_A, no A, T_S, B_S, no B_A, no F, no Y	Shin *et al*. (1995); Baker *et al*. (1997)
suberitenone B	ST	−	no C_A, no A, CE, T_S, B_S, no B_A, no F, no Y	
suberitenone C and D	ST	−	no S, no B_A, no F	Lee *et al*. (2004)
suberiphenol	ST	−	no S, no B_A, no F	
O. DENDROCERATIDA				
Dendrilla membranosa				
methanolic extract	−	−	I_A, no B_A, T_S, no Y	McClintock (1987);
			no T_S	McClintock *et al*. (1993a, 1994b); Baker & Yoshida (1994)
methanol-toluenic extract	−	−	B_A, Y, F	McClintock & Gauthier (1992)
dichlorometane extract	−	−	B_A	Molinski & Faulkner (1987)
aqueous extract	−	−	C_S, R_S, T_S	McClintock *et al*. (1990)
hexane extract (mainly norditerpenes)	−	−	no T_S	Baker *et al*. (1995)
hexane extract	−	−	no B_A, no T_S, T_S, no Y	
chloroform extract	−	−	no B_A, T_S, no Y	
non polar extract	−	−	FO_S	Amsler *et al*. (2000b)
polar extract	−	−	FO_S	
picolinic acid	NA	−	T_S?	
7-methyladenine	NC	−	T_S?	
4, 5,8-trihydroxyquinoline-2-carboxylic acid	QA	−	B_A, −	Molinski & Faulkner (1988)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
9,11-dihydrogracillin A (DGHA)	DT	−	−, no T_S	Baker *et al*. (1993); Puliti *et al*. (1993)
membranolide	DT	−	−, no T_S	Manríquez *et al*. (1990); Díaz-Marrero *et al*. (2004b)
membranolide B	DT	−	−	Ankisetty *et al*. (2004a)
membranolide C and D	DT	−	B_A, F	
dendrinolide	DT	−	−	Fontana *et al*. (1997)
DGHA epoxy derivative	DT	−	no T_S	
dendrillin	DT	−	no T_S	
norditerpene gracilane skeleton derivative	DT	−	−	
3 C-20 aplysulphurane type diterpenes	DT	−	−	
polyrhaphin D	DT	−	−	
shinorine	MA	−	UV	McClintock & Karentz (1997)
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
O. HALICHONDRIDA				
Halichondria sp.				
aqueous extract	−	−	C_S, R_S, T_S	McClintock *et al*. (1990)
bromochlorophenol	HP	−	−	Vetter & Janussen (2005)
2,4-dibromophenol	HP	−	−	
2,6-dibromophenol	HP	−	−	
dibromoanisole	HP	−	−	
dibromochlorophenol	HP	−	−	
2,4,6-tribromoanisole	HP	−	−	
tribromooctenone	HP	−	−	
2,4,6-tribromophenol	HP	−	−	
mixed halogenated compound (MHC-1)	HP	B? or MI?	−	
PH. CNIDARIA, CL. ANTHOZOA, SUBCL. ZOANTHARIA (= HEXACORALLIA), O. ACTINIARIA (SEA ANEMONES)				
Unidentified species (#1)				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Isotealia antarctica				
mycosporine-glycine	MA	−	UV	McClintock & Karentz (1997)
shinorine	MA	−	UV	
porphyra-334	MA	−	UV	
mycosporine-glycine-valine	MA	−	UV	
palythine	MA	−	UV	
asterina-330	MA	−	UV	
SUBCL. ALCYONARIA (= OCTOCORALLIA), O. ALCYONACEA				
Alcyonium paessleri				
aqueous extract	−	−	C_S	McClintock *et al*. (1991b)
aqueous methanolic extract	−	−	no FO_S, G_S, L_S, T_S	Slattery *et al*. (1995); Slattery & McClintock (1995)
aqueous homogenate	−	−	L_S	
hexane extract	−	−	no FO_S, no G_S, no L_S, T_S	
chloroform extract	−	−	FO_S, G_S, L_S, T_S	
methanolic extract	−	−	no FO_S, no G_S, no L_S, T_S	
tissue	−	−	D_{SF}	
tissue without metabolites	−	−	no D_{SF}	
mycosporine-glycine	MA	−	UV	McClintock & Karentz (1997)
alcyopterosins A, B, C, D, E, F, G, H, I, J, K, L, M, N and O	SQ	−	−	Palermo *et al*. (2000)
paesslerins A and B	SQ	−	−	Rodríguez-Brasco *et al*. (2001)
cholesterol	TS	−	T_S, YM_S	Slattery *et al*. (1997a)
22-dehydrocholesterol / 24-methylene-cholesterol	TS	−	T_S	
24-methylenecholesterol	TS	−	no T_S	
22-dehydro-7β-hydroxycholesterol	TS	−	T_S	
progesterone	TS	−	−	Slattery *et al*. (1997b)
androstenedione	TS	−	−	
testosterone	TS	−	−	
estradiol	TS	−	−	
Anthomastus bathyproctus				
methyl 3-oxocholesta-1,4-dien-26-oate	TS	−	no S	Mellado *et al*. (2005)
methyl (24E)-3-oxocholesta-1,4,24-trien-26-	TS	−	S	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
oate				
(20S)-20-hydroxyergosta-1,4,24(28)-trien-3-one	TS	−	S	
triterpenes [7, 8]	TS	−	S	
triterpenes [9, 10]	TS	−	no S	
Clavularia frankliniana				
hexane extract	−	−	no FO_S, no G_S, no L_S, T_S	Slattery *et al*. (1995); Slattery & McClintock (1995)
chloroform extract	−	−	no FO_S, no G_S, no L_S, T_S	
methanolic extract	−	−	no FO_S, no G_S, no L_S, T_S	
aqueous methanolic extract	−	−	no FO_S, no G_S, no L_S, T_S	
aqueous homogenate	−	−	no L_S	
tissue	−	−	D_{SF}	
tissue without metabolites	−	−	no D_{SF}	
chimyl alcohol	FA	−	D_{SS}	McClintock & Baker (2001)
Gersemia antarctica				
hexane extract	−	−	no FO_S, no G_S, no L_S, T_S	Slattery *et al*. (1995); Slattery & McClintock (1995)
chloroform extract	−	−	FO_S, G_S, L_S,T_S	
methanolic extract	−	−	no FO_S, no G_S, no L_S, T_S	
aqueous methanolic extract	−	−	FO_S, G_S, L_S, T_S	
aqueous homogenate	−	−	L_S	
tissue	−	−	D_{SF}	
tissue without metabolites	−	−	no D_{SF}	
organic extract	−	−	G_S	Slattery *et al*. (1997a)
homarine	NA	−	B_S, G_S	
trigonelline	NA	−	B_S, no G_S	
progesterone	TS	−	−	Slattery *et al*. (1997b)
androstenedione	TS	−	−	
testosterone	TS	−	−	
estradiol	TS	−	−	
O. GORGONACEA (GORGONIANS)				
Ainigmaptilon antarcticus				
diethyl ethereal extract	−	−	D_{SS}	Iken & Baker (2003)
ainigmaptilon A	SQ	−	D_{SS}, B_S, FO_S	
ainigmaptilon B	SQ	−	−	
Dasystenella acanthina				
furanoeudesmane	SQ	−	I_A, no D_A	Gavagnin *et al*. (2003c)
isofuranodiene	SQ	−	I_A, no D_A	
trans-β-farnesene (pheromone)	SQ	−	no I_A, no D_A, −	Mellado *et al*. (2004)
(24R,22E)-24-hydroxycholest-4,22-dien-3-one	TS	−	S	
23-acetoxy-24,25-epoxycholest-4-en-3-one	TS	−	S	
12β-acetoxycholest-4-en-3,24-dione	TS	−	S	
12β-acetoxy-24,25-epoxycholest-4-en-3-one	TS	−	S	
(22E)-25-hydroxy-24-norcholest-4,22-dien-3-one	TS	−	S	
3α-acetoxy-25-hydroxycholest-4-en-6-one	TS	−	S	
3α,11α-diacetoxy-25-hydroxycholest-4-en-6-one	TS	−	S	
steroid	TS	−	S	
PH. CTENOPHORA				
Bolinopsis n. sp.				
no mycosporine-like amino acids	−	−	−	Karentz *et al*. (1991)
Callianira antarctica				
no mycosporine-like amino acids	−	−	−	Karentz *et al*. (1991)
PH. PLATYHELMINTHES, O. TRICLADIDA				
Obrimoposthia wandeli				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
O. EULECITHOPHORA				
Unidentified planarian (#2, tentatively named *Plagiostomum* n. sp)				
palythine	MA	−	UV	Karentz *et al*. (1991)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
PH. NEMERTEANS, CL. ANOPLA, O. HETERONEMERTEA				
Parborlasia corrugatus				
aqueous extract	−	−	C_S, D_{SF}	Heine *et al*. (1991);
tissue	−	−	D_{SF}	McClintock *et al*. (1991b)
intact animal	−	−	D_{SF}	
porphyra-334	MA	−	UV	Karentz *et al*. (1991)
mycosporine-glycine	MA	−	UV	
shinorine	MA	−	UV	McClintock & Karentz (1997)
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythine	MA	−	UV	
parborlysin (from mucus)	NC	−	no CR, H	Berne *et al*. (2003)
liophilized extract of integumentary tissues	−	−	H	
liophilized extract of non integumentary tissues	−	−	no H	
Parborlasia fueguina				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
O. HOPLONEMERTEA				
Amphiporus michaelseni (both in adults and embryos)				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
PH. MOLLUSCA, CL. POLYPLACOPHORA				
Tonicina zschaui				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
CL. GASTROPODA, SUBCL. PROSOBRANCHIA				
Margarella antarctica				
porphyra-334	MA	−	UV	Karentz *et al*. (1991)
shinorine	MA	−	UV	
asterina-330	MA	−	UV	
palythine (in body, shell and egg ribbons)	MA	−	UV	
Marseniopsis mollis				
living animal	−	−	D_{SS}	McClintock *et al*. (1994a)
homarine (in mantle, viscera and foot)	NA	E	D_{SS}	McClintock *et al*. (1994d)
mycosporine-glycine	MA	−	UV	McClintock & Karentz (1997)
shinorine	MA	−	UV	
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
aqueous extract of mantle	−	−	C_S, T_S, E_S	McClintock *et al*. (1992a)
mantle tissue	−	−	D_{SF}	
Nacella concinna				
no mycosporine-like amino acids (in shell)	−	−	−	Karentz *et al*. (1992)
shinorine (in body, gut, gonads and eggs)	MA	−	UV	
porphyra-334 (in body, gut, gonads and eggs)	MA	−	UV	
Paludestrina antarctica				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
asterina-330	MA	−	UV	
Trophon cf. *geversianus*				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
asterina-330	MA	−	UV	
no mycosporine-like amino acids in egg masses	−	−	−	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
SUBCL. OPISTOBRANCHIA, O. THECOSOMATA				
Limacina helicina				
sterols	TS	−	−	Kattner *et al*. (1998)
shinorine	MA	P	UV	Whitehead *et al*. (2001)
porphyra-334	MA	P	UV	
mycosporine-glycine	MA	MO	UV	
palythine	MA	MO	UV	
palythenic acid	MA	MO	UV	
Limacina helicina ssp. *antarctica*				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
O. GYMNOSOMATA (PTEROPODA)				
Clione antarctica				
hexanic extract	−	−	D_{SF}	McClintock & Janssen (1990)
chloroformic extract	−	−	no D_{SF}	McClintock *et al*. (1994d)
methanolic extract	−	−	no D_{SF}	Bryan *et al*. (1995)
aqueous methanolic extract	−	−	no D_{SF}	
hexanic extract	−	−	D_{SF}	
pteroenone	PK	B?, −	D_{SF}	Yoshida *et al*. (1995)
triglyceride	FA	−	D_{SF}	
2 fatty acids	FA	−	no D_{SF}	
sterol	TS	−	no D_{SF}	
sterols	TS	−	−	Kattner *et al*. (1998)
odd-chain length fatty acids	FA	B?	F?	
shinorine	MA	M	UV	Whitehead *et al*. (2001)
porphyra-334	MA	M	UV	
mycosporine-glycine	MA	M	UV	
palythine	MA	M	UV	
palythenic acid	MA	M	UV	
O. NUDIBRANCHIA				
Unidentified species (#1, tentatively named *Telarma antarctica*)				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Austrodoris kerguelenensis				
acetoxyglyceryd [11] from mantle	DT	B?	−	Davies-Coleman & Faulkner (1991)
acetoxyglyceryd [12] from mantle	DT	B?	−	
2 diketones	DT	B?	−	
glyceryl (5R,10R,13R)-7-ketolabda-8-en-15-oate	DT	B?	−	
austrodorin from mantle	DT	−	−	Gavagnin *et al*. (1995)
diterpene diacylglicerides (in mantle, gills, foot and mucus)	DT	−	−	Iken *et al*. (2002)
diterpene diacylglycerol metabolite from mantle	DT	B?	D_{SS}	
diterpene monoacylglycerides from mantle	DT	B?	D_{SS}	
austrodorin A and B (in mantle and mucus)	DT	−	−	Gavagnin *et al*. (1999a)
2 1,3-diacylglyceryl esters (in mantle and mucus)	DT	−	−	Gavagnin *et al*. (1999b)
diterpene diacylglicerides (in gills and foot)	DT	−	−	
no diacylglicerides in viscera	DT	−	−	
diterpene diacylglicerides (from mucus)	DT	−	−	
aqueous extract of mantle	−	−	C_S, T_S, E_S	McClintock *et al*. (1992a)
living animal	−	−	D_{SS}	
mantle tissue	−	−	D_{SF}, D_{SS}	
butanolic extract of mantle	−	−	no D_{SS}	
ethereal extract of mantle	−	−	D_{SS}	
ethereal extract of viscera	−	−	no D_{SS}	
butanolic extract of viscera	−	−	no D_{SS}	
sterols from mantle	TS	−	no D_{SS}	
triglycerids + lipophilic compounds from mantle	FA	−	no D_{SS}	
fatty acids from mantle	FA	−	no D_{SS}	Gavagnin *et al*. (2003b)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
monoacylglycerides of regular fatty acids from mantle	FA	B?	D_{SS}	
2 2-monoacylglycerols from mantle	DT	−	−	
2 1,2-diacylglyceryl esters from mantle	DT	−	−	
austrodoral from mantle	SQ	−	−	Gavagnin *et al*. (2003a)
austrodoric acid from mantle	SQ	B?	−	
Bathydoris hodgsoni				
hodgsonal from mantle	SQ	B?	−, D_{SS}	Iken *et al*. (1998); Avila *et al*. (2000)
tissue (mantle and papillae)	−	−	D_{SS}	
butanolic extract of mantle	−	−	no D_{SS}	
ethereal extract of mantle	−	−	D_{SS}	
high and low Rf compounds from mantle	−	−	no D_{SS}	
fatty acids from mantle	FA	−	no D_{SS}	
sterols from mantle	TS	−	no D_{SS}	
ethereal extract of viscera	−	−	no D_{SS}	
butanolic extract of viscera	−	−	no D_{SS}	
Notaeolidia gigas				
mycosporine-glycine	MA	−	UV	McClintock & Karentz (1997)
Tritoniella belli				
chimyl alcohol	FA	C	D_{SS}	McClintock *et al*. (1994d)
mycosporine-glycine	MA	−	UV	McClintock & Karentz (1997)
shinorine	MA	−	UV	
mantle tissue	−	−	D_{SF}	McClintock *et al*. (1992a)
aqueous extract of mantle	−	−	C_S, T_S, E_S	
ethyl acetate extract of mantle	−	−	T_S	Bryan *et al*. (1998)
mantle mucus	−	−	T_S, D_{SF}	
egg masses	−	−	D_{SS}, no D_{SA}, no D_{SC}	McClintock & Baker (1997b)
CL. BIVALVIA				
Limatula hodgsoni				
shinorine	MA	−	UV	McClintock & Karentz (1997)
palythine	MA	−	UV	
Limatula cf. *ovalis*				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Cyamium cf. *commune*				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
PH. ANNELIDA, CL. POLYCHAETA				
Unidentified species (#2)				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
O. PHYLLODOCIDA				
Aglaophamus trissophyllus (=*Agalophamus ornatus*)				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
palythene	MA	−	UV	
Neanthes kerguelensis				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
Tomopteris carpenteri				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
mycosporine-glycine	MA	−	UV	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
O. TEREBELLIDA				
Terebella ehlersi				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
palythene	MA	−	UV	
asterina-330	MA	−	UV	
palythinol	MA	−	UV	
Thelepus extensus				
3,5-dibromo-4-hydroxybenzaldehyde	HP	−	−	Goerke *et al*. (1991)
3,5-dibromo-4-hydroxybenzyl alcohol	HP	−	−	
bis(3,5-dibromo-4-hydroxybenzyl)methane	HP	−	−	
bis(3,5-dibromo-4-hydroxybenzyl)ether	HP	−	−	
thelepin	HP	−	B?	
thelephenol	HP	−	−	
Thelepus cincinatus				
3,5-dibromo-4-hydroxybenzaldehyde	HP	−	−	Goerke *et al*. (1991)
3,5-dibromo-4-hydroxybenzyl alcohol	HP	−	−	
bis(3,5-dibromo-4-hydroxybenzyl)methane	HP	−	−	
bis(3,5-dibromo-4-hydroxybenzyl)ether	HP	−	−	
thelepin	HP	−	B?	
thelephenol	HP	−	−	
CL. CLITELLATA, O. HIRUDINEA				
Trachelobdella australis				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
asterina-330	MA	−	UV	
palythinol	MA	−	UV	
PH. ARTROPODA, CL. CRUSTACEA, SUBCL. COPEPODA				
Calanus propinquus				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
palythene	MA	−	UV	
SUBCL. MALACOSTRACA, O. EUPHAUSIACEA				
Euphasia superba				
palythenic acid	MA	−	−	Nakamura & Kobayashi (1982)
palythine	MA	−	−, UV	Karentz *et al*. (1991)
porphyra-334	MA	−	−, UV	
shinorine	MA	−	−, UV	
asterina-330	MA	−	−, UV	
palythinol	MA	−	−, UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
mycosporine-like amino acid	MA	A	UV	Newman *et al*. (2000)
O. ISOPODA				
Cymodocella tubicauda				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
Notasellus sarsii				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
Glyptonotus antarcticus				
palythine	MA	−	UV	McClintock & Karentz (1997)
living juveniles	−	−	D_{SS}	McClintock *et al*. (2003)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
lipophilic extract (dichloromethane/methanol) of juveniles	–	–	D_{SS}	
hydrophilic extract (methanol/water) of juveniles	–	–	no D_{SS}	
O. AMPHIPODA				
Bovallia gigantea				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Halirages sp.				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Jassa sp.				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Orchomene sp.				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Paraceradocus sp.				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
Pariphimedia integricauda				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
Pontogeneia sp.				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
CL. PYCNOGONIDA (= PANTOPODA)				
Unidentified species				
shinorine	MA	–	UV	McClintock & Karentz (1997)
palythine	MA	–	UV	
Achelia spicata				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
PH. BRYOZOA				
Unidentified species				

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
palythine	MA	−	UV	McClintock & Karentz (1997)
Beania livingstonei				
lipid soluble fraction	−	−	no B_A	Colon-Urban *et al*. (1985)
porphyra-334	MA	−	UV	Karentz *et al*. (1991)
shinorine	MA	−	UV	
Carbasea curva				
crude extract	−	−	H	Winston & Bernheimer (1986)
Caberea darwinii				
lipid soluble fraction	−	−	B_A	Colon-Urban *et al*. (1985)
crude extract	−	−	no H	Winston & Bernheimer (1986)
Cycliopora polaris				
lipid soluble fraction	−	−	B_A	Colon-Urban *et al*. (1985)
Flustra thysanica				
lipid soluble fraction	−	−	B_A	Colon-Urban *et al*. (1985)
crude extract	−	−	no H	Winston & Bernheimer (1986)
Himantozoum antarcticum				
lipid soluble fraction	−	−	B_A	Colon-Urban *et al*. (1985)
crude extract	−	−	no H	Winston & Bernheimer (1986)
Inversiula nutrix				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
Klugeflustra vanhoffeni				
crude extract	−	−	no H	Winston & Bernheimer (1986)
Nematoflustra flagellata				
lipid soluble fraction	−	−	B_A	Colon-Urban *et al*. (1985)
PH. BRACHIOPODA				
Liothyrella uva				
homogenated tissue	−	−	T_S	McClintock *et al*. (1993b)
homogenated & freezed	−	−	T_S	
liophilized	−	−	no D_{AF}	
living male	−	−	D_{SS}	Mahon *et al*. (2003)
living female	−	−	D_{SS}	
juvenile	−	−	D_{SS}	
hydrophobic extract	−	−	D_{SS}, no D_{SF}	
liophilized tissue (whole animal)	−	−	D_{SS}	
tissue of the lophophore	−	−	no D_{SS}	
liophilized tissue of the lophophore	−	−	no D_{SS}, no D_{SF}	
hydrophobic extract of the lophophore	−	−	B_S	
hydrophilic extract of the lophophore	−	−	B_S	
male liophilized reproductive tissue	−	−	D_{SS}, no D_{SF}	
female liophilizedreproductive tissue	−	−	no D_{SS}, no D_{SF}	
male hydrophobic extract of reproductive tissue	−	−	no B_S	
male hydrophilic extract of reproductive tissue	−	−	no B_S	
female hydrophobic extract of reproductive tissue	−	−	B_S	
female hydrophilic extract of reproductive tissue	−	−	no B_S	
liophilized tissue of pedicle	−	−	D_{SS}, D_{SF}	
hydrophobic extract of pedicle	−	−	no B_S	
hydrophilic extract of pedicle	−	−	no B_S	
liophilized tissue of intestine-stomach	−	−	D_{SS}, no D_{SF}	
hydrophobic extract of intestine-stomach	−	−	B_S	
hydrophilic extract of intestine-stomach	−	−	B_S	
PH. CHAETOGNATA				
Unidentified species				
no mycosporine-like amino acids	−	−	−	Karentz *et al*. (1991)
PH. ECHINODERMATA, CL. CRINOIDEA				
Promachocrinus kerguelensis				
aqueous extract of arms	−	−	no D_{AF}	McClintock (1989)
mycosporine-glycine	MA	−	UV	McClintock & Karentz (1997)
shinorine	MA	−	UV	
porphyra-334	MA	−	UV	
palythine	MA	−	UV	
CL. ASTEROIDEA				

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
Unidentified species (family Asteriidae)				
asterasterol A and B	TS	−	no S	De Marino *et al*. (1997b)
asterasterol C	TS	−	S	
asteriidoside A, B, C, D, E, F, I and L	GS	−	S	De Marino *et al*. (1998)
asteriidosides G and H	GS	−	−	
Unidentified species (tentatively named *Henricia* sp., family Echinasteridae)				
brasiliensoside	GS	−	S	De Marino *et al*. (1996); Iorizzi *et al*. (1996)
24S-methylbrasiliensoside	GS	−	S	
pectinoside A	GS	−	S	
24S-methylpectinoside	GS	−	S	
antarcticoside A and B	GS	−	S, −	
antarcticoside C, D, G, H, J, K and L	GS	−	S	
antarcticosides E, F, M, N, O and P	GS	−	−	
antarcticoside I	GS	−	no S	
polyhydroxylated steroids (compound #14, 16, 20, 21, 22, 23, 24 and 25)	TS	−	S	
polyhydroxylated steroid (compound #15)	TS	−	no S	
polyhydroxylated steroids (compounds #17, 18, 19, 26, 27)	TS	−	−	
Acodontaster conspicuus				
aqueous extract of body wall	−	−	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
3 asterosaponins	GS	−	no B_S	De Marino *et al*. (1997a)
halityloside I	GS	−	no B_S	
acodontasteroside A, B and C	GS	−	no B_S	
acodontasteroside D, E, F, G, H and I	GS	−	B_S	
polyhydroxylated steroids (compound #14 and 16)	TS	−	no B_S	
polyhydroxylated steroid (compound #15, 18 and 19)	TS	−	B_S	
polyhydroxylated steroid (compound #17)	TS	−	−	
Acodontaster hodgsoni				
aqueous extract of body wall	−	−	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
Bathybiaster loripes				
aqueous extract of body wall	−	−	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
Cueonotaster involutus				
aqueous extract of body wall	−	−	no D_{AF}	McClintock (1989)
Diplasterias brucei				
mixture of saponins	GS	−	H	Mackie *et al*. (1977)
marthasterone	TS	−	−	
dihydromarthasterone	TS	−	−	
liophilized tissue of egg mass & embryos	−	−	D_{AF}	McClintock & Vernon (1990)
tissue of embryos	−	−	D_{SS}, no D_{SA}, no D_{SC}	McClintock & Baker (1997b)
lipophilic extract of embryos	−	−	no D_{SS}, D_{SA}	
hydrophilic extract of embryos	−	−	D_{SS}, no D_{SA}	
aqueous extract of body wall	−	−	D_{AF}	McClintock (1989)
palythine	MA	−	UV	McClintock & Karentz (1997)
Granaster nutrix				
palythine	MA	−	UV	Karentz *et al*. (1991)
porphyra-334	MA	−	UV	
shinorine	MA	−	UV	
mycosporine-glycine	MA	−	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
asterina-330	MA	−	UV	
living animal	−	−	D_{SS}	McClintock *et al*. (2006)
methanolic extract of body wall	−	−	D_{SS}	
Labidiaster annulatus				
labidiasteroside A	GS	−	−	Díaz de Vivar *et al*. (2000)
ovarian asterosaponin 1	GS	−	−	
Lophaster gaini				
aqueous extract of body wall	−	−	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
Lysasterias perrieri				
embryos tissue	−	−	D_{SS}	McClintock *et al*. (2003)
methanolic extract of embryos	−	−	D_{SS}	
juvelines tissue	−	−	D_{SS}	
methanolic extract of juveniles	−	−	no D_{SS}	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
Macroptychaster accrescens				
aqueous extract of body wall	−	−	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
Neosmilaster georgianus				
santigoside	GS	−	−	Vázquez *et al*. (1992)
hydrophilic extract	−	−	AV_S	Mahon *et al*. (2000)
living animal	−	−	D_{SS}	McClintock *et al*. (2006)
embryos tissue	−	−	D_{SS}	McClintock *et al*. (2003)
methanolic extract of embryos	−	−	no D_{SS}	
juvelines tissue	−	−	D_{SS}	
body wall tissue	−	−	D_{SS}	
fresh mucus (pH=7.75)	−	−	D_{SS}	
methanolic extract of body wall	−	−	D_{SS}	
Notasterias armata				
aqueous extract of body wall	−	−	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	D_{AF}	McClintock & Vernon (1990)
Odontaster meridionalis				
aqueous extract of body wall	−	−	no D_{AF}	McClintock (1989)
no mycosporine-like amino acids	−	−	−	McClintock & Karentz (1997)
Odontaster validus				
aqueous extract of body wall	−	−	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
ovaries tissue	−	−	no D_{SS}, no D_{SC}, no D_{SA}	McClintock & Baker (1997b)
mycosporine-glycine (in body wall)	MA	−	UV	McClintock & Karentz (1997)
palythine (in ovaries)	MA	−	UV	
Perknaster fuscus				
aqueous extract of body wall	−	−	D_{AF}, L_S, R_S, T_S	McClintock (1989); McClintock *et al*. (1992b)
ethanolic extract of body wall	−	−	−	Kong *et al*. (1992)
fuscusine (in body wall)	NC	B?	−, L_S?, R_S?, T_S?	
liophilized tissue of egg mass & embryos	−	−	D_{AF}	McClintock & Vernon (1990)
embryos tissue	−	−	D_{SS}, D_{SA}, D_{SC}	McClintock & Baker (1997b)
larvae tissue	−	−	D_{SS}, D_{SA}, D_{SC}	
no mycosporine-like amino acids (in ovaries)	−	−	−	McClintock & Karentz (1997)
Porania antarctica				
aqueous extract of body wall	−	−	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	D_{AF}	McClintock & Vernon (1990)
Psilaster charcoti				
aqueous extract of body wall	−	−	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
larvae tissue	−	−	D_{SS}, D_{SA}, D_{SC}	McClintock & Baker (1997b)
embryos tissue	−	−	D_{SS}, D_{SA}, D_{SC}	
carotenoids (in embryos and eggs)	CA	−	UV?	Karentz & Bosch (2001)
no mycosporine-like amino acids	−	−	−	
CL. OPHIUROIDEA				
Amphioplus affinis				
palythine	MA	−	UV	Karentz *et al*. (1991)
Astrotoma agassizii				
aqueous extract of arms	−	−	no D_{AF}	McClintock (1989)
sterols [13, 14, 15]	TS	−	−, A	Roccatagliata *et al*. (1998); Comin *et al*. (1999)
2 sulphated polyhydroxysteroids	TS	−	−	
Gorgonocephalus chilensis				
5 disulphated polyhydroxysteroids	TS	−	−	Maier *et al*. (2000)
mixture of monosulfated steroids	TS	−	−	
Ophionotus victoriae				
aqueous extract of arms	−	−	no D_{AF}	McClintock (1989)
sterols [16, 17, 18]	TS	−	−	D'Auria *et al*. (1995)
2 sulphated polyhydroxysteroids	TS	−	−	
(22E)-24-norcholesta-5,22-dien-3β-ol	TS	−	−	Duque *et al*. (1997)
24-methyl-27-norcholesta-5,22-dien-3β-ol	TS	−	−	
22-dehydrocholesterol	TS	−	−	
24-methylcholesta-5,24(28)-dien-3β-ol	TS	−	−	
(22E)-24S-methylcholesta-5,22-dien-3β-ol	TS	−	−	
(22E)-24R-methylcholesta-5,22-dien-3β-ol	TS	−	−	
24ξ-ethylcholesta-5,24(28)-dien-3β-ol	TS	−	−	
24ξ-n-propylcholesta-5,24(28)-dien-3β-ol	TS	−	A	
cholest-5-en-3β-ol	TS	−	−	
24ξ-ethylcholesta-5,22-dien-3β-ol	TS	−	−	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
24ξ-ethylcholesta-5-en-3β-ol	TS	−	−	
Ophiosparte gigas				
aqueous extract of arms	−	−	no D_{AF}	McClintock (1989)
cholest-5-ene-2α,3α,4β,21-tetraol 3,21-disulphate	TS	−	C	D'Auria *et al*. (1993)
cholest-5-ene-2β,3α,21-triol 2,21-disulphate	TS	−	A	
steroid	TS	−	A	
CL. ECHINOIDEA (SEA URCHINS)				
Abatus nimrodi				
aqueous extract of testes	−	−	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
Abatus shackletoni				
aqueous extract of testes	−	−	no D_{AF}	McClintock (1989)
liophilized tissue of embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
no mycosporine-like amino acids	−	−	−	McClintock & Karentz (1997)
Ctenocidaris perrieri				
aqueous extract of testes	−	−	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
Sterechinus neumayeri				
mycosporine-glycine (in digestive tract, eggs and ovaries)	MA	−	UV	McClintock & Karentz (1997); Karentz *et al*. (1997)
mycosporine-glycine:valine (in ovaries and testes)	MA	−	UV	
shinorine (in body wall, digestive tract, eggs,ovaries and testes)	MA	−	UV	
porphyra-334 (in body wall, digestive tract, eggs, ovaries and testes)	MA	−	UV	
palythine (in body wall, digestive tract, eggs, ovaries and testes)	MA	−	UV	
lipophilic extract of eggs	−	−	no D_{SS}, no D_{SA}, no D_{SC}	McClintock & Baker (1997b)
hydrophilic extract of eggs	−	−	no D_{SS}, no D_{SA}, no D_{SC}	
lipophilic extract of larvae	−	−	no D_{SA}	
hydrophilic extract of larvae	−	−	no D_{SA}	
CL. HOLOTHUROIDEA (SEA CUCUMBERS)				
Bathyplotes moseleyi				
aqueous extract of body wall	−	−	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	−	−	no D_{AF}	McClintock & Vernon (1990)
Cucumaria ferrari				
aqueous extract of body wall	−	−	no D_{AF}	McClintock (1989)
mycosporine-glycine (in ovary and eggs)	MA	−	UV	McClintock & Karentz (1997)
shinorine (in ovary and eggs)	MA	−	UV	
porphyra-334 (in ovary and eggs)	MA	−	UV	
palythine (in ovary)	MA	−	UV	
mycosporine-glycine:valine (in eggs)	MA	−	UV	
Cucumaria cf. *georgiana*				
no mycosporine-like amino acids in body wall	−	−	−	Karentz *et al*. (1991)
Cucumaria steineni				
aqueous extract of body wall	−	−	D_{AF}	McClintock (1989)
Ekmocucumis steineri				
no mycosporine-like amino acids in body wall	−	−	−	Karentz *et al*. (1991)
porphyra-334 (in ovarian tubule)	MA	−	UV	
shinorine (in ovarian tubule)	MA	−	UV	
mycosporine-glycine (in ovarian tubule)	MA	−	UV	
mycosporine-glycine:valine (in ovarian tubule)	MA	B?, MO?	UV	
Staurocucumis liouvillei				
liouvilloside A and B	GS	−	A	Maier *et al*. (2001)
PH. TUNICATA, CL. ASCIDIACEA				
Unidentified benthic species tunicate				
mycosporine-glycine	MA	−	−	McClintock & Karentz (1997)
shinorine	MA	−	−	
Cnemidocarpa verrucosa				
tunic tissue	−	−	I_S, D_{SF}	McClintock *et al*. (1991a,b)
liophilized tunic tissue	−	−	I_A	
aqueous extract of tunic	−	−	C_S, no C_S	
body wall tissue	−	−	no I_S, no D_{SF}	
endocarps tissue	−	−	I_S, no D_{SF}	
intestines tissue	−	−	no I_S, no D_{SF}	
ovistestes tissue	−	−	I_S	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
tissue of the branchial basket	–	–	I_S, no D_{SF}	
shinorine	MA	–	–	McClintock & Karentz (1997)
porphyra-334	MA	–	–	
palythine	MA	–	–	
Distaplia cylindrica				
body tissue	–	–	D_{SS}	McClintock *et al*. (2004)
lipophilic extract (CH_2Cl_2:MeOH)	–	–	D_{SS}, FO_S	
lipophilic extract ($CHCl_3$)	–	–	D_{SS}, FO_S	
hydrophilic extract (butanolic extract)	–	–	D_{SS}, FO_S	
hydrophilic extract (MeOH:H_2O)	–	–	no D_{SS}, FO_S	
Molgula enodis				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
Synoicum adareanum				
palmerolide A	PK	–	S	Diyabalanage *et al*. (2006); Jiang *et al*. (2007)
CL. THALIACEA (SALPS)				
Ihlea racovitzai				
24-nor-cholesta-5,22-dien-3β-ol	TS	–	–	Schor & Seldes (1989)
24-nor-5α-cholest-22-en-3β-ol	TS	–	–	
27-nor-24ξ-methyl-cholesta-5,22-dien-3β-ol	TS	–	–	
cholesta-5,22-dien-3β-ol	TS	–	–	
5α-cholest-22-en-3β-ol	TS	–	–	
cholest-5-en-3β-ol	TS	–	–	
5α-cholestan-3β-ol	TS	–	–	
brassicasterol	TS	–	–	
cholesta-5,24-dien-3β-ol	TS	–	–	
24ξ-methyl-5α-cholest-22-en-3β-ol	TS	–	–	
24ξ-methyl-cholest-5-en-3β-ol	TS	–	–	
24ξ-methyl-5α-cholestan-3β-ol	TS	–	–	
24-methyl-cholesta-5,24(28)-dien-3β-ol	TS	–	–	
24ξ-ethyl-cholesta-5,22-dien-3β-ol	TS	–	–	
24ξ-ethyl-cholesta-5-en-3β-ol	TS	–	–	
24ξ-ethyl-5α-cholestan-3β-ol	TS	–	–	
24-ethyl-cholesta-5,24(28)-dien-3β-ol	TS	–	–	
24-propyl-cholesta-5,24(28)-dien-3β-ol	TS	–	–	
Salpa thompsoni				
(22E)-24-norcholesta-5,22-dien-3β-ol	TS	MO?	–	Mimura *et al*. (1986)
(22E)-24-nor-5α-cholest-22-en-3β-ol	TS	MO?	–	
sterol [19]	TS	–	–	
sterols [20, 21]	TS	PC?	–	
cholesterol	TS	B	–	
cholestanol (5α-cholestan-3β-ol)	TS	PC?	–	
desmosterol (cholesta-5,24-dien-3β-ol)	TS	PC?	–	
(22E)-(24ξ)-24-methylcholesta-5,22-dien-3β-ol	TS	D?	–	
(22E)-(24ξ)-24-methyl-5α-cholest-22-en-3β-ol	TS	D?	–	
sterols [22, 23]	TS	D?	–	
(22E)-(24ξ)-24-ethylcholesta-5,22-dien-3β-ol	TS	D?	–	
(22E)-(24ξ)-24-ethyl-5α-cholest-22-en-3β-ol	TS	D?	–	
fucosterol	TS	D?	–	
(24ξ)-24-ethylcholest-5-en-3β-ol	TS	D?	–	
(24ξ)-24-ethyl-5α-cholest-3β-ol	TS	D?	–	
fucostanol	TS	D?	–	
methanolic extract	–	–	H	
acetate extract	–	–	H	
sterols + fatty acids	–	–	H	
sterols	TS	–	H	
fatty acids	FA	–	H	
no mycosporine-like amino acids	–	–	–	Karentz *et al*. (1991)
PH. VERTEBRATES, CL. OSTEICHTHYES (Fish)				
Unidentified larvae of an ice-fish species				
palythine	MA	–	UV	Karentz *et al*. (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure[a]	Origin[b]	Activity[c]	References
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	−	UV	
Lycodichthys dearborni				
no mycosporine-like amino acids	−	−	−	McClintock & Karentz (1997)
Trematomus bernacchii				
shinorine	MA	−	UV	McClintock & Karentz (1997)
palythine	MA	−	UV	

Codes are described in the text. Superscript numbers refer to long names and are reported here.
Long-named compounds: [1]:(2'E,6'E,10'E,14'E)-2-(8'-one-3',7',11',15'-tetramethylhexadeca-2',6',10',14'-tetraenyl)-6-methyl-1,4-benzoquinone; [2]:(2'E,6'E,10'E,14'E)-2-(8',9'-dione-15'-formyl-3',7',11'-trimethylhexadeca-2',6',10',14'-tetraenyl)-6-methyl-1,4-benzoquinone; [3]: 2,4-dichloro-trans-1-chlorovinyl-1-methyl-5-methylene-cyclohexane; [4]: 2-chloro-4-bromo-*trans*-1-chlorovinyl-1-methyl-5-methylene-cyclohexane; [5]:2-chloro-trans-1-chlorovinyl-1-methyl-5-chloromethyl-4-cyclohexane; [6]:2,5-dichloro-4-bromo-*trans*-1-chlorovinyl-1-methyl-5-bromomethyl-cyclohexane; [7]: methyl (22R,24E)-22-acetoxy-3-oxocholesta-1,4,24-trien-26-oate; [8]: methyl (22E)-3-oxo-24-norcholesta-1,4,22-trien-26-oate; [9]: (22E)-11*β*-hydroxy-24-norcholesta-1,4,22-trien-3-one; [10]: (20S,22E)-20-hydroxy-24-norcholesta-1,4,22-trien-3-one; [11]: 2'-acetoxyglyceryl (5R,10R,13R)-labda-8-en-15-oate; [12]: 3'-acetoxyglyceryl (5R,10R,13R)-labda-8-en-15-oate; [13]: (20R)-cholesta-5,24-diene-2β,3α,21-triol 2,21-disulphate; [14]: (20R)-5α-cholest-24-ene-2β,3α,21-triol 3,21-disulphate; [15]: (20R)-cholesta-5,24-diene-2α,3α,4β,21-tetrol 3,21-disulphate; [16]: (20R)-cholest-5-ene-2β,3α,21-triol 3,21-disulphate; [17]: (20R,22E)-cholesta-5,22-diene-2β,3α,21-triol 3,21-disulphate; [18]: (20R)-cholest-5-ene-3α,4β,21-triol 3,21-disulphate; [19]: (22E)-24-nor-(24ξ)-24-methylcholesta-5,22-dien-3β-ol; [20]: *trans*-22-dehydrocholesterol:(22E)-cholesta-5,22-dien-3β-ol; [21]: *trans*-22-dehydrocholestanol:(22E)-5α-cholest-22-en-3β-ol; [22]: 24-methylenecholesterol:24-methylene-cholest-5-en-3β-ol; [23]: 24-methylenecholestanol:24-methylene-5α-cholestan-3β-ol.

[a]*Chemical structure*. AA, aromatic aldehydes; BA, brominated alkaloids; CA, carotenoids; CR, chromenes; DA, discorhabdin alkaloids; DK, diketopiperazine alkaloids; DT, diterpenes; FA, fatty acids and glyceryl derivatives; GS, glycosides and saponins; HP, halogenated products; IC, inorganic compounds; MA, mycosporine-like amino acids; MT, monoterpenes; NA, pyridinic alkaloids; NC, nitrogenated compounds; PA, phenazine alkaloids; PK, polyketides; PT, phlorotannins; PY, pyridopyrrolopyrimidine alkaloids; QA, quinolinic alkaloids; QN, quinones; SF, stilbene flavonoids; SQ, sesquiterpenes; ST, sesterterpenes; TS, triterpenes, sterols and steroids; VH, volatile halogenated organic compounds.

[b]*Origin*. A, algae; B, *de novo* biosynthesis; C, cnidarians; D, diet in general (not specified); E, epibionts; M, molluscs; MI, associated microorganisms; MO, modification of an existing compound; P, plankton; PC, precursor of cholesterol; S, sea water sequestration.

[c]*Activity*. A, antiviral; AVS, avoidance behavior to sympatric species (*Nacella concinna*); B, antibacterial activity (undetermined); BA, antibacterial activity against allopatric species; BS, antibacterial activity against sympatric species; C, cytotoxicity (undetermined); CA, cytotoxicity to allopatric species; CS, cytotoxicity to sympatric species (usually gametes or spermatozoa of *Sterechinus neumayeri*); CE, inhibition of cholesteryl ester transfer protein; CR, toxic- ity to crayfish (*Procambarus clarkii*); DS, deterrent to sympatric species (undetermined); DA, deterrent to allopatric species (undetermined); DAF, deterrent to allopatric fish; DAI, deterrent to allopatric insects; DSA, deterrent to sympatric anemone *Isotealia antarctica*; DSC, deterrent to sympatric crustaceans; DSF, deterrent to sympatric fish; DSS, deterrent to sympatric sea stars; ES, arm retraction in sympatric sea stars; F, antifungal activity; FOS, antifouling against sympatric diatoms; FT, antifungal activity applied to TLC plate; GS, defended against grazing by sympatric grazers (undetermined); GSM, defended against grazing by sympatric molluscs; H, hemolytic activity; I, ichthyotoxicity (undetermined); IA, ichthyotoxicity to allopatric species; IS, ichthyotoxicity to sympatric species; IN, insecticidal activity; L, inhibitor for embryos and⁄or larvae (undetermined); LA, inhibitor for embryos and⁄or larvae in allopatric sea urchin bioassay; LS, inhibitor for embryos and⁄or larvae in sympatric sea urchin bioassay; MS, molt inhibition in sympatric crustaceans; MI, mating induction (pheromone) between cells of complementary strains; PSU, phagostimulation in sympatric sea urchin *Sterechinus neumayeri*; PPS, physical protection from the sympatric anemone *Isotealia antarctica*; RS, rightening response in sympatric sea stars; S, antitumor; TS, tube-foot retraction in sympatric species; UV, UV radiation protectant; X, antioxidative activity; Y, antiyeast activity; YMS, chemo-avoidance in Y-maze experiment to sympatric species.

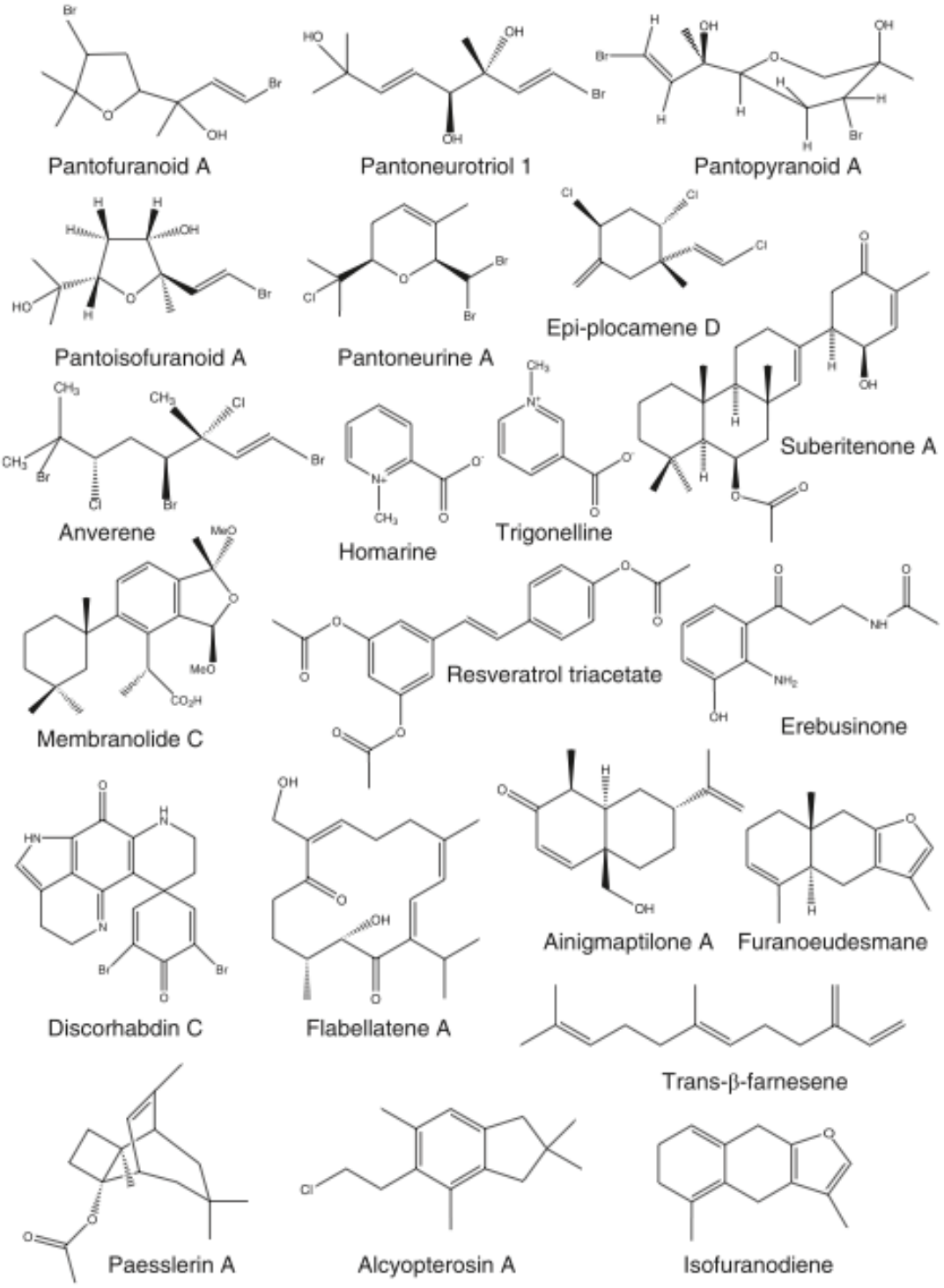

Figure 1. Chemical structure of some natural products described from Antarctic algae, poriferans and cnidarians

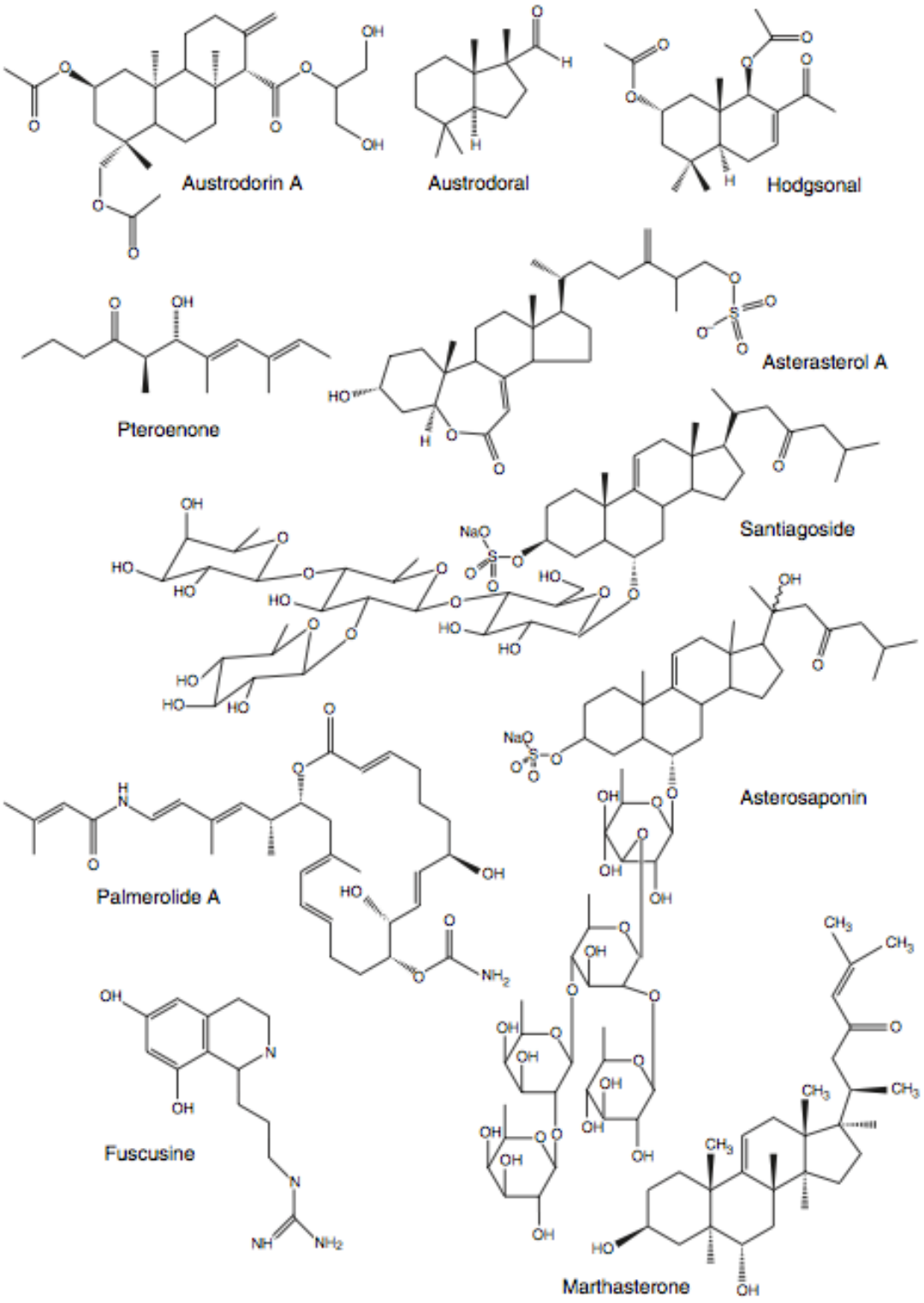

Figure 2. Chemical structure of some natural products described from Antarctic molluscs, echinoderms and tunicates

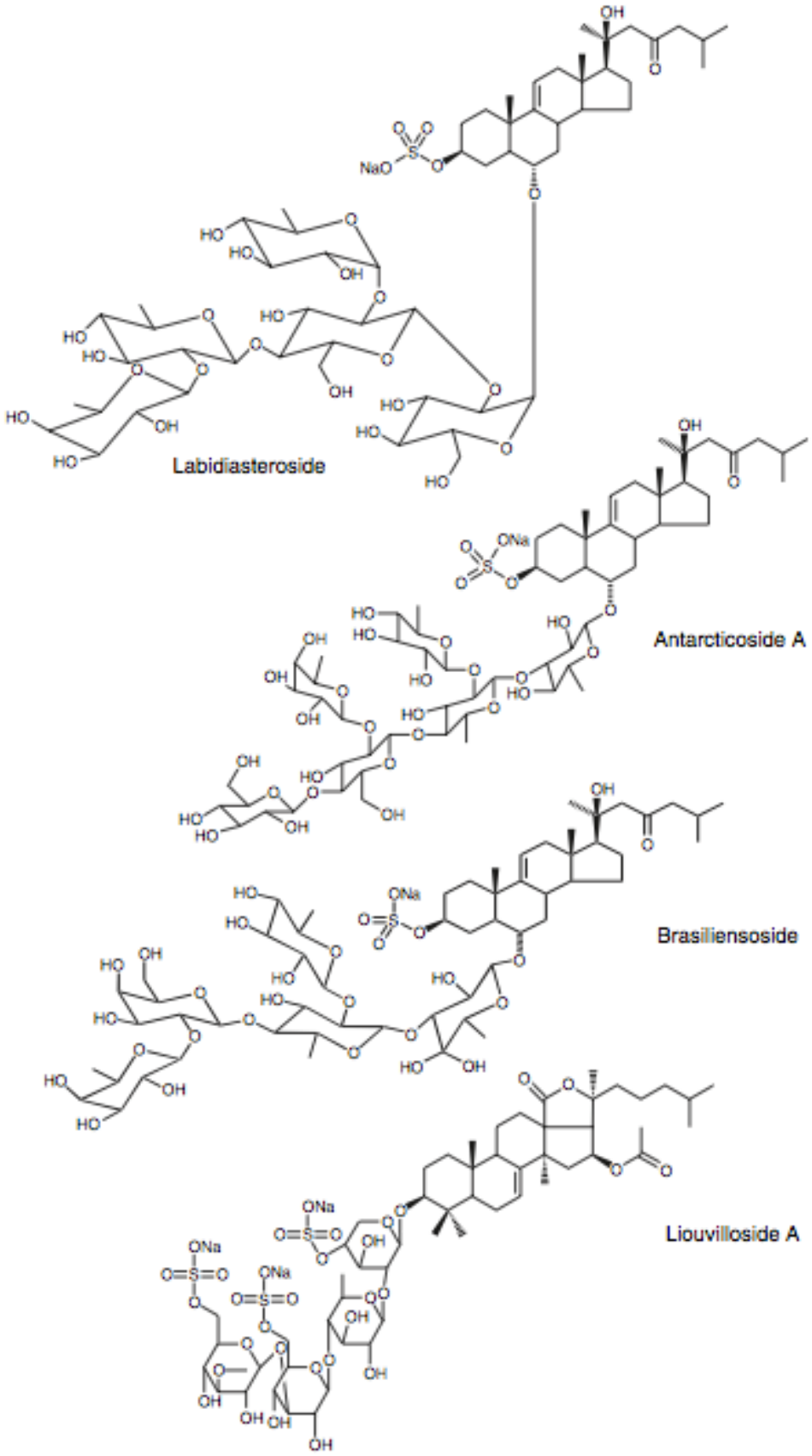

Figure 3. Chemical structure of some natural products described from Antarctic echinoderms

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Chapter 2

Feeding repellence of Antarctic and sub-Antarctic benthic invertebrates against the omnivorous sea star *Odontaster validus*

Photos by C. Avila

Chapter 2

Feeding repellence of Antarctic and sub-Antarctic benthic invertebrates against the omnivorous sea star *Odontaster validus*

Abstract. Antarctic and sub-Antarctic benthic invertebrates are subjected to intense predation by mobile macroinvertebrates. Accordingly, chemical protection, as well as other defensive mechanisms, are expected to be common in organisms inhabiting these ecosystems. In order to evaluate anti-predation activities and allocation of chemical defenses within the anatomy of marine benthic Antarctic and sub-Antarctic invertebrates, 55 species were tested for feeding repellence against the sea star *Odontaster validus*, a common eurybathic sympatric predator. The invertebrates tested were collected from the deep-waters of two poorly surveyed areas in terms of chemical ecology studies: the eastern Weddell Sea (Antarctica) and the vicinities of Bouvet Island (sub-Antarctica). Experiments were conducted at the Spanish Antarctic Base in Deception Island. In the feeding deterrence experiments, shrimp pieces were treated with crude lipophilic fractions obtained from each species, and were offered to the sea stars. A total of 29 species (53%) from 7 different phyla (Porifera, Cnidaria, Chordata, Bryozoa, Echinodermata, Mollusca, and Annelida) showed feeding repellence against *O. validus*, and are therefore chemically protected against this keystone predator. Furthermore, 25 species were dissected into parts to investigate the possible allocation of defensive compounds. Some of the results obtained from these analyses support the prediction that the most exposed/vulnerable tissues concentrate chemical defenses to avoid predation against the sea stars. In summary, the results obtained in our survey support the hypothesis that deep-water Antarctic and sub-Antarctic benthic invertebrates are well protected chemically against sympatric predators, similarly to what has been reported in previous studies investigating shallow-water Antarctic species.

Introduction

Marine natural products act as important mediators in intra- and interspecific biological interactions, and in regulating the structure of marine communities, as it has been demonstrated in temperate and tropical ecosystems (*e.g.* Scheuer 1990, Paul 1992a, Pawlik 1993, Hay 1996). The Antarctic seafloor, with a very predictable and relatively constant physical environment below the zone of ice scour and anchor ice, also appears to be intensively influenced by biotic relationships. Certainly, predation and competition play a crucial role in structuring these communities (Dayton *et al.* 1974, Arntz *et al.* 1994). In these extremely stable environments, the largest proportion of benthic fauna is made up of a rich and diverse community of suspension feeders, usually conforming tridimensional structures (Dayton *et al.* 1974, Arntz *et al.* 1994, Clarke & Johnston 2003, Brandt *et al.* 2007). All these suspension feeders, chiefly sessile and sluggish animals, have survived thanks to developing mechanisms against predation and competition for space, but also through strategies that inhibit settling and fouling by other organisms (*e.g.* Dayton *et al.* 1974, Amsler *et al.* 2000b, Peters *et al.* 2009, Núñez-Pons *et al.* 2010, Koplovitz *et al.* 2011). Accordingly, to ensure survival, most of these species possess structural defenses (*e.g.* long siliceous spicules, shells) and/or defensive secondary metabolites (Lebar *et al.* 2007, Avila *et al.* 2008).

The role that chemical defenses play mediating predator-prey interactions has attracted the greatest attention in tropical and temperate areas as well as in shallow Antarctic waters (Scheuer 1990, Paul 1992a, Pawlik 1993, Hay 1996, McClintock & Baker 1997a, Amsler *et al.* 2001, Avila *et al.* 2008). Unlike lower latitudes, in Antarctic communities asteroids have replaced fish as major potential predators, and the predation pressure caused by these macrobenthic invertebrates has demonstrated to be as intense as that reported in temperate and even tropical areas (Dearborn 1977, McClintock 1994). This pressure, added to the environmental stability and the period that Antarctic ecosystems have remained isolated from the surrounding waters (*ca.* 23–41 My; Scher & Martin 2006, Lylle *et al.* 2007), has acted as a selective force for the evolution and acquisition of defensive secondary metabolites in many invertebrates (*e.g.* McClintock & Baker 1997a, Amsler *et al.* 2000a, 2001, Avila *et al.* 2008). In this sense, a large number of natural products and putative chemical defenses have been discovered from Antarctic marine organisms in the last years (for review see Lebar *et al.* 2007, Avila *et al.* 2008). Although some of these compounds have been reported to have a defensive function, in most cases the full understanding of either the molecular structure or the ecological relevance of most metabolites is still lacking (Avila *et al.* 2008).

Here, an approach to better comprehend predator-prey interactions mediated by secondary metabolites has been done by testing ecological theories such as the Optimal Defense Theory (ODT; Rhoades 1979). According to this theory, an organism exposed to high predation rates should preferably allocate its chemical defensive metabolites in the most vulnerable and/or valuable tissues. This indeed is directly correlated with the risk of attacks by sympatric predators in a particular environment, and with the relative contribution of the protected parts to the prey's fitness (Rhoades 1979, Hay 1996). In the literature, there are many examples of marine invertebrates

where the allocation of defensive metabolites has been established. Some of these examples deal with opisthobranch molluscs occurring in temperate and tropical waters (*e.g.* Faulkner & Ghiselin 1983, Avila, 1995, Wägele *et al.* 2006). These gastropods, with a general tendency towards the loss of the shell, have gradually acquired chemical defenses that deter fish from predation. Conversely, in the Southern Ocean, where sea stars are the major macrobenthic predators, almost nothing is known about chemical defense allocation, except for a few studies on sponges, molluscs and deep-water tunicates (*e.g.* Avila *et al.* 2000, Iken *et al.* 2002, Furrow *et al.* 2003, Peters *et al.* 2009, Núñez-Pons *et al.* 2010).

To date, chemical protection reported from Antarctic benthic invertebrates is mostly based on the study of shallow-water organisms (accessible via scuba diving), mainly collected from McMurdo Sound (Ross Sea) and the Western Antarctic Peninsula. A few studies also investigated some sub-Antarctic Islands and deep-water species from the Weddell Sea (reviewed in McClintock & Baker 1997a, Davies-Coleman 2006, Avila *et al.* 2008, McClintock *et al.* 2010). Aiming at evaluating the incidence and allocation of chemical defenses against predation in deep-water benthic invertebrates, we conducted an extensive study with samples from a very wide bathymetric range. Organisms were collected from two poorly known areas in terms of chemical ecology: (i) the eastern Weddell Sea (Antarctica), mainly dominated by suspension feeders (Arntz *et al.* 1994), where the bulk of the samples were collected; (ii) and the vicinities of Bouvet Island (sub-Antarctica), an area characterized by a potent predatory community (Arntz *et al.* 2006, Jacob *et al.* 2006). Our survey included the study of the lipophilic fractions from 55 species belonging to 9 phyla (Porifera, Cnidaria, Nemertea, Mollusca, Annelida, Bryozoa, Echinodermata, Hemichordata, and Chordata), most of them being sessile or sluggish organisms with no apparent physical defenses. These organisms were tested for feeding repellence against a keystone predator, the sympatric omnivorous sea star *Odontaster validus*. This species, one of the most abundant and voracious Antarctic predators, has a wide bathymetric range and a circumpolar distribution, extending into the sub-Antarctic (Dayton *et al.* 1974, Dearborn 1977, McClintock 1994, Janosik *et al.* 2011). According to *O. validus* extraoral feeding mode and to the predictions of the ODT (Rhoades 1979), the most exposed surfaces should be the most vulnerable regions in potential preys. In order to test the validity of the ODT, 25 deep-water invertebrate species were dissected into different parts. Therefore, we present here the results of a study on feeding repellence in deep-water Antarctic and sub-Antarctic benthic invertebrates, as well as of testing the ODT for several of these organisms.

Material and Methods

Sample collection and identification

Invertebrate benthic marine samples were collected in the eastern Weddell Sea (Antarctica) and the vicinities of Bouvet Island (sub-Antarctica) during the ANT XXI/2 cruise (November 2003-January 2004) on board the R/V Polarstern, from the Alfred Wegener Institute for Polar and Marine Research (Bremerhaven, Germany). In the 23 sampling stations, surveying a very wide bathymetric range (82–1,866 m depth), four sampling different devices were used: bottom trawl, Agassiz trawl, Rauschert dredge, and epibenthic sledge (Figure 1; Table 1). Sorting of samples was carried out on deck: invertebrates from different phyla were selected based on the availability of specimens, the approximate required biomass for the tests, and the *in situ* observations of characters related to the presence of chemical natural products (*i.e.* sessile nature, absence of physical defenses, soft-bodied texture, particular color and/or smell, absence of epibionts). After this qualitative selection, organisms were immediately frozen to -20 °C and later transferred to the laboratory in Spain. A voucher specimen or a portion of each sample was fixed in 10% formalin or 70% ETOH for taxonomical determination. These vouchers are deposited at the Dept. of Animal Biology (Invertebrates), University of Barcelona, Spain. Additionally, pictures of the living organisms were also taken for further taxonomical identification.

Odontaster validus specimens (n = 527) used during the feeding deterrence tests were collected in the South Shetland Islands area (Livingston and Deception Island, and their proximities; Figure 1) during January 2006. The bulk of the sea stars (474 specimens) were obtained by scuba diving at Whalers Bay (Deception Island: 62º 59.37' S, 60º 33.42' W) from 3 to 15 m depth; the rest of sea stars (53 specimens) were collected using an Agassiz trawl at about 100 m deep on board the R/V BIO Hespérides. The size of the sea stars collected ranged between 4.5–10.5 cm diameter. After the experiments, the sea stars were brought back alive to the sea at Whalers Bay. In relation to the origin of the sea star used during the experiments, it is worth mentioning that despite the sea stars and the species tested come from different areas (Figure 1), it has recently been proved that Antarctic and sub-Antarctic *O. validus* populations show great connectivity over long distances (Janosik *et al.* 2011).

Chemical extraction

Frozen specimens were chemically extracted in the laboratories at the Faculty of Biology, University of Barcelona. When needed, in order to yield enough extract for the tests, several conspecific specimens or pieces of colonies from the same station were extracted together. When possible, samples were carefully dissected into different parts in order to locate the compounds responsible for defense within the anatomy of the organisms. These parts were divided according to the taxonomic group (*e.g.* mantle, foot, and viscera, in molluscs; internal or visceral tissues, and external tissues or tunic, in tunicates; external/internal, and apical/basal regions, in sponges), and were processed separately (Table 1). Each species (whole organism or dissected parts) was

extracted with acetone. After removing the organic solvent under reduced pressure, the remaining aqueous residues were sequentially partitioned into diethyl ether and *n*-butanol fractions. All steps were repeated thrice, except for the butanol fraction which was done once. Organic solvents were evaporated under reduced pressure, resulting in dry diethyl ether (EE) and butanolic fractions (BE), and an aqueous residue (WR) (see Annex 1). Thin-layer chromatography (TLC) screenings were carried out to check the chemical profile of all the fractions obtained. An aliquot of all the lipophilic extracts was used at natural concentration (see Annex 1) in the feeding repellence tests (see below). Butanolic extracts and water residues (hydrophilic) were not tested in this study and will be assayed in future experiments. The main reason for using lipophilic extracts is due to the fact that the nature of many of the known products displaying interesting chemical activity is mainly lipophilic (Sotka *et al.* 2009, Blunt *et al.* 2011).

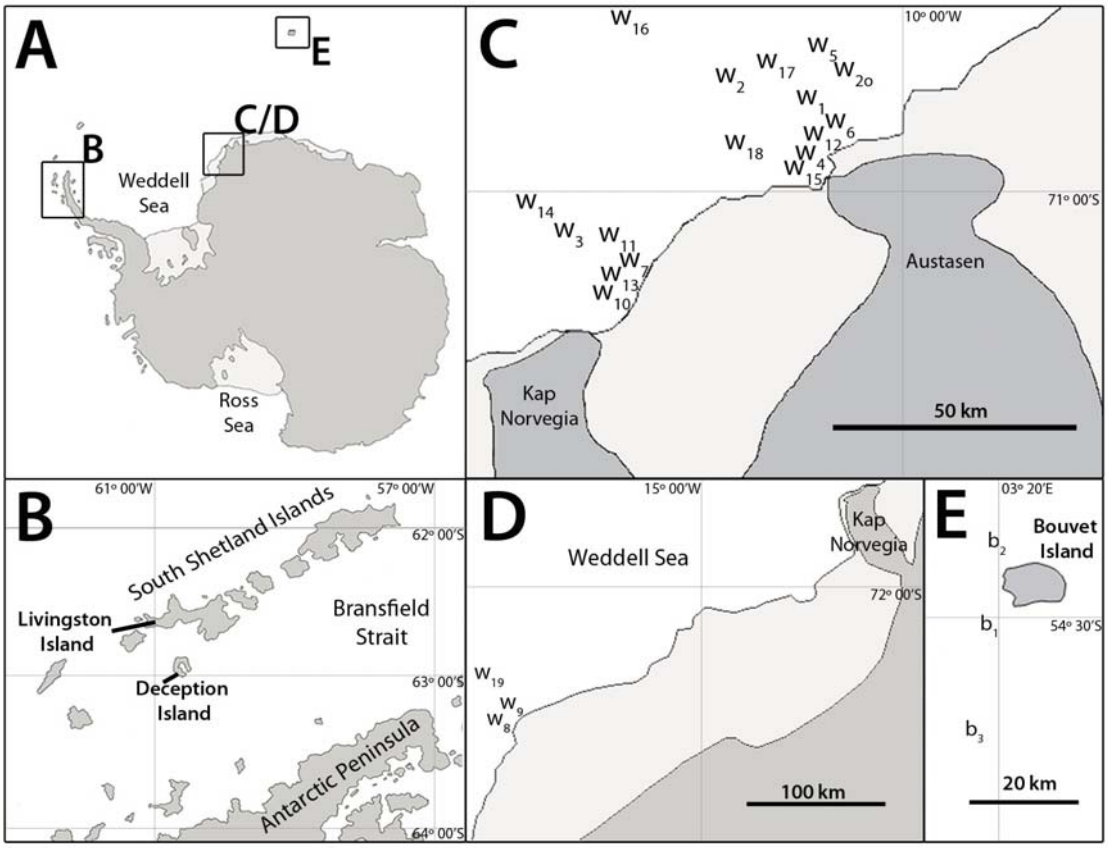

Figure 1. Sampling stations surveyed during the study (see also Table 1 for details). **A.** General map of Antarctica; **B.** South Shetland Islands area; **C.** Eastern Weddell Sea area part 1; **D.** Eastern Weddell Sea area part 2; **E.** Bouvet Island

Feeding repellence tests

In the Antarctic marine benthic environment, asteroids are the dominant consumers of sessile, slow-moving and sluggish invertebrates. Hence, the abundant eurybathic (down to 941 m depth) Antarctic and sub-Antarctic sea star *Odontaster validus*, with voracious omnivorous habits (Dayton *et al.* 1974, Dearborn 1977,

McClintock 1994, Janosik *et al.* 2011), was chosen as a potential generalist predator for carrying out our assays, as done in previous studies (Avila *et al.* 2000, Iken *et al.* 2002, Núñez-Pons *et al.* 2010). Sea stars were collected and maintained in large tanks with sea water pumped directly from the sea, in the laboratory at the "Gabriel de Castilla" Antarctic Spanish Base, Deception Island (South Shetland Islands; Figure 1). They were acclimated and starved for 3–5 days before being used in the feeding assays. The methodology used for the assays was the same as in the study by Núñez-Pons *et al.* (2010). Briefly, shrimp cubes, prepared after processing frozen peeled shrimps, were treated with ethereal extracts and offered to the sea stars to test their repellent activity. Shrimp cubes had an approximate volume of 0.5 cm^3, 68.92 $\pm$ 11.01 mg average wet weight (WW), and 13.09 $\pm$ 3.43 mg average dry weight (DW). Shrimp pieces were slowly soaked with the ethereal extracts of each species at natural concentrations, allowing the extract to be uniformly absorbed throughout the food item. Subsequently, the solvent (diethyl ether) was allowed to evaporate from the treated shrimp cubes. Natural concentrations were calculated referring the EE weight to the total dry weight (DW_T = DW of the sample + EE weight + BE weight) yielded for each species. We chose dry weight rather than other parameters, such as wet weight or volume, in order to standardize the calculations for all our species, since they may contain uneven water content and volumetric features. Thus, natural extract concentrations ([N]) were related to the average dry weight of the shrimp cubes. In a few cases, we also assessed higher or lower concentrations several fold the natural one: (i) when there was enough quantity left, some inactive extracts were assessed using twice the natural concentration ([X2]) to investigate whether higher concentrations would cause repellence; (ii) we assayed half the natural concentration ([1/2]), for two parts of two dissected molluscs that did not yield enough extract to be tested at natural concentration (see Annex 1).

The assays were performed in single 2.5 L buckets, and there were 10 replicates per treatment, each containing one sea star and one food item. A control, also with 10 replicates, using shrimp cubes treated only with solvent, was run simultaneously every day for each set of experiments. In both treatments and controls, the piece of shrimp was placed at the bottom in the center of the bucket, and the sea star was then carefully placed with its oral opening in direct contact with the food item. After 24 h, a shrimp cube was considered rejected when *O. validus* lost physical contact with it, and considered eaten when it was completely ingested by the sea star. Some of those sea stars that did not feed after a treatment were used again only once, after at least a three-day period of starvation. Sea stars which had consumed in a feeding assay were discarded for further experiments. Non-ingested shrimp cubes treated with extracts were frozen after the experiments. TLC screenings of the extracted shrimp pieces confirmed that the chemical profile of the extracts remained unchanged after the assays, ruling out the possibility of a major loss of extracts by diffusion to the water.

Statistics were calculated for each treatment referred to the control run simultaneously by applying the Fisher's exact Test (Sokal & Rohlf 1995).

Table 1. Benthic invertebrates collected in the Weddell Sea and the vicinities of Bouvet Island during the ANT XXI/2 cruise

Taxonomic group (phylum, class) and species name	N specimens	Location[a]	Latitude	Longitude	Gear[b]	Depth (m)
PORIFERA, Demospongiae						
Antho (*Acarnia*) *gaussiana* (Henstschel, 1914)	1	Weddell (w_1)	70° 55,92' S	010° 32,37' W	AT	288
Cinachyra barbata Sollas, 1886	3	Weddell (w_2)	70° 52,75' S	010° 51,24' W	BT	295
Homaxinella cf *balfourensis* (Ridley & Dendy, 1886)	Piece	Weddell (w_3)	71° 06,30' S	011° 32,04' W	AT	175
Iophon unicorne Topsent, 1907	1	Weddell (w_4)	70° 57,00' S	010° 33,02' W	BT	333
Isodictya erinacea (Topsent, 1916)	3	Weddell (w_2)	70° 52,75' S	010° 51,24' W	BT	295
Isodictya kerguelenensis (Ridley & Dendy, 1886)	1	Weddell (w_5)	70° 50,08' S	010° 34,76' W	AT	274
Isodictya setifera (Topsent, 1901)	Piece	Weddell (w_5)	70° 50,08' S	010° 34,76' W	AT	274
Isodictya toxophila Burton, 1932	4	Weddell (w_4)	70° 57,00' S	010° 33,02' W	BT	333
Lissodendoryx (*Ectyodoryx*) *anacantha* (Hentschel, 1914)	5	Weddell (w_4)	70° 57,00' S	010° 33,02' W	BT	333
Mycale (*Oxymycale*) *acerata* Kirkpatrick, 1907	Piece	Weddell (w_2)	70° 52,75' S	010° 51,24' W	BT	295
Phorbas glaberrimus (Topsent, 1917)	2	Weddell (w_2)	70° 52,75' S	010° 51,24' W	BT	295
Pyloderma latrunculioides (Ridley & Dendy, 1886)	Piece	Weddell (w_6)	70° 56,42' S	010° 31,61' W	BT	284
Tedania oxeata Topsent, 1916	1	Weddell (w_7)	71° 07,15' S	011° 26,23' W	AT	228
Hexactinellida						
Rossella cf *vanhoeffeni* (Schulze & Kirkpatrick, 1910)	Piece	Weddell (w_5)	70° 50,08' S	010° 34,76' W	AT	274
CNIDARIA, Anthozoa						
Alcyonium grandis Casas, Ramil & van Ofwegen, 1997	Piece	Weddell (w_8)	72° 51,43' S	019° 38,62' W	BT	598
Primnoisis antarctica (Studer, 1878)	Piece	Weddell (w_5)	70° 50,08' S	010° 34,76' W	AT	274
Primnoisis antarctica (Studer, 1878)	Piece	Weddell (w_2)	70° 52,75' S	010° 51,24' W	BT	295
Thouarella (*Epithouarella*) *laxa* Versluys, 1906	Piece	Weddell (w_9)	72° 50,18' S	019° 35,94' W	RD	622
Thouarella (*Epithouarella*) *viridis* Z.-Guardiola & L.-González, 2009	Piece	Weddell (w_9)	72° 50,18' S	019° 35,94' W	RD	622
Hydrozoa						
Eudendrium sp. Ehrenberg, 1834	Piece	Weddell (w_3)	71° 06,30' S	011° 32,04' W	AT	175
Staurotheca antarctica Hartlaub, 1904	Piece	Weddell (w_8)	72° 51,43' S	019° 38,62' W	BT	598
Symplectoscyphus glacialis (Jäderholm, 1904)	Piece	Weddell (w_3)	71° 06,30' S	011° 32,04' W	AT	175
Unidentified hydrocoral	Piece	Weddell (w_8)	72° 51,43' S	019° 38,62' W	BT	598
BRYOZOA, Gymnolaemata						
Alcyonidium flabelliforme Kirkpatrick, 1902	1	Weddell (w_{10})	71° 07,51' S	011° 29,94' W	AT	120
Austroflustra vulgaris (Kluge, 1914)	Piece	Bouvet (b_1)	54° 30,01' S	003° 13,97' E	AT	260
Bostrychopora dentata (Waters, 1904)	Piece	Weddell (w_4)	70° 57,00' S	010° 33,02' W	BT	333
Cellaria diversa Livingstone, 1928	Piece	Weddell (w_3)	71° 06,30' S	011° 32,04' W	AT	175
Cornucopina polymorpha (Kluge, 1914)	Piece	Bouvet (b_1)	54° 30,01' S	003° 13,97' E	AT	260
Isoschizoporella secunda Hayward & Taylor, 1984	Piece	Weddell (w_{11})	71° 06,44' S	011° 27,76' W	AT	277
Isosecuriflustra tenuis (Kluge, 1914)	Piece	Weddell (w_2)	70° 52,75' S	010° 51,24' W	BT	295
MOLLUSCA, Gastropoda						
Marseniopsis conica (Smith, 1902)	1	Weddell (w_2)	70° 52,75' S	010° 51,24' W	BT	295
Bathyberthella antarctica Willan & Bertsch, 1987	1	Weddell (w_{12})	70° 56,67' S	010° 32,05' W	BT	302

Table 1. (Continued)

Taxonomic group (phylum, class) and species name	N specimens	Location[a]	Latitude	Longitude	Gear[b]	Depth (m)
Philine alata Thiele, 1912	6	Bouvet (b_2)	54° 22,49' S	003° 17,58' E	AT	134
Tritonia challengeriana Bergh, 1884	1	Weddell (w_{13})	71° 07,32' S	011° 28,45' W	RD	82
Tritoniella belli Eliot, 1907	2	Weddell (w_{13})	71° 07,32' S	011° 28,45' W	RD	82
CHORDATA, Ascidiacea						
Aplidium falklandicum Millar, 1960	2	Weddell (w_{14})	71° 04,30' S	011° 33,92' W	BT	309
Aplidium millari Monniot & Monniot, 1994	1	Weddell (w_{14})	71° 04,30' S	011° 33,92' W	BT	309
Cnemidocarpa verrucosa (Lesson, 1830)	1	Weddell (w_1)	70° 55,92' S	010° 32,37' W	AT	288
Molgula pedunculata Herdman, 1881	10	Weddell (w_3)	71° 06,30' S	011° 32,04' W	AT	175
Pareugyrioides arnbackae (Millar, 1960)	7	Weddell (w_{15})	70° 57,33' S	010° 33,86' W	BT	352
Synoicum adareanum (black & white morph) (Herdman, 1902)	2	Weddell (w_6)	70° 56,42' S	010° 31,61' W	BT	284
Synoicum adareanum (orange morph) (Herdman, 1902)	53	Weddell (w_1)	70° 55,92' S	010° 32,37' W	AT	288
ECHINODERMATA, Asteroidea						
Porania antarctica E.A. Smith, 1876	7	Bouvet (b_2)	54° 22,49' S	003° 17,58' E	AT	134
Ophiuroidea						
Ophionotus victoriae Bell, 1902	62	Bouvet (b_3)	54° 36,95' S	003° 12,42' E	AT	553
Holothuroidea						
Ekmocucumis steineri (Ludwig, 1886)	2	Weddell (w_7)	71° 07,15' S	011° 26,23' W	AT	228
Paradota weddellensis Gutt, 1988	1	Weddell (w_{16})	70° 47,88' S	011° 24,13' W	AT	1,525
Peniagone cf *vignioni* Hérouard, 1901	16	Weddell (w_{16})	70° 47,88' S	011° 24,13' W	AT	1,525
Psolus charcoti Vaney, 1906	14	Weddell (w_6)	70° 56,42' S	010° 31,61' W	BT	284
Psolus ephippifer (Thompson, 1876)	27	Weddell (w_1)	70° 55,92' S	010° 32,37' W	AT	288
Rhipidothuria racowitzai Hérouard, 1901	23	Weddell (w_{17})	70° 56,98' S	010° 48,04' W	ES	407
Staurocucumis liouvillei (Vaney, 1914) Ekman, 1927	21	Bouvet (b_2)	54° 22,49' S	003° 17,58' E	AT	134
Taeniogytus contortus (Ludwig, 1874)	3	Weddell (w_{18})	70° 52,16' S	010° 43,69' W	BT	291
Crinoidea						
Encrinus cf *liliformis*	25	Weddell (w_{16})	70° 47,88' S	011° 24,13' W	AT	1,525
NEMERTEA, Anopla						
Parborlasia corrugatus (McIntosh, 1876)	4	Weddell (w_{16})	70° 47,88' S	011° 24,13' W	AT	1,525
ANNELIDA, Polychaeta						
Polyeunoa laevis McIntosh, 1885	16	Weddell (w_{18})	70° 52,16' S	010° 43,69' W	BT	291
Travisia sp. Johnston, 1840	3	Weddell (w_{19})	72° 46,91' S	019° 37,40' W	RD	1,866
HEMICHORDATA, Pterobranchia						
Cephalodiscus sp. McIntosh, 1882	Piece	Weddell (w_{20})	70º 50,75' S	10º 28,01' W	AT	281

[a]w_n: sampling station from the eastern Weddell Sea, b_n: sampling station from Bouvet Island. See also Figure 1 for details; [b]AT: Agassiz Trawl, BT: Bottom Trawl, RD: Rauschert Dredge, ES: Epibenthic Sledge

Results

Of the 55 species assayed from 9 different phyla, a total of 29 species (53%) pertaining to 7 phyla showed feeding repellence against *Odontaster validus*, thus indicating the presence of lipophilic defensive chemical metabolites. The remaining 26 species (47%) did not show any activity (Figure 2; Annex 1). Both sponges and cnidarians, with 6 repellent species each (21% each), provide the major contribution to the active percentage in the whole survey. These are followed by bryozoans and echinoderms with 5 active species each (17% each), chordates with 4 active species (14%), molluscs with 2 species (7%), and annelids with one active species (3%). Even though the evident bias in the sampling effort for some phyla, the majority of the groups studied demonstrated repellent activity against the generalist sympatric predator *O. validus*. In this sense, the most surveyed phyla are also those presenting the largest percentage of activity (Figure 3).

Concerning the location of the chemical defensive activity, some groups appear to accumulate protective metabolites in certain parts of their anatomy (Figure 2; Annex 1). Of the 7 sponges dissected into parts 3 displayed defensive activity against *O. validus*. Two out of these 3 active dissected sponges (*Cinachyra barbata* and *Tedania oxeata*), concentrated the defensive metabolites in their external tissues. For *T. oxeata*, the internal extract tested at both natural and two-fold the natural concentration did not show deterrent activity against the sea star. *Isodictya toxophila*, also dissected into parts, presented repellent activity in both the apical and basal parts; thus, its defensive metabolites were homogeneously distributed within the sponge anatomy. The remaining active sponges (*Rossella* cf *vanhoeffeni*, *Isodictya setifera* and *Lissodendoryx* (*Ectyodoryx*) *anacantha*) were not dissected, and so the allocation of defensive activity cannot be determined here. Three of the 5 different species of tunicates dissected into parts reported feeding repellence activity: *Aplidium millari* and the orange morph of *Synoicum adareanum* concentrated their activity in the internal part, while *Pareugyrioides arnbackae* presented activity only in its apical part. When considering molluscs, *Bathyberthella antarctica* protected both its visceral tissues and foot, while the mantle neither at natural nor at two-fold the natural concentration deterred the sea star. The viscera of the opisthobranch *Philine alata*, only assayed at half the natural concentration due to lack of enough extract, also deterred *O. validus.* Finally, for echinoderms, defensive chemical compounds accumulated in the arms of the brittle star *Ophionotus victoriae* as well as in the tentacles of the sea cucumber *Ekmocucumis steineri*, while the sea star *Porania antarctica* concentrated its chemical defenses in its basal part.

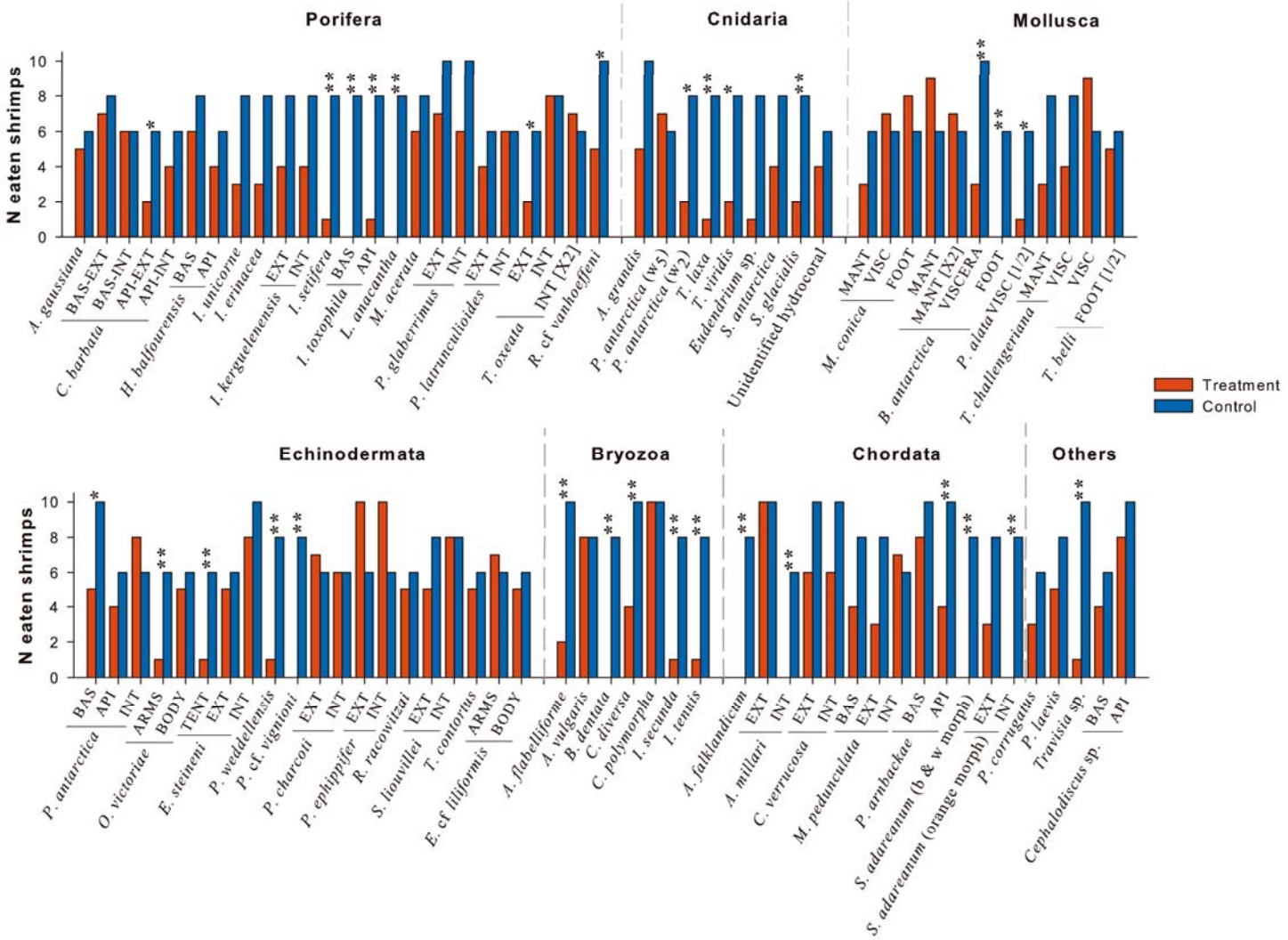
Porifera
Cnidaria
Mollusca
Echinodermata
Bryozoa
Chordata
Others
N eaten shrimps
0
2
4
6
8
10
Treatment
Control
A. gaussiana
BAS-EXT
BAS-INT
API-EXT
API-INT
C. barbata
H. balfourensis
BAS
API
I. unicorne
I. erinacea
EXT
INT
I. kerguelenensis
I. setifera
BAS
API
I. toxophila
L. anacantha
M. acerata
EXT
INT
P. glaberrimus
P. latrunculoides
EXT
INT
T. oxeata
EXT
INT
INT [X2]
R. cf. vanhoeffeni
A. grandis
P. antarctica (w5)
P. antarctica (w2)
T. laxa
T. viridis
Eudendrium sp.
S. antarctica
S. glacialis
Unidentified hydrocoral
MANT
VISC
M. conica
FOOT
MANT
MANT [X2]
VISCERA
B. antarctica
FOOT
P. alata VISC [1/2]
T. challengeriana
MANT
VISC
VISC
FOOT [1/2]
T. belli
P. antarctica
BAS
API
INT
ARMS
BODY
O. victoriae
TENT
E. steineni
EXT
INT
P. weddellensis
P. cf. vignioni
EXT
INT
P. charcoti
EXT
INT
P. ephippifer
R. racovitzai
S. liouvillei
EXT
INT
T. contortus
ARMS
BODY
E. cf. liliformis
A. flabelliforme
A. vulgaris
B. dentata
C. diversa
C. polymorpha
I. secunda
I. tenuis
A. falklandicum
EXT
INT
A. millari
EXT
INT
C. verrucosa
M. pedunculata
BAS
EXT
INT
P. arnbackae
BAS
API
S. adareanum (b & w morph)
EXT
INT
S. adareanum (orange morph)
P. corrugatus
P. laevis
Travisia sp.
Cephalodiscus sp.
BAS
API

Figure 2. Feeding deterrence tests with lipophilic fractions added to shrimp pieces offered to *Odontaster validus*. Each set of experiments and controls consisted of 10 replicates. All the fractions were assayed at their natural tissue concentration except: [X2], twice the natural concentration; [1/2], half the natural concentration. Abbreviations: API, apical part; BAS, basal part; EXT, external part; INT, internal part; MANT, mantle; TENT, tentacles; VISC, viscera. Statistical differences calculated for each set of experiments respect to the control run simultaneously using Fisher's exact test; *p ≤ 0.05, **p ≤ 0.01

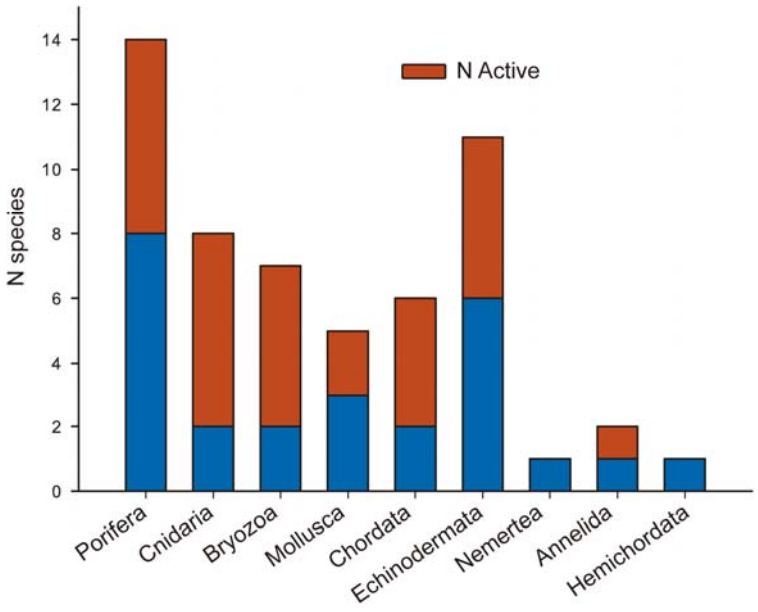

Figure 3. Number of active species versus number of inactive species for each phylum

Discussion

Our study shows that more than half (53%) of the deep-water Antarctic and sub-Antarctic benthic invertebrates tested are chemically protected against predation from a sympatric keystone predator, the sea star *Odontaster validus*. Thus, these results clearly support the hypothesis that chemical defenses in marine sessile and sluggish invertebrates play an important role in predator-prey interactions in the deep-water Antarctic and sub-Antarctic benthos. During the last two decades, similar results mostly from shallow-water Antarctic marine invertebrates have reinforced this statement (Amsler *et al.* 2000a, Lebar *et al.* 2007, Avila *et al.* 2008, Peters *et al.* 2009, McClintock *et al.* 2010), leading to a reevaluation of the latitudinal hypothesis (Amsler *et al.* 2000a). This hypothesis, originally predicting a negative gradient in the occurrence of predation and chemical defenses from the tropics to the poles (Bakus & Green 1974), is no longer accepted for the Southern Ocean benthic environment. Our findings are in clear agreement with the highly structured and biologically accommodated communities that dominate the benthos under the ice scouring area (Dayton *et al.* 1974, Arntz *et al.* 1994).

The existence of chemical repellence mechanisms has been assessed in the past through a variety of experiments with Antarctic marine invertebrates (for a review see Avila *et al.* 2008). Among the research groups using *O. validus* as an Antarctic model for testing predation interactions, different methodologies have been employed (*e.g.* tube-foot and arm retraction to tissues, to freeze-dried tissues mixed in alginate solution or to extracts; McClintock *et al.* 1992, 1993a, Slattery and McClintock 1995, Mahon *et al.* 2003; placing tissues, paper filter disks soaked with extracts, or alginate-krill pellets soaked with extracts in the ambulacral grooves of the arms and observing movement to the mouth; McClintock *et al.* 1994c, McClintock and Baker 1997b, Peters *et al.* 2009). Hence, comparison of results using different methodologies is difficult. Apart from the methodological aspects, other biotic (*e.g.* individual variation related to age, presence/absence of bacterial symbionts, genetic variation between populations) and abiotic (*e.g.* seasonal changes, geography, bathymetry) sources of variation should also be taken into account when comparing the experimental results for the same species from different studies (Hay 1996, Paul & Puglisi 2004, Sharp *et al.* 2007). Also, since we only present here the results of testing lipophilic extracts, further studies are needed to test the hydrophilic fractions of our samples.

To the best of our knowledge, 43 of the 55 species (78%) tested in our survey are studied now for the first time in repellency bioassays. These data are not surprising since most of the species investigated here occur in deep waters, as opposed to most of the species studied so far. The remaining 12 species, comprising 6 sponges, 2 echinoderms, 3 tunicates, and one mollusc, have been examined in previous surveys.

A recent study concluded that 78% out of 27 sponges coming from the shallow-waters along the Western Antarctic Peninsula caused repellence to *O. validus* (Peters *et al.* 2009). Porifera, our best represented phylum (14 species), yielded a lower active percentage (43%), but had a smaller sample size respect to that study. Although more extensive studies should be done in both shallow- and deep-water environments to

confirm a clear tendency, perhaps a heavier predation pressure occurring in the shallow-waters of the Antarctic Peninsula may explain the higher incidence of chemical defenses in these environments (Peters *et al.* 2009). Other than this, deterrent activities may remain hidden in the hydrophilic extracts not assayed here.

Comparative approximations of our results in sponges with the available literature deserve some discussion. The demosponge *Isodictya setifera* showed significant unpalatability in our assays, as previously observed for its brooded eggs (McClintock & Baker 1997b), however, a previous investigation found the extracts of shallow-water adults to be palatable for the sympatric sea star *Perknaster fuscus* (McClintock *et al.* 1993). On the other hand, some of the sponges that did not cause feeding deterrence to *O. validus* in our experiments, showed anti-predatory effects in previous surveys from shallow-waters. Although in our case the effects of the hydrophilic extracts still need to be investigated, it is important to note that *Homaxinella balfourensis*, *Mycale acerata*, *Isodictya kerguelenensis, I. erinacea,* and *Iophon unicorne*, showed anti-predatory activity against the sympatric sea stars *P. fuscus* and *O. validus* in other assays (McClintock *et al.* 1990, 1993a, 1994b, Baker *et al.* 1993, Baker & Yoshida 1994, Moon *et al.* 1998, Peters *et al.* 2009). In our study, 7 sponges were dissected for chemical defense allocation, and none of them had been previously investigated for this (Figure 2; Annex 1). Only *Cinachyra barbata* and *Tedania oxeata* (showing a negative result in its internal part even at two-fold the natural concentration) accumulated chemical defenses in their outermost parts. These results follow the predictions of the ODT (Rhoades 1979) for an environment chiefly affected by sea star predation, in contrast with some results obtained by Peters *et al.* (2009). In their survey on common shallow-water sponges, the outer portion of 78% of the sponges were rejected by *O. validus*, while 62% of the inner portions also caused repellence.

Antarctic ascidians have lately received a great deal of attention (Koplovitz *et al.* 2009, 2011, Núñez-Pons *et al.* 2010). In a recent study with 12 different solitary and colonial species from the Western Antarctic Peninsula, Koplovitz *et al.* (2009) included 2 of the species investigated here. One of them, the solitary ascidian *Cnemidocarpa verrucosa*, yielded a palatable lipophilic extract according to our experiments, and proved palatability also when the fresh tunic was offered to *O. validus* (Koplovitz *et al.* 2009). Conversely, fresh tunic pieces deterred the sympatric fish *Notothenia coriiceps*, while both the lipophilic and hydrophilic extracts resulted palatable. Protection from fish was in this case attributed to the toughness of the ascidian's tunic (McClintock *et al.* 1991, Koplovitz *et al.* 2009). The other previously assessed species, the colonial *Synoicum adareanum*, exhibited strong repellent activity in the two morphotypes tested in our survey. This species showed repellent activity to *O. validus* and *N. coriiceps* when they were offered fresh tunic tissues, although neither lipophilic nor hydrophilic extracts deterred the sea star, the fish, as well as a common omnivorous amphipod (Koplovitz *et al.* 2009). The colonial ascidian *Aplidium falklandicum* is another previously investigated species reporting feeding deterrence in our experiments. Specimens from the Weddell Sea proved that the internal and external lipophilic fractions of this species strongly deterred *O. validus*, and that bioactive alkaloids, the meridianins A-G, also present in the congeneric ascidian *A. meridianum*, were responsible for this activity (Núñez-Pons *et al.* 2010). The also colonial ascidian *A. millari* was significantly rejected in our assays, along with *Pareugyrioides arnbackae*.

This last solitary lollipop-shaped ascidian, whose biology and ecology is poorly known, stored its defensive chemicals in its apical part, according to the ODT (Rhoades 1979).

In our study, echinoderms are the second group in number of species, being Holothuroidea the most represented clade. Holothurians, previously investigated in the shallow waters of McMurdo Sound (McClintock 1989), showed remarkable results within our survey. The species *Psolus charcoti* and *P. ephippifer* lacked chemical defenses against *O. validus.* This is supported by the fact that both species have a tough leathery skin, suggested as a physical protection against potential predation (Gutt 1991). On the other hand, the sediment feeder sea cucumber *Rhipidothuria racowitzai*, showed no feeding deterrence against the sea star in our tests, although having a vulnerable, gelatinous body wall. This species (formerly named *Achlyonice violaecuspidata*) is vagile and able to swim (Gutt 1991), a mechanism that may help to escape from sea bottom predators. *Taeniogytus contortus*, another holothurian that showed no feeding deterrence against *O. validus*, may as well avoid sea star predation thanks to living as epizoic, sheltered by dense colonies of bryozoans (Gutt 1991), similarly as what has also been observed for *P. charcoti* (Moyano & Wendt 1981). Of the 4 holothurians dissected into parts, *Ekmocucumis steineri* is the only one that showed feeding repellence in our tests. This suspension feeding organism commonly occurs on or between fan-shaped bryozoans with the posterior part of its body hidden in the sediment, extending the tentacles into the water for feeding (Gutt 1991). This strategy could explain why this holothurian concentrates chemical defenses in the tentacles, its most exposed and vulnerable tissues, again following the ODT (Rhoades 1979). In all the cases mentioned above, further studies focusing on the hydrophilic fractions should be conducted in order to confirm our hypothesis. As for the rest of echinoderms, the basal part of the sea star *Porania antarctica* and the arms of the ophiuroid *Ophionotus victoriae*, showed unpalatability for *O. validus*. These species were previously tested for deterrency in other experiments using an allopatric fish (McClintock 1989, McClintock & Vernon 1990). The deterrent activity we observed in the arms of *O. victoriae* is surprising since this common ophiuroid displays very rapid escape movements when disturbed (authors' pers. obs.). In this case, the deterrent activity observed could be related to other potential, faster predators such as fishes.

Molluscs, and particularly those from the group of the opisthobranchs, have been the focus of a large number of chemical ecology studies in other latitudes (Avila 1995). However, as reported for other groups, molluscs have received very little attention in Antarctic waters (see Avila *et al.* 2008). In our survey a prosobranch and 4 opisthobranchs were investigated (Figure 2; Annex 1). The two opisthobranch nudibranchs studied (*Tritonia challengeriana* and *Tritoniella belli*) did not show repellence activity against *O. validus*, although *T. belli* specimens from the McMurdo Sound area are chemically protected against different sympatric predators (McClintock *et al.* 1992, 1994c, Bryan *et al.* 1998). This protection was attributed to chymil alcohol, a compound probably sequestered from one of the nudibranch's primary preys, the soft coral *Clavularia frankliana* (McClintock 1994c). Instead, the cephalaspidean *Philine alata* showed repellent activity in our experiments. Studies on congeneric species from other geographic areas, concluded that some species afford protection against predation by burrowing into the sediment and by secretion of acid mucus (Thompson 1960). In our study we could only demonstrate a moderate repellence to the sea star

caused by the viscera, tested only at half the natural concentration. Unfortunately, no other anatomical parts could be assayed due to the lack of extract for this organism with a neutral pH when alive (unpublished results from the authors). The last opisthobranch displaying feeding deterrence activity in our tests was *Bathyberthella antarctica*. For this pleurobranchid both viscera and foot resulted unpalatable to *O. validus*, while the mantle (very exposed and prominent in this species and in the whole family) resulted palatable at the natural concentration as well as after testing twice the natural concentration. This fact, that appears to contradict the ODT (Rhoades 1979), could be explained because the mantle of *B. antarctica* produces an extremely acid secretion (pH=1; unpublished results from the authors). This secretion could provide protection against sea stars, as it has been already demonstrated experimentally. Actually, agar food pellets acidified with H_2SO_4 displayed significant deterrence to *O. validus* in the laboratory when reproducing the acidic tissues of some ascidians (McClintock *et al.* 2004, Koplovitz *et al.* 2009). Since the mantle of *Marseniopsis conica* was also acid when measured in alive animals (unpublished results from the authors), we postulate a similar defensive strategy for this prosobranch to avoid predation.

A total of 8 cnidarians were assayed here for the first time, and yielded the highest percentage (75%) of activity among the different phyla. All the octocoral species (Anthozoa) tested demonstrated feeding repellence to *O. validus*. These organisms, along with gorgonians, have no massive calcium carbonate skeleton and have been intensively investigated by natural products chemists in tropical latitudes (Paul 1992b, Paul & Puglisi 2004). In Antarctic waters, however, little investigation has been conducted for both soft corals and gorgonians. So far, only 3 common shallow-water soft corals from the McMurdo Sound area and one deep-water gorgonian from the eastern Weddell Sea have proved the existence of chemical defenses against *O. validus* (Slattery & McClintock 1995, Slattery *et al.* 1997, Iken & Baker 2003). Back to our study, it is noteworthy that 2 out of the 4 hydrozoans also showed deterrence to the asteroid.

Although bryozoans have been barely investigated for secondary metabolites either in Antarctic waters as well as in the rest of the planet (Sharp *et al.* 2007, Avila *et al.* 2008), in our survey, they constitute the second phylum displaying the highest relative activity. *Bostrychopora dentata* and *Isosecuriflustra tenuis*, have both weakly calcified forms, and *Alcyonidium flabelliforme* is characterized by a membranaceous body structure. All of them displayed significant repellency towards *O. validus*, thus giving support to the postulates of Winston and Berheimer (1986), who suggested that weakly calcified bryozoan species are likely to develop chemical defenses. However, the also weakly calcified *Austroflustra vulgaris* appeared not to be defended against the asteroid (although in this case we should also check hydrophilic fractions to confirm the lack of deterrents). Moreover, the calcified bryozoans *Cellaria diversa* and *Isoschizoporella secunda* were also repellent to the sea star.

Annelids are also a scarcely investigated group for chemical defense in Antarctica (Avila *et al.* 2008). When collected, the polychaete *Travisia* sp. gave off a strong smell, similar to that reported for its Atlanto-Mediterranean relative *Phylo foetida* (author's pers. obs.). The chemicals causing the smell could be behind the strong deterrence activity observed in our experiments. However, since the station where the polychaete was collected is deeper (Table 1) than the maximum bathymetric depth

reported for the sea star, these results should be carefully interpreted. On the other hand, the polynoid *Polyeunoa laevis*, commonly occurring in symbiotic association with different gorgonians from the genus *Thouarella* (Pettibone 1969), did not cause repellence in our assays. Specimens of this polychaete were collected in association with *Thouarella* (*Epithouarella*) *viridis* and *T.* (*E.*) *laxa*, octocorals that showed a strong feeding deterrence against *O. validus*. Thus, although both polychaete and corals tested in this study were collected in different sampling stations (Table 1), our results suggest a commensalistic relationship in which the polychaete may use the host as a shelter to avoid potential predation. In fact, in other stations sampled during the same cruise both species were collected often together, with the polychaete living in between the gorgonian branches (CA personal observations). Similar results, but involving an octocoral and its amphipod host, have recently been observed in the shallow-waters of the Japanese coast (Kumagai 2008).

Ecologically relevant assays using naturally co-occurring predators, greatly contribute to enhance our knowledge on chemical interactions. This ecological approach is particularly useful in the highly predictable Antarctic deep-water ecosystems, where community structure seems to be ruled by biological factors (Dayton *et al.* 1974, Arntz *et al.* 1994), and also because deep-sea organisms have greater probabilities to contain structurally unique metabolites (Skropeta 2008). Further studies in Antarctic and sub-Antarctic waters will be directed to prospecting in understudied ecosystems (*e.g.* deep water), and to identify and locate the natural products responsible for not only the anti-predatory activity, but also for other roles that secondary metabolites may play (Paul 1992a). All this, together with the increasing amount of autoecological and functional information of the species involved, will make possible to better understand the chemical processes affecting predator-prey interactions, and will allow to establish proper comparisons with similar interactions occurring in other depths and latitudes.

Annex 1. Data of the extract yields of the studied species, including the statistics obtained in repellency tests against the sea star *Odontaster validus* using lipophilic fractions. Statistics were calculated for each set of experiments respect to the simultaneous control, by using the Fisher's Exact test. WW: wet weight of the sample; DW: dry weight of the sample; EE: dry weight of the diethyl ether fraction; [N]: natural concentration of the ether fraction in the sample, calculated by dividing the EE by DW (%); [X2]: twice the natural concentration; [1/2]: half the natural concentration; API: apical part; BAS: basal part; EXT: external part; INT: internal part; MANT: mantle; TENT: tentacles; VISC: viscera; n.a.: not available; (w_5), (w_2) sampling stations (see Fig. 1) *: significantly different from the control; n.s.: not significant

Taxonomic group (phylum, class) and species name	Body part and [EE]	WW (g)	DW (g)	EE (mg)	[N] respect DW (%)	Shrimp eaten (out of 10)	Statistics
	CONTROL 1					8	
	CONTROL 2					6	
	CONTROL 3					10	
	CONTROL 4					6	
	CONTROL 5					8	
PORIFERA, Demospongiae							
Antho (*Acarnia*) *gaussiana*	[N]	16.6	2.4	179.8	7.46	5	n.s.
Cinachyra barbata	BAS-EXT [N]	484	127.1	180.9	0.14	7	n.s.
	BAS-INT [N]	603	123.4	392.9	0.32	6	n.s.
	API-EXT [N]	342	93	249.3	0.27	2	p=0.023*
	API-INT [N]	458	80.9	451.2	0.56	4	n.s.
Homaxinella balfourensis	BAS [N]	14.7	2.8	326.9	11.67	6	n.s.
	API [N]	32.1	4.7	362.7	7.78	4	n.s.
Iophon unicorne	[N]	9.8	0.5	14.8	2.77	3	n.s.
Isodictya erinacea	[N]	58	17.3	247.4	1.43	3	n.s.
Isodictya kerguelenensis	EXT [N]	110	29.8	151.9	0.51	4	n.s.
	INT [N]	48.7	15.3	269.3	1.76	4	n.s.
Isodictya setifera	[N]	61.8	18.8	190.7	1.01	1	p=0.005*
Isodictya toxophila	BAS [N]	61	12.3	83.5	0.68	0	p<0.001*
	API [N]	88	17.3	91.3	0.53	1	p=0.005*
Lissodendoryx (*Ectyodoryx*) *anacantha*	[N]	31.6	4.7	71.6	1.52	0	p<0.001*
Mycale (*Oxymycale*) *acerata*	[N]	149	26.3	63	0.24	6	n.s.
Phorbas glaberrimus	EXT [N]	94	23.2	167.5	0.72	7	n.s.
	INT [N]	89	19.5	207.8	1.06	6	n.s.
Pyloderma latrunculioides	EXT [N]	26.3	7.3	86.9	1.2	4	n.s.
	INT [N]	71.9	15.7	279	1.78	6	n.s.
Tedania oxeata	EXT [N]	1,234.2	125.7	466.8	0.37	2	p=0.023*
	INT [N]	358	34.3	280.7	0.82	8	n.s.
	INT [X2]	368	36.9	291.4	1.58	7	n.s.
Hexactinellida							
Rossella cf *vanhoeffeni*	[N]	112	19.8	395.5	2	5	p=0.033*
CNIDARIA, Anthozoa							
Alcyonium grandis	[N]	18.6	4.3	544.1	12.73	5	p=0.033*
Primnoisis antarctica (w_5)	[N]	66.9	39.1	380.4	0.98	7	n.s.
Primnoisis antarctica (w_2)	[N]	32.3	14	81.1	0.5	2	p=0.023*

Annex 1. (Continued)

Taxonomic group (phylum, class) and species name	Body part and [EE]	WW (g)	DW (g)	EE (mg)	[N] respect DW (%)	Shrimp eaten (out of 10)	Statistics
Thouarella (Epithouarella) laxa	[N]	54.2	17.2	492.6	2.87	1	p=0.005*
Thouarella (Epithouarella) viridis	[N]	108.7	6.4	196.6	3.12	2	p=0.023*
Hydrozoa							
Eudendrium sp.	[N]	63.9	13.1	237.8	1.83	1	p=0.005*
Staurotheca antarctica	[N]	28.4	5.1	201.8	3.96	4	n.s.
Symplectoscyphus glacialis	[N]	140.6	22.5	229.3	1.02	2	p=0.023*
Unidentified hydrocoral	[N]	246.3	216	16.6	0.01	4	n.s.
BRYOZOA, Gymnolaemata							
Alcyonidium flabelliforme	[N]	215.2	3.5	177.4	5.22	2	p<0.001*
Austroflustra vulgaris	[N]	165	18.3	674.7	3.68	8	n.s.
Bostrychopora dentata	[N]	24.2	9.7	73.8	0.76	0	p<0.001*
Cellaria diversa	[N]	221	51.6	285.8	0.55	4	p=0.011*
Cornucopina polymorpha	[N]	67.4	5.8	215.4	3.69	10	n.s.
Isoschizoporella secunda	[N]	19.2	7.6	57	0.75	1	p=0.005*
Isosecuriflustra tenuis	[N]	18.5	2.7	69.5	3.47	1	p=0.005*
MOLLUSCA, Gastropoda							
Marseniopsis conica	MANT [N]	194.7	2.4	40.6	1.73	3	n.s.
	VISC [N]	29.2	3.7	499.4	13.54	7	n.s.
	FOOT [N]	6.6	0.7	28.4	4.25	8	n.s.
Bathyberthella antarctica	MANT [N]	n.a.	6.3	281.3	4.56	9	n.s.
	MANT [X2]	n.a.	6.3	281.3	9.12	7	n.s.
	VISC [N]	n.a.	34.5	4,954.5	14.38	3	p=0.003*
	FOOT [N]	n.a.	4.3	69.6	0.73	0	p=0.011*
Philine alata	VISC [1/2]	1.2	0.1	9.7	3.82	1	p=0.05*
Tritonia challengeriana	MANT [N]	4.4	0.2	31.9	16.95	3	n.s.
	VISC [N]	2.4	0.3	21.8	6.82	4	n.s.
Tritoniella belli	VISC [N]	2.7	0.4	40.9	9.61	9	n.s.
	FOOT [1/2]	2.4	0.1	7.9	4.26	5	n.s.
CHORDATA, Ascidiacea							
Aplidium falklandicum	[N]	73.2	1.4	111.1	7.81	0	p<0.001*
Aplidium millari	EXT [N]	68.3	1.3	51.1	4.09	10	n.s.
	INT [N]	63.1	0.5	40.8	8.37	0	p<0.001*
Cnemidocarpa verrucosa	EXT [N]	43.6	7.5	106.8	1.43	6	n.s.
	INT [N]	99.1	6	436	7.44	6	n.s.
Molgula pedunculata	BAS [N]	76.3	11.1	10.2	0.09	4	n.s.
	EXT [N]	100.3	9.6	385.9	4.01	3	n.s.
	INT [N]	132.5	8.3	645.5	7.81	7	n.s.
Pareugyrioides arnbackae	BAS [N]	5.6	1.6	11.8	0.73	8	n.s.
	API [N]	14.7	1.1	99.8	8.74	4	p=0.011*
Synoicum adareanum (black & white morph)	[N]	14.6	1.7	35.5	2.11	0	p<0.001*
Synoicum adareanum (orange morph)	EXT[N]	820	49.1	1.002.2	2.04	3	n.s.
	INT [N]	522	6.6	48.4	0.73	0	p<0.001*

Annex 1. (Continued)

Taxonomic group (phylum, class) and species name	Body part and [EE]	WW (g)	DW (g)	EE (mg)	[N] respect DW (%)	Shrimp eaten (out of 10)	Statistics
ECHINODERMATA, Asteroidea							
Porania antarctica	BAS [N]	148.1	32.1	780.5	2.43	5	p=0.033*
	API [N]	58.5	11.4	379.1	3.31	4	n.s.
	INT [N]	207.7	9.7	1,370.3	14.07	8	n.s.
Ophiuroidea							
Ophionotus victoriae	ARMS [N]	299	83.6	152	0.18	1	p=0.005*
	BODY [N]	236	86.5	732.6	0.85	5	n.s.
Holothuroidea							
Ekmocucumis steineri	TENT [N]	86	3	170.2	5.62	1	p=0.005*
	EXT [N]	276.4	16.5	84.1	0.51	5	n.s.
	INT [N]	443	6.9	679.1	9.9	8	n.s.
Paradota weddellensis	[N]	13.6	1.5	117.9	7.82	1	p=0.005*
Peniagone cf *vignioni*	[N]	361.9	8.7	190.9	2.19	0	p<0.001*
Psolus charcoti	EXT [N]	44.5	10.7	669.1	6.27	7	n.s.
	INT [N]	62.9	3.1	153.5	4.94	6	n.s.
Psolus ephippifer	EXT [N]	87	21.5	1,196.7	5.75	10	n.s.
	INT [N]	250	9	422.5	5.12	10	n.s.
Rhipidothuria racowitzai	[N]	243.6	8.8	61.8	0.7	5	n.s.
Staurocucumis liouvillei	EXT [N]	76.6	9.5	1,596.5	16.84	5	n.s.
	INT [N]	462.3	13.6	1,599.1	11.77	8	n.s.
Taeniogytus contortus	[N]	8.1	0.3	30.6	9.18	5	n.s.
Crinoidea							
Encrinus cf *liliformis*	ARMS [N]	12.6	8.5	16.9	0.2	7	n.s.
	BODY [N]	11.2	3	122.5	4.16	5	n.s.
NEMERTEA, Anopla							
Parborlasia corrugatus	[N]	5.2	0.4	44.7	12.19	3	n.s.
ANNELIDA, Polychaeta							
Polyeunoa laevis	[N]	13	1.2	111.9	9.93	5	n.s.
Travisia sp.	[N]	0.8	0.1	3.1	6.2	1	p<0.001*
HEMICHORDATA, Pterobranchia							
Cephalodiscus sp.	BAS [N]	252	41.6	144.7	0.35	4	n.s.

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Chapter 3

Antitumoral activity in Antarctic and sub-Antarctic benthic organisms

Photo by Pharmamar S.A.U.

Chapter 3

Antitumoral activity in Antarctic and sub-Antarctic benthic organisms

Abstract. A prospecting search for antitumoural activity in polar benthic invertebrates was conducted on Antarctic and sub-Antarctic benthos in three different areas: Bouvet Island (sub-Antarctic), eastern Weddell Sea (Antarctica) and the South Shetland Islands (Antarctica). A total of 770 benthic invertebrate samples (corresponding to at least 290 different species) from 12 different phyla were assayed to establish their pharmacological potential against three human tumour cell lines (colorectal adenocarcinoma, lung carcinoma and breast adenocarcinoma). Bioassays resulted in 15 different species showing anticancer activity corresponding to five different phyla: Chordata (5), Porifera (4), Cnidaria (3), Echinodermata (2) and Annelida (1). This appears to be the largest pharmacological study ever carried out in Antarctica and it shows very promising antitumoural activities in the Antarctic and sub-Antarctic benthos.

Introduction

Modern marine pharmacology starts with the work by Bergmann & Feeney (1951) who studied the chemical activity of a Caribbean sponge and reported the first marine chemical compounds displaying antitumoural activity. This discovery shifted part of the attention from terrestrial organisms to marine organisms and expanded the research conducted in the marine environment to the pharmacological field. Since then, *ca*. 21,500 structurally diverse natural products with different activities have been discovered from marine natural sources (MarinLit database - http://www.chem.canterbury.ac.nz/marinlit/marinlit.shtml, accessed 2009), many of them providing the basis for the investigation of new compounds for human use.

During the past 15 years, despite the promising results in the search for new natural drugs, there has been a decrease in the investment of large companies in natural products research (Lam 2007). Against this trend in downgrading the effort invested in exploring nature, the percentage of new leads currently and over the last century with direct or indirect origins in naturally occurring compounds is still very high, always exceeding in importance the synthetically derived compounds (Paterson & Anderson 2005, Mayer & Gustafson 2006, Harvey 2007, Lam 2007, Newman & Cragg 2007). As an example, an investigation reviewing the new drugs from 1981 to 2006 stated that only 22.2% of the total number of anticancer drugs were synthetic (Newman & Cragg 2007). Interestingly, several of these future anticancer leads are originally from marine-derived compounds currently in clinical and preclinical trials (Simmons *et al.* 2005, Mayer & Gustafson 2006).

Marine environments are considered to be the largest potential sources of biodiversity on Earth. Experts estimate that biodiversity in certain marine ecosystems is higher than in tropical rain forests (Haefner 2003). This is probably due to the fact that seas cover about 70% of the Earth surface as well as that life had its origin in the primordial oceans. Furthermore, seas harbour a greater proportion of phyla –some of them exclusively marine– when compared with terrestrial habitats (Clarke & Johnston 2003). This appears to be strongly correlated with the possibility of finding new compounds since when searching across phyla, the probability of finding unique classes of compounds is higher than when sampling different species within one phylum (Devlin 1997, Munro *et al.* 1999).

Many marine organisms are sessile and have no physical mechanism of defence. This could have led them to develop strategies to chemically defend themselves from predators and/or competitors (Amsler *et al.* 2001, Simmons *et al.* 2005). Evidence for the connection between marine biodiversity and the field of marine natural products are well documented. In 2005, 812 new marine compounds were described, an increase of *ca.* 13% on the number of compounds reported the previous year. Interestingly, this increasing trend in the number of new marine chemical compounds has been steady since 1965 (Blunt *et al.* 2007).

Antarctica is amongst the regions that are likely to harbour many new and promising chemical products. Evidence for chemical defensive compounds exist in many Antarctic invertebrate phyla (Blunt *et al.* 1990, McClintock & Baker 1997, Lebar

et al. 2007, Avila *et al.* 2008). There are only a few examples in the Antarctic literature of interesting antitumoural/cytotoxic compounds in sponges (Perry *et al.* 1994, Trimurtulu *et al.* 1994, Fontana *et al.* 1999), cnidarians (Mellado *et al.* 2004, 2005), echinoderms (De Marino *et al.* 1998), bryozoans (Winston & Bernheimer 1986) and tunicates (Diyabalanage *et al.* 2006, Reyes *et al.* 2008). However, very few Antarctic specimens have been tested to date from the *ca.* 4000 currently described invertebrate species in the Southern Ocean (Clarke & Johnston 2003, Avila *et al.* 2008). Since it was recently predicted that there must be more than 17 000 macrozoobenthic species inhabiting the entire Antarctic Shelf in the Southern Ocean (Gutt *et al.* 2004), it is reasonable to assume that high percentages of chemical activity may exist in these waters.

We collected and analysed 770 benthic animals (corresponding to at least 290 different species) from 12 different phyla in order to investigate the antitumoural potential of the invertebrates inhabiting the Southern Ocean and adjacent waters,. In this study we present the results of an extensive antitumoural pharmacological screening performed with marine invertebrates from the eastern Weddell Sea, the South Shetland Islands (Antarctica) and the Bouvet Island (sub-Antarctic) areas. The aim of this work is to highlight the antitumoural possibilities that these geographic areas can provide, considering macrozoobenthic organisms from a wide bathymetric range.

Material and Methods

Study area and field sampling

Invertebrate benthic marine samples were collected on two different Antarctic cruises: ANTXXI/2 (November 2003–January 2004) and ECOQUIM-2 (January 2006). ANTXXI/2 expedition surveyed mostly the eastern Weddell Sea area (Antarctic) but also the vicinity of Bouvet Island (sub-Antarctic waters). Sampling was performed on board the RV *Polarstern,* from the Alfred Wegener Institute for Polar and Marine Research (Bremenhaven, Germany), using seven different sampling devices: Agassiz trawl, bongo net, bottom trawl, epibenthic sledge, giant box corer, plankton multinet and Rauschert dredge. A total of 55 stations were sampled ranging from 0–1,866m depth (see Arntz & Brey 2005 for details). Sorting of the samples was carried out on deck, and invertebrates from different phyla were selected based on the availability of the specimens, the required biomass for the pharmacological tests, and the *in situ* observations of feasible characters related to the presence of chemical natural products (*i.e.* absence of physical defences, particular colour and/or smell, absence of epibionts). Each sample corresponded to one invertebrate species and every specimen to be chemically analysed was immediately frozen to -20ºC. Some individuals from each of the corresponding samples were fixed for later taxonomic identification in the laboratory by specialists on each of the different phyla. In addition, images of live animals were taken when possible for the same purpose.

The ECOQUIM-2 cruise was carried out around Deception Island, Livingston Island and their vicinities (South Shetland Islands) on board the Spanish RV *BIO-Hespérides.* Two different sampling devices (Agassiz trawl and rocky dredge) were used to obtain the samples at depths from 25–215 m. Dredging range in all stations was not higher than a few metres except for a station where it started at 65 m and finished at 215 m depth. Sorting was performed as described above. Also in this case, specimens to be chemically analysed were frozen at -20ºC and the procedure for the later identification of animals with the fixed material was the same as described before.

In vitro tests

All frozen samples from invertebrates collected from both expeditions were analysed by the biopharmaceutical company PharmaMar SA to search for antitumoural activity. Two grammes of frozen samples were extracted in distilled water using an ultraturrax homogenizer. The aqueous extract was decanted and stored at -30ºC. The remaining solid pellet was dried using a speed-vac centrifuge and extracted in 1:1 dichloromethane/methanol. The organic extract was also decanted and stored at -30ºC. To analyse the putative pharmacological potential of the extracts, equal ‘‘weight/volume’’ amount of each tissue homogenate was assayed *in vitro,* using three different final concentrations (50, 15 and 5 mg ml^{-1}), against the following human tumour cell lines: HT-29 (ATCC HTB-38) colorectal adenocarcinoma; A-549 (ATCC CCL 185) lung carcinoma; and MDA-MB 231 (ATCC HTB-26) breast adenocarcinoma. Briefly, cells were seeded in 96-well microtitre plates and allowed to stand for 24 h in a

drug-free medium before treatment with vehicle alone or test extracts for 72 h period. For viability quantification, a colorimetric assay (sulphurhodamine B, SRB) was used. Cells were washed twice with PBS, fixed for 15 min in 1% glutaraldehyde solution, rinsed twice in PBS, and stained in 0.4% SRB solution for 30 min at room temperature. Cells were then rinsed several times with 1% acetic acid solution and air-dried. SRB was then extracted in 10 mM trizma base solution and the absorbance measured at 490 nm. The cytostatic or cytotoxic effect of the compounds was estimated applying the algorithm developed by the American National Cancer Institute (NCI). Being Tz the number of control cells at time zero, C the number of cells in control wells at 72 h, and T the number of cells in the test wells at 72 h then: if Tz<T<C (no effect or growth inhibition), cell survival is 100x([T-Tz]/[C-Tz]); if T<Tz (net cell killing), cell survival is 100x([T-Tz]/Tz). Three dose response parameters were calculated for each experimental agent: (i) GI50, or compound concentration that produces 50% inhibition on cell growth compared to control cells; (ii) TGI, or compound concentration that produces total growth inhibition as compared to control cells; and (iii) LC50, or compound concentration that produces 50% net cell killing. GI50 is used as reference value. Results represented the mean of at least three independent experiments.

Results

A total of 770 samples (corresponding to at least 290 different species) were collected, 658 from the ANTXXI/2 expedition and 112 from the ECOQUIM-2 cruise. To date, the number of species identified is 260 for the ANTXXI/2 expedition and 61 for the ECOQUIM-2 cruise. A taxonomic list of these species and the number of samples for any given species is reported in Table 1. Samples consisted of benthic invertebrates belonging to 12 different phyla: Porifera, Cnidaria, Nemertina, Priapulida, Mollusca, Annelida, Arthropoda, Bryozoa, Brachiopoda, Echinodermata, Hemichordata and Chordata. Results from the *in vitro* tests carried out against the three different human tumour cell lines indicated that 19 samples (corresponding to 15 different species) presented relevant antitumoural activity (Tables 2–3). This represents the 2.5% of the total number of tested samples, and 5.2% when considering the number of assayed species (290) versus the number of active species (15). In every active sample detected in the study, the three tumour cell lines tested presented a similar behaviour, in the sense that a similar effect for every tumour cell line was detected, except for the tunicate *Aplidium cyaneum.* In this specific case, the antitumoural effects of the tested fractions were mild for A-549 lung carcinoma and strong for the other two tumour cell lines (HT-29 colorectal adenocarcinoma and MDA-MB 231 breast adenocarcinoma). For the remaining cases, there was no significant difference among the results in the different tumour cell lines assays for every analysed sample (Table 2). Antitumour activity was detected in both the aqueous and organic extracts in some of the cases (five out of the 15 species showed activity in both fractions) indicating a distribution of the active metabolites between both extracts, probably due to medium polarity compounds being responsible for the bioactivity. In the rest of the cases, the bioactivity was found only in one of the fractions, most probably indicating that the antitumour properties are due to the presence of very polar compounds (activity found only in aqueous extracts) or non-polar compounds (activity found in organic extracts) (Table 2).

Samples with antitumoural activity belonged to only five phyla: Porifera, Cnidaria, Annelida, Echinodermata and Chordata. Considering just the number of species, Chordata is the group with the higher relative percentage of activity (13.2%), followed by Annelida with more than 9% activity. The last three phyla, in decreasing order of antitumoural activity, are Cnidaria, Porifera and Echinodermata with 7.1%, 5.3% and 4.7% activity, respectively (Figure 1). A comparison of the relative number of active versus inactive species is shown for each phyla possessing antitumoural activity in Figure 2. In the analysis of activity by phyla, Chordata (with five species) contains the largest number of active species, representing more than 33% of the total activity observed in the whole screening. Porifera reaches more than 25% of the activity observed with four active species, while Cnidaria and Echinodermata are the following groups in order of importance, with three and two active species, respectively. Finally, just one Annelid species was found to show antitumoural activity (Figure 3; Table 3).

Bouvet Island (sub-Antarctica)

The four sampling stations studied from the Bouvet Island area yielded 28 different species (32 samples when considering the replicates). Specimens analysed were from seven different phyla (Porifera, Nemertina, Mollusca, Annelida, Bryozoa, Echinodermata and Chordata) with the Echinodermata the most represented phylum in our survey, with 10 species. The rest of phyla presented five or less species each (Table 3). Antitumoural activity was observed in two species: one holothurian (*Psolus paradubiosus)* and one sponge (*Latrunculia brevis).* Both samples were collected using Agassiz trawl at depths of 553 and 259 m, respectively (Figure 4; Table 4). About 50% of the samples analysed in this area were collected at *ca.* 260 m depth. The rest of the samples were collected at three different depths, with the highest percentage of samples concentrated at depths around 375 m and 550 m (Figure 5).

Eastern Weddell Sea (Antarctica)

The eastern Weddell Sea was the largest area sampled, as well as being the most surveyed region. A total of 232 different species (626 samples when considering the replicates) were collected from 51 different sampling stations. Specimens from ten phyla were tested (Porifera, Cnidaria, Nemertina, Mollusca, Annelida, Bryozoa, Brachiopoda, Echinodermata, Hemichordata, and Chordata). From these, Porifera (4 active species), Cnidaria (3), Chordata (2), Echinodermata (1) and Polychaeta (1) presented antitumoural activity (Table 3). Although the bathymetry of stations ranged from 0 to more than 1,800 m, most of the active samples were collected from depths *ca.* 300 m. Only in one deeper station, more than 900 m deep, the cnidarian *Fannyella mawsoni* presented antitumoral activity (Figure 4; Table 4). Most samples in this area (>80%) were collected at depths ranging between 200–400 m (Figure 5).

South Shetland Islands (Antarctica)

Sampling in the South Shetland Islands yielded 61 different species (112 samples when considering the replicates) belonging to 11 phyla (Porifera, Cnidaria, Nemertina, Priapulida, Mollusca, Annelida, Arthropoda, Bryozoa, Brachiopoda, Echinodermata and Chordata). A total of 13 sampling stations, ranging from a few metres to more than 200 m depth were surveyed. Only two stations –both in the vicinity of Livingston Island– presented organisms with antitumoural activity; in particular three different tunicate species: *Polysyncraton trivolutum, Tylobranchion speciosum* and *Aplidium falklandicum.* These sampling stations were at relatively shallow depths, in the very first 100m depth (Figure 4; Table 4). Most of the samples from the South Shetland Islands area were obtained from the first 150m depth. Only 13 samples were collected from a deeper station that ranged from 69–215 m deep (Figure 5).

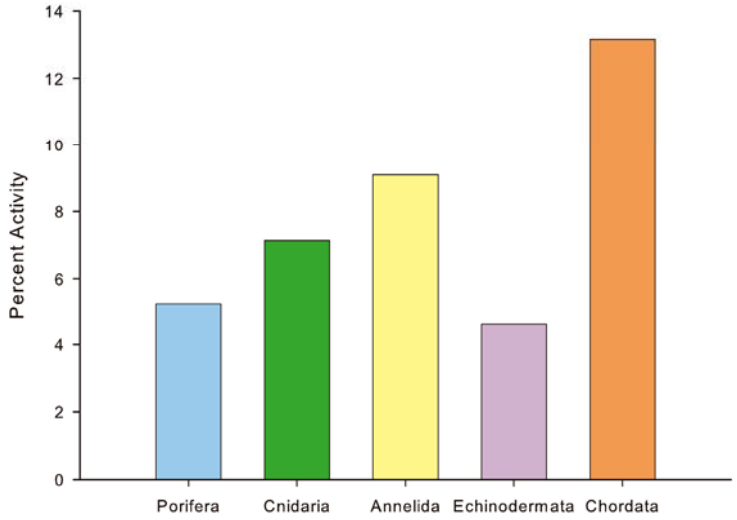

Figure 1. Percentages of antitumoural activity (number of species with antitumoural activity respect to the total of species tested) within each active phyla

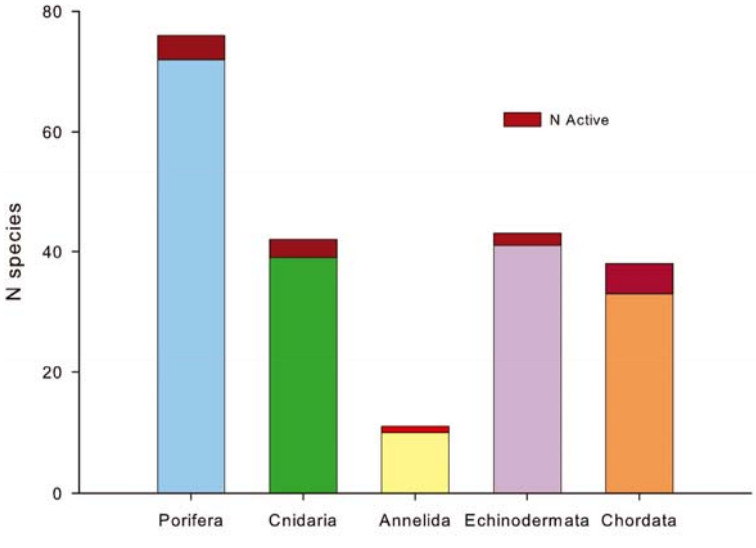

Figure 2. Number of active versus inactive species in phyla presenting activity (N = number of species

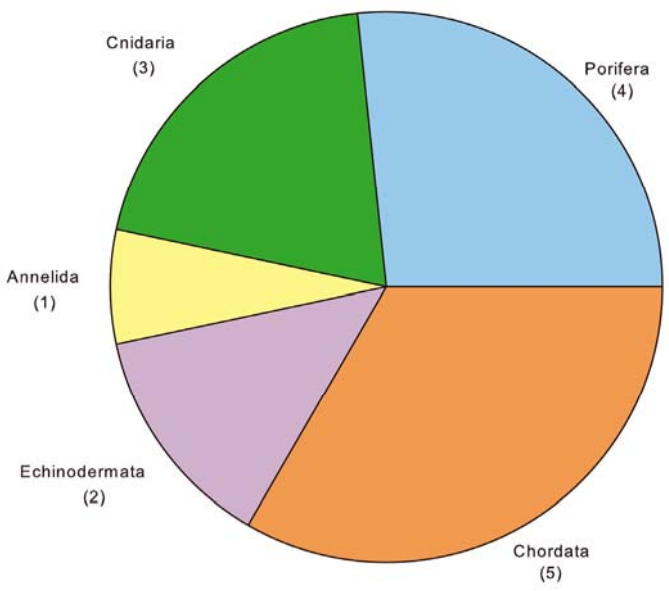

Figure 3. Relative proportions of antitumoural activity for each active phylum considering species number

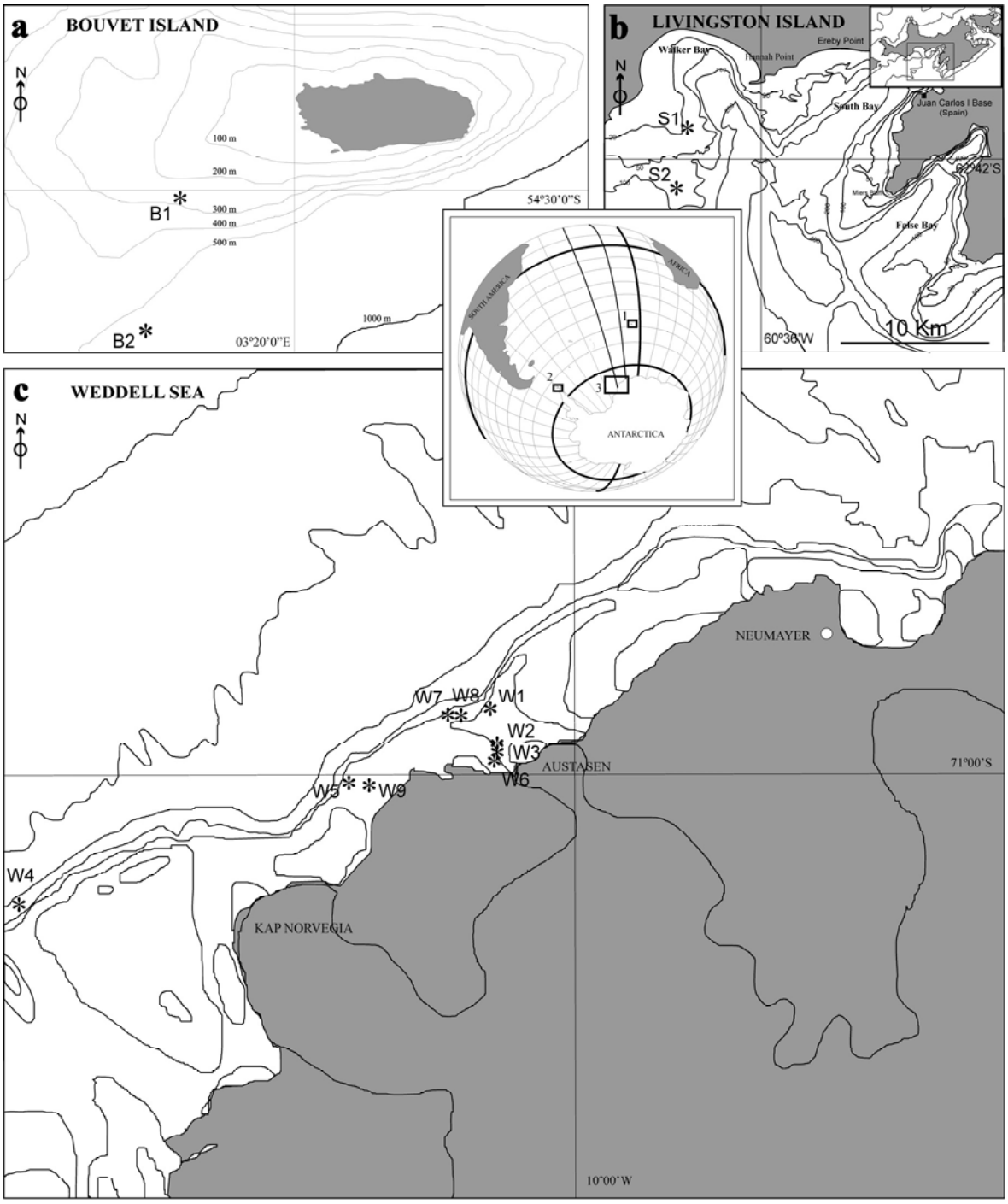

Figure 4. Map representing the stations that presented active samples at the three different surveyed areas: **a.** Bouvet Island (B1–2); **b.** South Shetland Islands-Livingston Island (S1–2); and **c.** eastern Weddell Sea (W1–9)

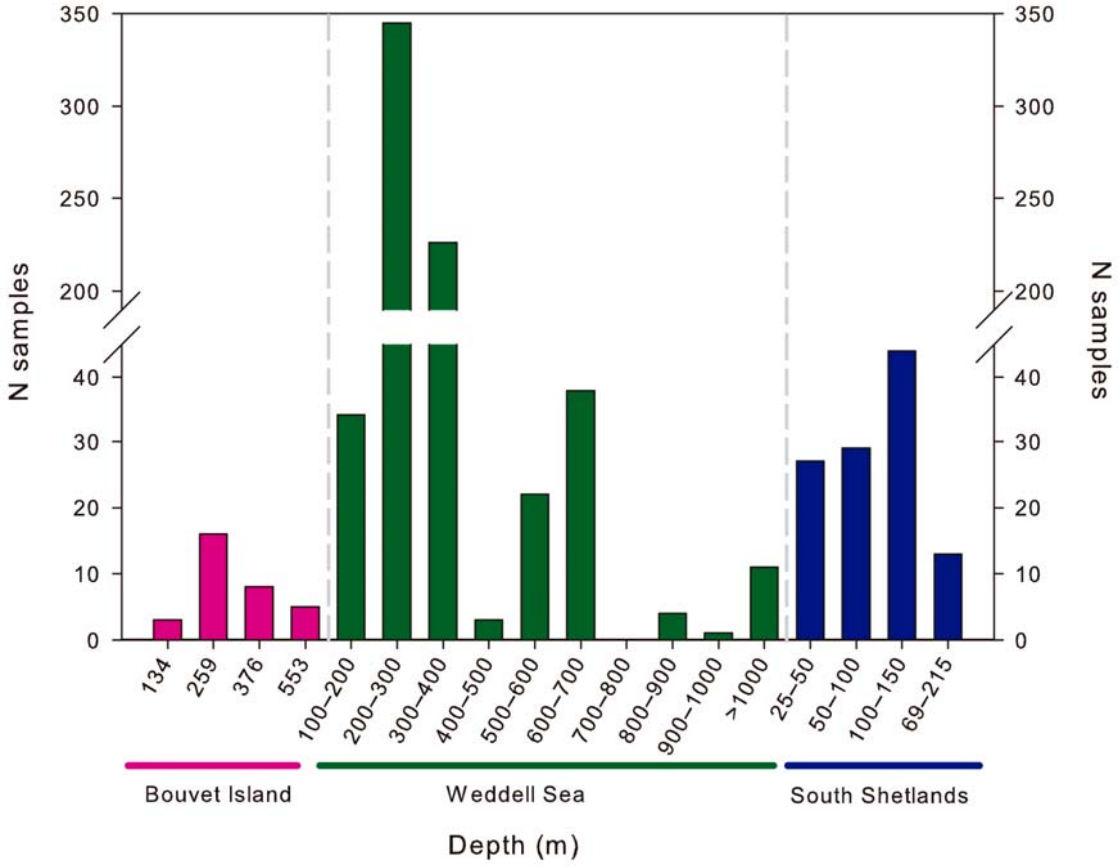

Figure 5. Number of samples analyzed in the stations from the Bouvet Island, the Weddell Sea and the South Shetland Islands areas at different depths

Table 1. Taxonomic list of the species of this survey grouped by phylum. Number of samples used and geographic area in brackets: (B), Bouvet Island; (S), South Shetland Islands; (W), Weddell Sea. +: two species tested together. * antitumoral activity detected

PHYLUM PORIFERA	
Anoxycalyx ijimai	1(W)
Antho (*Acarnia*) *gaussiana*	1(W)
Astrophorida sp.	8 (W)
Axinellidae sp.	1(S)
Bubaris sp.	1(B)
Cinachyra barbata	2(W), 1(S)
Cinachyra vertex	7(W), 1(S)
Cinachyra sp.	4(W)
Clathria (*Axosuberites*) *nidificata*	2(W)
Clathriidae sp.	1(W)
Dendrilla antarctica	1(S)
Hadromerida sp.	7(W)
Haplosclerida sp.	8(W)
Gellius sp.	1(W)
? *Gellius* sp.	1(W)
Homaxinella balfourensis	1(S)
Homaxinella cf *balfourensis*	1(W)
Iophon unicorne	2(W)
Iophon cf *unicorne*	4(W)
Iophon cf *unicorne* or *Isodictya* sp.	1(W)
Iophon sp. 1	2(W), 3(S)
Iophon sp. 2	5(W)
Iophon sp. 3	1(W)
Isodictya bentarti	4(S)
Isodictya erinacea	5(W)
Isodictya kerguelenensis	4(W)
Isodictya lankesteri	1(W), 1(S)
Isodictya setifera	3(W)
Isodictya toxophila	4(W), 1(S)
Isodictya cf *verrucosa*	1(W)
Isodictya sp. 1–2	1(W) of each
*Latrunculia biformis**	2(W)
*Latrunculia brevis**	2(W), 1(B)
Lissodendoryx (*Ectyodoryx*) *anacantha*	1(W)
Lissodendoryx (*E.*) cf *ramilobosa*	1(W)
Mycale (*Mycale*) sp.	2(W)
Mycale (*Oxymycale*) *acerata*	5(W), 2(S)
Mycale (*Oxymycale*) cf *acerata*	6(W)
Mycale sp.	2(W)
Myxilla (*Burtonanchora*) *asigmata*	1(W)
Myxilla (*Burtonanchora*) *lissostyla*	1(W), 2(S)
Myxilla (*Burtonanchora*) sp.	1(W)
Myxilla sp.	5(W)
Myxillidae sp.	8(W)
Phorbas glaberrima	1(W)
Poecilosclerida sp.	5(W)
Polymastia sp.	2(W)
Pyloderma latrunculioides	2(W)
Rossella cf *antarctica*	3(W)
Rossella fibulata	3(W)
Rossella cf *fibulata*	1(W)
Rossella nuda	1(W)
Rossella cf *nuda*	2(W)
Rossella cf *vanhoffeni*	4(W)
Rossella sp. 1*	1(W)
Rossella sp. 2*	1(W)
Rossella sp.	10(W), 2(B)
Scolymastra cf *joubini*	6(W)
Sphaerotylus antarcticus	1(S)
Stylocordyla sp.	4(W), 2(S)
Tedania (*Tedaniopsis*) *charcoti*	1(W)
Tedania (*Tedaniopsis*) *oxeata*	3(W)
Tedania (*Tedaniopsis*) *tantula*	4(W), 2(B)
Tedania sp.	1(W), 1(B), 2(S)
Tetilla leptoderma	1(W)
Calcarea sp.	3(W)
Demospongiae sp.	2(W)
Hexactinellida sp.	18(W)
Porifera sp. 1–7	1(W) of each
PHYLUM CNIDARIA	
Ainigmaptilon cf *antarcticum*	1(W)
Alcyonium grandis	2(W)
Alcyonium cf *roseum*	1(W)
Antarctoscyphus elongatus	2(W)
Antarctoscyphus sp.	1(W)
Echinisis spicata	3(W)
Eudendrium sp.	1(W)
Fannyella aurora	5(W)
Fannyella mawsoni *	1(W)
Fannyella rossii	2(W)
Hormathia sp.	2(S)
Isididae sp.	6(W)
Oswaldella billardi	3(W)
Primnoisis ambigua	1(W)
Primnoisis antarctica	9(W)
Staurotheca antarctica	1(W)
Staurotheca dichotoma	1(W)
Staurotheca glomulosa	1(W)
Staurotheca sp.	1(S)
Symplectoscyphus cf *glacialis*	1(W)
Symplectoscyphus sp.	1(S)
Thauroprimnoa cf *austasensis*	1(W)
Thouarella cf *laxa*	2(W)
Thouarella cf *minuta*	1(W)
Thouarella sp. 1	3(W)
Thouarella sp.2	17(W)
Thouarella sp. 2 + *Primnoisis antarctica*	1(W)
Thouarella sp. 2 + *Thouarella* sp. 5	1(W)
Thouarella sp. 3	1(W)
Thouarella sp. 4	4(W)
Thouarella sp. 5	12(W)
Thouarella sp. 6	5(W)
Thouarella sp. 7	2(W)
Thouarella sp. 8	1(W)
?*Thouarella* sp.	8(W)
Cnidarian sp. 1–2	1(W) of each
Cnidarian sp.	5(W)
Gorgonacea sp. 1–2*	1(W) of each
Hydrozoa sp.	4(W)
Unidentified cnidarians	14(W)
PHYLUM NEMERTEA	
Parborlasia corrugatus	5(S)
Nemertean sp. 1–2	1(B) of each
Nemertean sp. 3–5	1(W) of each
Unidentified nemerteans	1(W)
PHYLUM PRIAPULIDA	
Priapulus cf *tuberculatospinosus*	4(S)
PHYLUM MOLLUSCA	
Austrodoris kerguelenensis	2(W), 1(S)
A. kerguelenensis (eggs)	1(W)
Lamellaria sp.	2(S)

Table 1. (Continued)

Nacella concinna	2(S)
Philine sp.	3(S)
Thracia meridionalis	1(S)
Tritonia challengeriana	1(B)
Yoldia eightsi	2(S)
Solenogastres sp.	2(S)
PHYLUM ANNELIDA	
Aglaophamus trissophyllus	1(S)
Aglaophamus cf *trissophyllus*	1(W)
Amphitrite sp.	1(S)
Antarctinoe spicoides	1(B)
Flabelligera mundata	1(B), 1(S)
Laetmonice sp.	1(B)
Pista sp.	1(S)
Polyeunoa cf *laevis*	13(W)
Polynoidae sp. 1–2	1(B) of each
Terebellidae sp. 1*	1(W)
PHYLUM CRUSTACEA	
Glyptonotus cf *antarcticus*	1(S)
PHYLUM BRYOZOA	
Alcyonidium flabelliforme	1(W)
Alcyonidium cf *flabelliforme*	1(W)
Alcyonidium sp.	4(W), 1(S)
Austroflustra vulgaris	1(W), 1(B)
Bostrychopora dentata	13(W)
Camptoplites angustus	3(W)
Camptoplites bicornis	3(W)
Camptoplites tricornis	2(W), 1(S)
Carbasea curva	2(W)
Carbasea ovoidea	3(S)
Cellaria diversa	2(W), 2(S)
Cellaria incula	1(W)
Cellaria sp. 1–2	1(S) of each
Cellarinella nutti	8(W)
Cellarinella sp.	1(W)
Cornucopina polimorpha	1(B)
Dakariella dabrowni	4(W)
Himantozoum antarcticum	1(W), 2(S)
Hornera sp.	1(W)
Isoschizoporella secunda	2(W)
Isoschizoporella tricuspis	2(W)
Isoschizoporella sp.	1(W)
Isosecuriflustra tenuis	2(W)
Isosecuriflustra sp.	1(W)
Klugella echinata	2(W)
Melicerita obliqua	2(W)
Nematoflustra flagellata	5(W), 1(S)
Notoplites drygalskii	5(W)
Osthimosia curtioscula	5(W), 1(B)
Paracellaria wandeli	1(W)
Pemmatoporella marginata	1(W)
Reteporella antarctica	1(W)
Reteporella frigida	4(W)
Reteporella hippocrepis	1(W), 1(B)
Reteporella lepralioides	1(W)
Reteporella sp.	2(W)
Smittina antarctica	1(W)
Smittoidea albula	1(W)
Smittoidea sp.	1(W)
Staurotheca sp.	1(W)
Stystenopora contracta	2(W)
Bryozoa sp. 1	2(W)
Bryozoa sp. 2–10	1(W) of each
Unidentified bryozoans	13(W)
PHYLUM BRACHIOPODA	
Brachiopoda sp.	1(W)
Liothyrella uva	1(S)
PHYLUM ECHINODERMATA	
Abatus sp.	1(S)
Abyssocucumis liouvillei	1(B)
Achlyonice violaecuspidata	2(W)
Cidaridae sp.	1(W)
Chiridota weddellensis	1(W)
Diplasterias cf *brucei*	1(S)
Diplopteraster sp.	1(W)
Echinopsolus acanthocola	1(W)
Ekmocucumis steineri	3(W)
Ekmocucumis cf *steineri*	1(W), 1(S)
Ekmocucumis sp. 1	2(W)
Ekmocucumis sp. 2	1(W)
Ekmocucumis sp. 3	2(W)
Encrinus liliformis	1(W)
Labidiaster annulatus	3(S)
Lysasterias hemiora	2(W)
Lysasterias sp.	1(S)
Macroptychaster sp.	1(W)
Odontaster validus	2(S)
Ophionotus victoriae	3(S)
Ophiurolepis sp. + *Iophon* cf *unicorne*	1(W)
Ophiurolepis sp.	1(W)
Ophionotus victoriae	1(B)
Peniagone vignioini	1(W)
Porania antarctica	1(B)
Porania antarctica glabra	1(B)
Pseudostichopus villosus	1(W)
Psolus charcoti	7(W)
Psolus ephipiffer	1(W)
*Psolus paradubiosus**	1(B)
Psolus sp.	1(W)
Sterechinus neumayeri	3(S)
*Taeniogytus contortus**	4(W)
Crinoidea sp.	1(W)
Holothuroidea sp. 1	1(W)
Holothuroidea sp. 2	1(W), 1(B)
Holothuroidea sp. 3–4	1(B) of each
Holothuroidea sp. 5–7	1(W) of each
Ophiuroidea sp. 1	2(B)
Ophiuroidea sp. 2	1(B)
PHYLUM HEMICHORDATA	
Cephalodiscus cf *nigrescens*	9(W)
Cephalodiscus sp. 1	9(W)
Cephalodiscus sp. 2	4(W)
Cephalodiscus sp. 3	3(W)
Cephalodiscus sp. 4	6(W)
Cephalodiscus sp. 5	7(W)
Cephalodiscus sp. 6	1(W)
PHYLUM CHORDATA	
Agnezia biscoei	1(S)
*Aplidium cyaneum**	2(W)
*Aplidium falklandicum**	2(W), 2(B), 1(S)
Aplidium millari	1(W), 1(S)
Ascidia challengeri	4(S)

Table 1. (Continued)

Caenagnesia schmitti	1(S)	*Pyura obesa*	2(S)	Ascidiacea sp. 6	3(W)
Cnemidiocarpa verrucosa	10(W), 4(S)	*Styela wandeli*	1(S)	Ascidiacea sp. 7	1(W)
Corella eumyota	3(S)	*Synoicum adareanum*	9(W), 3(S)	Ascidiacea sp. 8	3(W)
Distaplia cylindrica	1(W)	*Synoicum* cf *adareanum*	1(W)	Ascidiacea sp.9	6(W)
Distaplia cf *cylindrica*	1(W)	*Tylobranchion speciosum**	2(S)	Ascidiacea sp. 10	2(W)
Molgula pedunculata	1(W), 4(S)	Ascidiacea sp. 1*	1(W)	Ascidiacea sp. 11	4(W)
Molgula cf *pedunculata*	1(W)	Ascidiacea sp. 2	2(W)	Ascidiacea sp. 12	1(W)
Paraeugyrioides arnbackae	1(W)	Ascidiacea sp. 3	3(W)	Ascidiacea sp. 13	12(W)
*Polysyncraton trivolutum**	3(S)	Ascidiacea sp. 4–5	1(W) of each	Ascidiacea sp. 14–19	1(W) of each

Table 2. Percentage of cell growth for the active samples against three human tumor cell lines (HT-29, A-549 and MDA-MB 231) at three concentrations (50, 15 and 5 μg/ml)

(Phylum[a]) Active species name	Station code[b]	Fraction[c]	Tumor cell lines		
			HT-29*	A-549*	MDA-MB 231*
			50/15/5	50/15/5	50/15/5
(POR) *Latrunculia biformis*	PS65/259-1	A	-86/-80/-16	-74/-83/71	-88/-48/-18
		DM	-90/-45/24	-90/-34/89	-88/-53/67
(POR) *Latrunculia biformis*	PS65/274-1	A	-78/3/99	-84/80/100	-91/-35/78
		DM	-86/-61/-35	-81/-87/-42	-86/-71/-56
(POR) *Latrunculia brevis*	PS65/019-1	A	-83/-29/13	-87/-65/107	-87/-37/35
		DM	-81/-79/-43	-85/-85/-36	-83/-76/-59
(POR) *Latrunculia brevis*	PS65/253-1	A	-89/-66/58	-90/-66/29	-87/-76/47
		DM	-84/-74/-41	-79/-86/44	-87/-68/-61
(POR) *Latrunculia brevis*	PS65/265-1	A	-88/-82/-43	-66/-83/-82	-92/-90/-77
		DM	-84/-73/-30	-76/-85/80	-75/-81/-21
(POR) *Rossella* sp. 1	PS65/253-1	DM	-76/-81/-73	-12/-1/3	-14/-30/-30
(POR) *Rossella* sp. 2	PS65/253-1	DM	-69/-75/-68	-4/-1/1	-15/-21/-21
(CNI) *Fannyella mawsoni*	PS65/232-1	DM	-88/-49/65	-83/-60/89	-97/-75/93
(CNI) Gorgonacea sp. 1	PS65/121-1	A	-96/-26/-8	-96/-14/23	-91/-72/-69
		DM	-92/-11/42	-90/21/75	-91/2/66
(CNI) Gorgonacea sp. 2	PS65/166-1	A	-94/2/29	-89/33/64	-93/18/57
(ANN) Terebellidae sp. 1	PS65/166-1	DM	-58/3/134	-72/71/115	-75/-18/123
(ECH) *Psolus paradubiosus*	PS65/020-1	A	-90/-66/58	-90/-66/29	-87/-76/47
		DM	-83/49/89	-85/11/97	-83/-5/113
(ECH) *Taenyogytus contortus*	PS65/265-1	A	-90/-51/28	-87/18/4	-90/11/57
(CHO) *Aplidium cyaneum*	PS65/148-1	A	-58/-48/42	8/12/65	-62/-1/11
		DM	-45/-39/-19	-4/19/22	-70/-57/-5
(CHO) *Aplidium cyaneum*	PS65/280-1	A	-68/-55/50	1/5/64	-30/-10/21
		DM	-59/-27/3	6/15/78	-65/-25/4
(CHO) *Aplidium falklandicum*	AGT-6	DM	-29/2/37	-80/-60/21	-64/-71/11
(CHO) *Polysyncraton trivolutum*	AGT-5	A	-54/-32/25	-47/-34/11	-89/-44/18
(CHO) *Tylobranchion speciosum*	AGT-5	A	-45/-30/-3	-59/-36/-15	-83/-19/2
(CHO) Ascidiacea sp. 1	PS65/166-1	DM	-80/18/121	-88/85/88	-90/-3/113

[a]ANN, Annelida; CHO, Chordata; CNI, Cnidaria; ECH, Echinodermata; POR, Porifera; [b]See Figure 4 for details; [c]A, aqueous extract; DM, dichloromethane/methanol extract; *active extracts when percentage of cell growth <50% at least at two concentrations in one of the cell lines. Positive values (+100 to 0), represent samples with no activity or some degree of cytostatic activity. Negative values (0 to -100), represent samples with cytotoxic activity (net cell death)

Table 3. Total number of samples (N spls.) and species (N sps.) analyzed by phylum in each surveyed area with the number of active species in brackets

Geographic area		Phylum[a]										
		POR	CNI	BRY	CHO	ECH	HEM	ANN	MOL	NEM	OTH*	Total
Bouvet Island	N spls.	7	-	4	2	11	-	5	1	2	-	32
	N sps.	5(1)	-	4	1	10(1)	-	5	1	2	-	28(2)
Weddell Sea	N spls.	202	128	116	76	42	39	15	3	4	1	626
	N sps.	70(4)	39(3)	49	30(2)	27(1)	7	3(1)	2	4	1	232(11)
South Shetlands	N spls.	23	4	12	30	15	-	4	13	5	6	112
	N sps.	14	3	8	13(3)	8	-	4	7	1	3	61(3)
Total	N spls.	232	132	132	108	68	39	24	17	11	7	770
	N sps.[b]	76(4)	42(3)	53	38(5)	43(2)	7	11(1)	9	7	4	290(15)

[a]ANN, Annelida; BRY, Bryozoa; CHO, Chordata; CNI, Cnidaria; ECH, Echinodermata; HEM, Hemichordata; MOL, Mollusca; NEM, Nemertina; OTH, Others; POR, Porifera; *This category includes the following phyla: Priapulida, Brachiopoda and Arthropoda; [b]The total number of species for every phylum does not correspond to the sum of species for the three geographic areas since some species are shared in the different area

Table 4. Data from the stations where active samples were collected

Geographic area	Station code	Coordinates	Gear[a]	Depth (m)	(Phylum[b]) Active species
Bouvet Island	PS65/019-1	54° 30.01' S / 003° 13.97' E	AT	259	(POR) *Latrunculia brevis*
Bouvet Island	PS65/020-1	54° 36.95' S / 003° 12.42' E	AT	553	(ECH) *Psolus paradubiosus*
Weddell Sea	PS65/121-1	70° 50.08' S / 010° 34.76' W	AT	274	(CNI) Gorgonacea sp. 1
Weddell Sea	PS65/148-1	70° 56.67' S / 010° 32.05' W	BT	302	(CHO) *Aplidium cyaneum*
Weddell Sea	PS65/166-1	70° 56.83' S / 010° 32.61' W	BT	338	(CNI) Gorgonacea sp. 2; (ANN) Terebellidae sp. 1; (CHO) Ascidiacea sp. 1
Weddell Sea	PS65/232-1	71° 18.61' S / 013° 56.12' W	ES	910	(CNI) *Fannyella mawsoni*
Weddell Sea	PS65/253-1	71° 04.30' S / 011° 33.92' W	BT	308	(POR) *Latrunculia brevis*; *Rossella* sp. 1 and sp. 2
Weddell Sea	PS65/259-1	70° 57.00' S / 010° 33.02' W	BT	332	(POR) *Latrunculia biformis*
Weddell Sea	PS65/265-1	70° 52.75' S / 010° 51.24' W	BT	294	(POR) *Latrunculia brevis;* (ECH) *Taenyogytus contortus*
Weddell Sea	PS65/274-1	70° 52.16' S / 010° 43.69' W	BT	290	(POR) *Latrunculia biformis*
Weddell Sea	PS65/280-1	71° 07.15' S / 011° 26.23' W	AT	228	(CHO) *Aplidium cyaneum*
South Shetlands	AGT-5	62º 40.56' S / 60º 42.41' W	AT	25	(CHO) *Polysyncraton trivolutum*; *Tylobranchion speciosum*
South Shetlands	AGT-6	62º 43.12' S / 60º 43.68' W	RD	94	(CHO) *Aplidium falklandicum*

[a]AT, Agassiz trawl; BT, Bottom trawl; ES, Epibenthic sledge; RD, Rocky dredge; [b]ANN, Annelida; CHO, Chordata; CNI, Cnidaria; ECH, Echinodermata; POR, Porifera

Discussion

The present work is, to the best of our knowledge, the largest pharmacological study ever carried out on Antarctic and sub-Antarctic marine benthic invertebrates. Different studies conducted on sessile marine invertebrates from other areas of the world have proved these organisms to have the highest probability of providing compounds with cytotoxic properties (Schmitz *et al.* 1993, Munro *et al.* 1999). In this sense, our results from the Antarctic and sub- Antarctic areas are consistent with this general trend, since the majority of the pharmacologically active hits (80%) correspond to strict sessile invertebrates belonging to the phyla Porifera, Cnidaria and Chordata.

There is only one previous study in a comparable geographic area dealing with pharmacological activity in marine invertebrates. Blunt *et al.* (1990) investigated a different region (Ross Sea) and restricted their bathymetry range of study to shallow waters (SCUBA diving). Although in their analysis they considered jointly the incidence of antiviral and cytotoxic activity of the different Antarctic phyla, and the number of surveyed benthic species was relatively small (59), it is remarkable that the main active phyla are coincident with our results.

In our survey, two main geographical areas were sampled: sub-Antarctic (Bouvet Island) and Antarctic (eastern Weddell Sea and South Shetland Islands). In the sub-Antarctic area, two different species out of the 28 analysed (7.4%) presented antitumoural properties. In contrast, the percentage of active samples in the Antarctic area reached 5.1% (14 active species out of the 277 species analysed). However, these differences cannot lead us to hypothesize any trend, since there is a significant difference in the sampling effort when comparing both areas. Further analysis should be conducted in order to compare, from the pharmacological point of view, Bouvet Island with the rest of Antarctic samples. This could be especially relevant since this island, situated just south of the Polar Front, is a transitional area considered to be a linking point between the High Antarctic and the adjacent temperate Atlantic ecosystems (Arntz *et al.* 2006).

As stated above, the majority of active species (*ca.* 90%) came from the Antarctic area (eastern Weddell Sea and the South Shetland Islands) and this area included also the largest number of bioassayed species (>90%). The Antarctic benthos is commonly characterized by presenting a very rich and diverse community of sessile suspension feeders (Arntz *et al.* 1994, Orejas *et al.* 2000, Clarke & Johnston 2003). This community has been quite well surveyed in our case, despite the fact that our sampling was qualitative; the Porifera, Cnidaria, Bryozoa and Chordata in our study represent >70% of the whole survey. The environment, below the area of ice scouring, believed to be very old and stable and with a high degree of physical environment predictability, is postulated to be ruled by biological factors (Dayton *et al.* 1974). Accordingly, it could be expected that marine benthic Antarctic invertebrates (mostly sessile) develop chemical means to defend themselves from predation, inhibition of settling, and prevention of fouling and overgrowth of other species (Amsler *et al.* 2001, Avila *et al.* 2008). These chemical compounds could be hypothesized to be involved in the antitumoural activity described here.

In our study, Porifera yielded the highest number of pharmacological hits (seven), although it is also true that it was the group with the highest percentage of tested samples (*ca.* 30% of our samples were sponges) and the highest percentage of tested species (*ca.* 30%) (Figure 2; Table 2–3). Among the species found to possess antitumoural activity, here are two species from the genus *Latrunculia* (*L. biformis* and *L. brevis).* Analysis of the biochemical composition of one of our *L. brevis* specimens (Table IV, PS/65-265-1 station code) confirmed the occurrence of discorhabdins A, C and G and also tsitsikammamine A (Figure 6; unpublished results from the authors), an alkaloid firstly described in a South African latrunculid sponge (Hooper *et al.* 1996). Similarly, specimens of *L. brevis* with its origin in New Zealand and Argentinean waters yielded some antitumoural alkaloids, discorhabdins A, D, L and I (Perry *et al.* 1988, Reyes *et al.* 2004). In addition, an Antarctic congeneric species, *Latrunculia apicalis,* was found to possess discorhabdin G located preferentially in the outermost layer of the sponge, where it could cause deterrence against predatory sea stars (Furrow *et al.* 2003). Apart from the latrunculids, two specimens of the genus *Rossella* (Rossella sp. 1 and sp. 2), still under taxonomic study, also displayed antitumoural activity. To the best of our knowledge, this is the first time that any specimen from the class Hexactinellida (glass sponges provided with long siliceous spicules that can act as a physical defence) is reported to show antitumoural activity. Porifera are one of the major targets of chemical investigations in marine environments due to their high biomass and their well-documented ability to possess interesting natural products (McClintock *et al.* 2005, Blunt *et al.* 2007, Avila *et al.* 2008, Peters *et al.* 2009). There are several examples in the literature providing evidence of pharmacologically active compounds from sponges presenting relevant antitumoural effects from tropical (e.g. Bergmann & Feeney 1951) and temperate waters (*e.g.* Burres & Clement 1989). As shown in this work, a similar pattern can be expected in the Southern Ocean since this group of invertebrates constitutes a basic element in the benthic ecosystem, both in terms of abundance and in number of described species (Orejas *et al.* 2000, Clarke & Johnston 2003). Actually, Antarctic sponges represent the group of invertebrates with the highest number of natural compounds described to date and have been extensively studied in terms of chemical compounds, when compared with the rest of invertebrate groups (McClintock *et al.* 2005, Avila *et al.* 2008). Interestingly, some Antarctic sponges have been previously found to present antitumoural activity, with variolin-B, a new alkaloid described from *Kirkpatrickia variolosa,* (Perry *et al.* 1994, Trimurtulu *et al.* 1994), and flabellatene A, a new antiproliferative cembrane isolated from *Lissodendoryx flabellata* (Fontana *et al.* 1999), the most remarkable ones.

In our pool of tested cnidarians three different species were active against the tumour cell lines assayed. The Gorgonacea *Fannyella mawsoni* is reported for the first time as possessing interesting pharmacological activity. The other two cnidarians (order Gorgonacea) presenting activity are still under taxonomic study. As in sponges, cnidarians also play an important ecological role in Antarctic marine benthic ecosystems (Orejas *et al.* 2000). Although very few species have been studied so far from the chemical point of view (Avila *et al.* 2008), there are examples of two different species pertaining to the orders Gorgonacea and Alcyonacea with compounds presenting cytotoxic activity against human tumour cell lines (Mellado *et al.* 2004, 2005). Cnidarians are one of the major sources of marine natural products in other geographical areas as well (Schmitz *et al.* 1993, Munro *et al.* 1999).

After the results of our survey, Antarctic Chordata represent a much more important potential source for pharmacological purposes than previously. In fact, this is the group with the highest percentage of activity in our tests (Figure 1). Among these interesting results there is one that stands out from the rest: aplicyanins A–F (Figure 6), new compounds from the ascidian *Aplidium cyaneum* yielding strong antitumoural activity (Reyes *et al.* 2008). Other examples with a similar relevance such as didemnin B (Rinehart *et al.* 1981) or Ecteinascidin (Rinehart *et al.* 1990), both derived from tropical ascidians, highlight the importance of these animals in the context of the marine drug discovery field. In our study, two of the tunicates found to be active against tumour cell lines, belong to the genus *Aplidium* (*A. cyaneum* and *A. falklandicum).* This genus has been widely recognized as a source of antitumoural compounds in different areas of the world (McKee *et al.* 1998, Le Tourneau *et al.* 2007). Another species to highlight is *Polysyncraton trivolutum,* from the family Didemnidae. This family is also recognized as a source of chemical products with potent biological properties (e.g. Rinehart *et al.* 1981) and a congeneric species from the Fiji Islands, *P. lithostrotum,* also displays relevant antitumoural effects (McDonald *et al.* 1996). On the other hand, this is the first time that the ascidian *Tylobrachion speciosum* is reported as a source for antitumoural activity. Tunicates, together with bryozoans and the above-mentioned sponges and cnidarians, all of them being sessile suspension feeders, conform the basis of the Antarctic benthic ecosystems (Orejas *et al.* 2000). Nevertheless, little chemical work has been conducted to date in tunicates from the Southern Ocean (Avila *et al.* 2008). It is also worth mentioning the antitumoural activity described in the Antarctic ascidian *Synoicum adareanum* (Diyabalanage *et al.* 2006).

Only bryozoans seem not to follow the suggestion that sessile marine invertebrates have a high probability of showing cytotoxic activities (Schmitz *et al.* 1993, Munro *et al.* 1999), since none of the 53 species assayed here showed any activity (this group was the second in number of tested species and also the second in number of samples analysed; see Table 3). Although they are very speciose and abundant in Antarctic waters (Orejas *et al.* 2000, Clarke & Johnston 2003), they have been little studied from a chemical perspective (Avila *et al.* 2008) and, to the best of our knowledge, there is only one reported case of Antarctic cytotoxic activity (haemolytic activity against erythrocytes from man and dog) in the bryozoan *Carbasea curva* (Winston & Bernheimer 1986). Nevertheless, there are examples from other marine geographical areas such as the cosmopolitan *Bugula neritina,* which possesses bryostatin 1, one of the strongest naturally derived antitumoural compounds known to date (Pettit *et al.* 1982).

Non-sessile invertebrates are usually considered less likely groups in which to find cytotoxic compounds (Munro *et al.* 1987). However, in our survey, there were some vagile invertebrates showing interesting antitumoural activity. Two echinoderm species (holothurians), *Psolus paradubiosus* and *Taenyogytus contortus,* presented antitumoural activity. These are not exceptional cases for these slow and soft-bodied organisms since echinoderms have been reported to have a remarkable incidence in cytotoxic activity in other areas of the world (Schmitz *et al.* 1993, Munro *et al.* 1999). This highly diverse group of Antarctic invertebrates (Clarke & Johnston 2003) has also been extensively studied for their chemical ecology (Amsler *et al.* 2001, Avila *et al.* 2008) yielding a large number of natural products. Among them, at least one of the

species analysed (an unidentified sea star from the family Asteriidae) has been observed to possess compounds with cytotoxic activity against human carcinoma cells (De Marino *et al.* 1998).

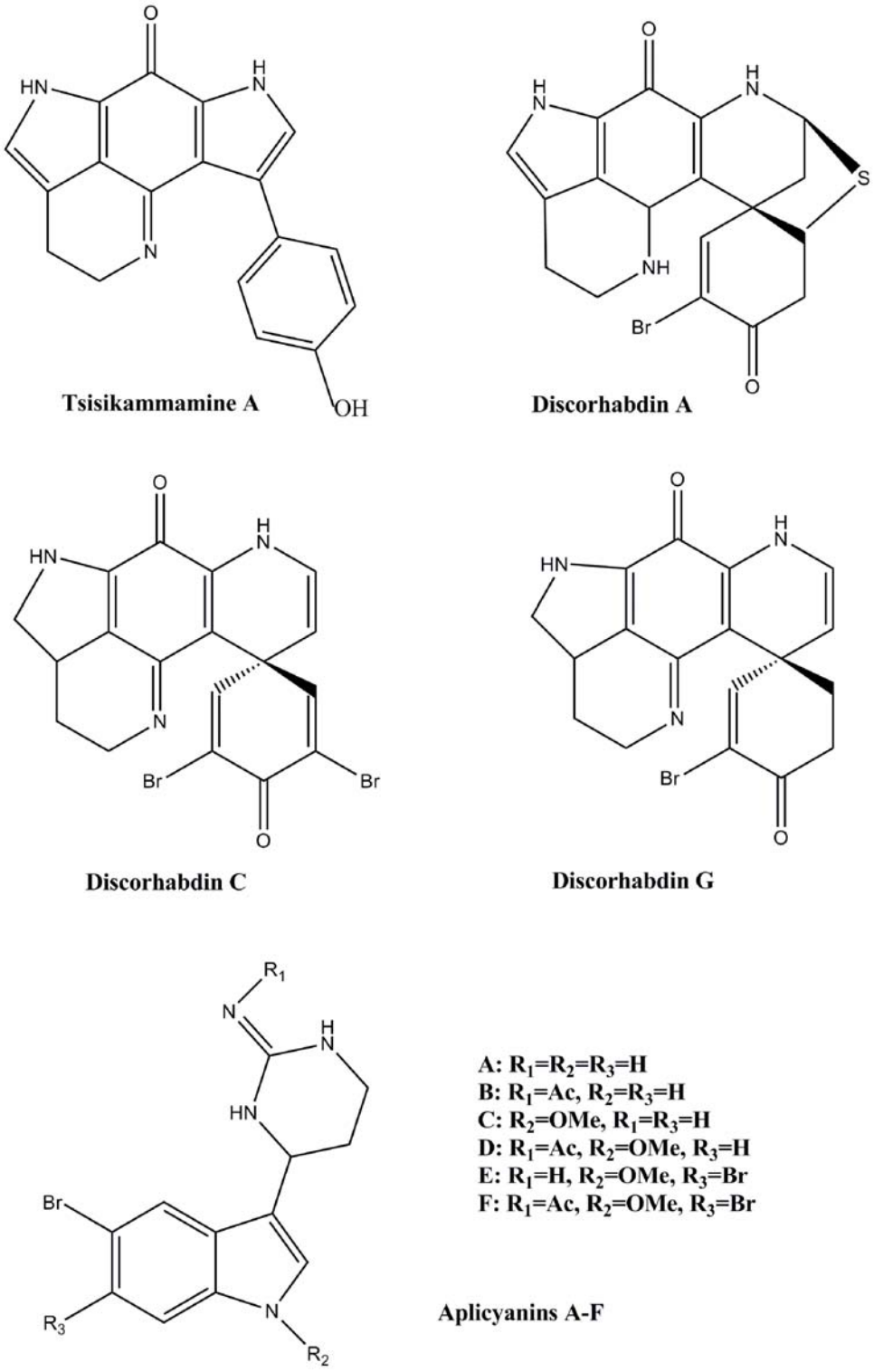

Figure 6. Chemical compounds found in the samples analyzed in the present survey

Annelids are the other group of invertebrates presenting antitumoural activity in this study. The active species belongs to the family Terebellidae. Terebellids are sessile deposit feeders that live attached to the substrate protected by a tube. We know of only one precedent of an annelid with antitumoural activity: the case of *Terebella* sp. (also from the family Terebellidae) showing a mild antitumour activity against P388 murine leukaemia cell line (Battershill *et al.* 1989). As reported for echinoderms, annelids also represent a high percentage of the invertebrate biodiversity in Antarctica; actually, they are the most speciose group in the Antarctic benthos (Clarke & Johnston 2003). However, they have been barely studied from the chemical point of view (Lebar *et al.* 2007, Avila *et al.* 2008), and it seems probable that further positive results may appear for this group.

Other phyla have also displayed antitumoural activity in other marine areas. Examples such as dolastatins in molluscs (Pettit *et al.* 1987) or cephalostatins in pterobranchs (Pettit *et al.* 1994) are just two of the many examples that can be found in the literature. Thus, we may hypothesize that the chances of finding interesting active chemicals in these and other groups in future analyses in Antarctica are reasonably high.

Sampling depth is also an important variable to take into account when bioprospecting. It was mentioned that there seems to be a greater probablility of finding cytotoxicity in animals at depths greater than 30 m (Munro *et al.* 1987). In our survey, samples showing antitumoural activity were predominately found in depths ranging from 250–500 m in the eastern Weddell Sea area and the Bouvet Island vicinities, and *ca.* 100 m depth in the South Shetland Islands area (Figure 5). Since our study was qualitative and the sampling effort was clearly biased to some depths (Figure 5), in our case no further inferences can be drawn when evaluating depth as a factor related to bioactivity.

As explained above, the collection of our samples was supported by a qualitative sampling design in order to maximize the return for the effort invested. Although the sampling effort was, therefore, clearly biased to some particular groups, we believe that results in terms of pharmacological activity are similar to what could be expected after a quantitative sampling, since samples tested were, in general, the most representative organisms in each station. In a similar way, the different number of hits registered in the three major areas studied are proportionally correlated with the sampling effort (eastern Weddell Sea>South Shetland Islands>Bouvet Island); this leads us to hypothesize that the study area was not a decisive factor in our survey.

In our study, two samples identified as the same species (Latrunculia *brevis)* had a similar pharmacological behaviour although they were collected in different áreas –Bouvet Island and eastern Weddell Sea (Table 2). This species has also been reported to display antitumoural effects in other nearby geographical areas such as South America and New Zealand (Perry *et al.* 1988, Reyes *et al.* 2004). It is common that individuals from the same species possess similar activity regardless of the geographical area, as it is the case of the ascidian *Ecteinascidia turbinata* (Munro *et al.* 1987). However, occasionally, individuals of the same species but from different geographical locations may possess distinctly different activity. An example is *Bugula neritina,* a bryozoan only found to present bryostatin 1 in certain geographical areas

(Pettit 1991). In our survey, we also found species that showed antitumoural activity in one sampling station and did not display any antitumoural effect in the rest of the stations where they were collected. These are the cases of the holothurian *Taeniogytus contortus* (only one out of four replicates analysed showed antitumoural activity), and the tunicates *Aplidium falklandicum* (only the sample collected in the South Shetland Islands displayed antitumoural activity), *Polysincraton trivolutum* (one replicate out of the three with activity) and *Tylobranchion speciosum* (one replicate out of the two with activity) (Table 1). Whether this situation is common or rare in nature is still to be established, and it could be related, among other reasons, to the presence of symbionts (Faulkner *et al.* 2000, König *et al.* 2006). We suggest, therefore, that it is important to bioprospect different areas even when sampling similar or the same species, since unexpected results may be obtained.

Since the beginnings of marine pharmacological studies in the 1950s, this discipline has mainly focused on tropical areas and, to a lesser extent, on temperate regions (Bergmann & Feeney 1951, Dietzman 1997, Avila *et al.* 2008). Polar regions have received much less attention, in part due to the difficulties of prospecting in these remote areas and in part also due to the traditional and incorrect belief that they hold low marine chemical diversity (challenged by Amsler *et al.* 2000). Results of this and previous works in the field of chemical ecology are uncovering a very promising future in the search for new leads in the Southern Ocean (Lebar *et al.* 2007, Avila *et al.* 2008). Since only *ca.* 25% of Antarctic fauna has been described so far (Gutt *et al.* 2004) and just a tiny part of it has been tested for biological activity (Avila *et al.* 2008), it can be assumed that natural products in this area will continue providing novel bioactive chemical structures. Furthermore, due to the particular characteristics of the Southern Ocean, which has been physically isolated from the surrounding oceans for 34 million years (Tripati *et al.* 2005), the chances of finding totally novel natural products seem to be higher in this area than in other parts of the world. Natural products are proving to be the most reliable way to find solutions to current and future human diseases (Amsler *et al.* 2001, Newman & Cragg 2007) and many new compounds wait to be discovered. As in an iceberg, which we believe to be very appropriate in this context, for chemical studies in general and pharmacological studies in particular, one could say that only the tip has been discovered so far.

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Chapter 4

A new species of *Cirratulus* (Annelida: Polychaeta) described from a shallow-water whale bone in Antarctica

Photos by C. Avila & S. Taboada

Chapter 4

A new species of *Cirratulus* (Annelida: Polychaeta) described from a shallow-water whale bone in Antarctica

Abstract. A new species of *Cirratulus* Lamarck, 1801 is described from the shallow Antarctic waters of Deception Island (South Shetland Islands). *Cirratulus balaenophilus* **sp. nov.** is the first cirratulid to be described from a fresh whale bone that was experimentally deployed for one year on the Antarctic sea floor. The species is characterized by the lack of spines, lack of eyes, the number of dorsal tentacles arranged in an arc, as well as the light yellow-orange color in life. The cytochrome *c* oxidase subunit I (COI) sequence is presented, as well as some remarks about its feeding preferences and ecology. A comparison with congeneric species occurring in Antarctica and adjacent waters is also provided.

Introduction

Whale bones around Deception Island constitute a relatively common hard substrate that has been systematically overlooked in studies of benthic fauna. These bones, which are very frequent and conspicuous in the intertidal and subtidal waters of Port Foster (authors' personal observations), originated from the Norwegian-Chilean whaling factory that operated in Whalers Bay in the early 20th century (Dibbern 2010). In order to describe the invertebrate community that whale bones could sustain, we deposited the caudal vertebra of a minke whale (*Balaenoptera acutorostrata* Lacépède, 1804) on the sea floor in the area of Whalers Bay in January 2009. Similar experiments using whale remains conducted in other geographic areas (*e.g.* east Pacific) emphasize the importance of polychaetes as the most abundant and diverse taxon to be associated with whale bones (Baco & Smith 2003). After retrieval and examination of the bone, we identified at least five undescribed polychaete species belonging to the families Cirratulidae, Terebellidae, Dorvilleidae, and Siboglinidae. One of the most abundant of these was a new species of the genus *Cirratulus* Lamarck, 1818.

The genus *Cirratulus*, the most speciose of the multitentaculate cirratulids, consists of more than 50 currently accepted species. Six of these species are described or recorded from the Southern Ocean and adjacent waters (see Table 1): *C. cirratus* (O.F. Müller, 1776), the type species for the genus considered as cosmopolitan with a wide bathymetric range; *C. concinnus* Ehlers, 1908, known only from moderate depths at Agulhas Bank, South Africa; *C. gilchristi* Day, 1961, recorded in the shallow waters of Saldanha Bay, South Africa; *C. nuchalis* (Ehlers, 1907), collected from the harbor of Auckland, New Zealand; *C. parafiliformis* Hartmann-Schröder & Rosenfeldt, 1989, occurring at moderate depths in Admiralty Bay, Antarctica; and *C. patagonicus* (Kinberg, 1866), known from the littoral waters of the Strait of Magellan. The aim of the present work is to formally describe *Cirratulus balaenophilus* **sp. nov.**, the first cirratulid to be described from whale bones, and provide comments on its probable feeding behavior and ecology. The cytochrome *c* oxidase subunit I (COI) sequence for *C. balaenophilus* **sp. nov.** and a comparison of congeneric species occurring in Antarctica and adjacent waters are also presented.

Material and Methods

Sample collection

The caudal vertebra of a minke whale was deposited at 21 m depth in Whalers Bay (62º 59.33' S; 60º 33.45' W) (Figure 1B; Sta. 1). The bone was obtained from a beached juvenile minke whale carcass found in the Cantabric Sea (Asturias, Spain) in May 2008. After removing the bulk of the flesh, the vertebra was frozen to -20ºC and shipped to Deception Island. On location, the bone was firmly attached to a heavy metallic grid by means of steel cables and deployed on January 2, 2009. An acoustic release (IXSEA OCEANO 500) connected to a piece of ballast and a buoy was connected to the grid. The mooring was recovered on January 25, 2010, by activating the acoustic release with a telecommand unit (IXSEA TT300 Mors). The recovered bone was brought to the laboratory at the "Gabriel de Castilla" Spanish Antarctic Base (Deception Island), where it was placed in a 3L aquarium containing 0.2-µm filtered seawater and kept at ambient temperature (0–5ºC). No additional oxygenation was supplied to the aquarium, thus forcing the system to go anoxic. Following several days of observation, specimens of an undescribed cirratulid were noticed crawling through the holes in the bone matrix; they were collected with a Pasteur pipette and transferred to a Petri dish containing 0.2-µm filtered seawater. Prior to preservation, animals were relaxed in 7% $MgCl_2$ in fresh water and photographed alive with a camera (Invenio 5S 5MPixel CMOS) mounted on a Zeiss Stemi 2000-C stereomicroscope.

An additional whale vertebra of unknown origin was collected via scuba diving at 15 m depth close to Colatinas on January 11, 2010 (62º 59.482' S; 60° 37.095' W) (Figure 1B; Sta. 2). This bone, examined in the laboratory following the same procedure described above, yielded no cirratulids.

Morphological analysis

Specimens for SEM were fixed in 3% glutaraldehyde in 0.1 mol l^{-1} phosphate buffer solution (PBS) with 0.3 mol l^{-1} sucrose (pH 7.8) and stored at -20ºC. Samples were then washed with cacodylate buffer. Postfixation was carried out for 60 min in 1% osmium tetroxide, followed by a distilled water wash. Specimens were subsequently dehydrated in a graded series of alcohol, critical point dried with a VGmicrotech CPD 7501 system, mounted, and coated with gold in a Fisons SC510 sputter coater. Samples were examined using a Hitachi H-4100FE scanning electron microscope at the University of Barcelona, Spain.

Specimens for standard morphology were fixed in 10% buffered formalin in seawater for 24 h, then transferred to 70% ETOH. Surface structures were observed by temporarily darkening with Shirlastain A. Specimens were also submerged in a concentrated solution of Methyl Green and 80% ETOH for a minimum of 60 seconds to determine the presence of staining patterns. Fixed, live and SEM photographs were edited using Adobe Photoshop CS4 to make the background black and enhance contrast.

Type material is deposited in the Centre of Biodiversity Resources (CRBA, formerly Museum of Zoology) in the Faculty of Biology, University of Barcelona, and vouchers for the sequencing are deposited in the Museum of Comparative Zoology (MCZ), Harvard University, Cambridge, Massaschusetts, USA. All animals not deposited as type material or specimen vouchers are held by the first author at the Department of Animal Biology, Faculty of Biology, University of Barcelona.

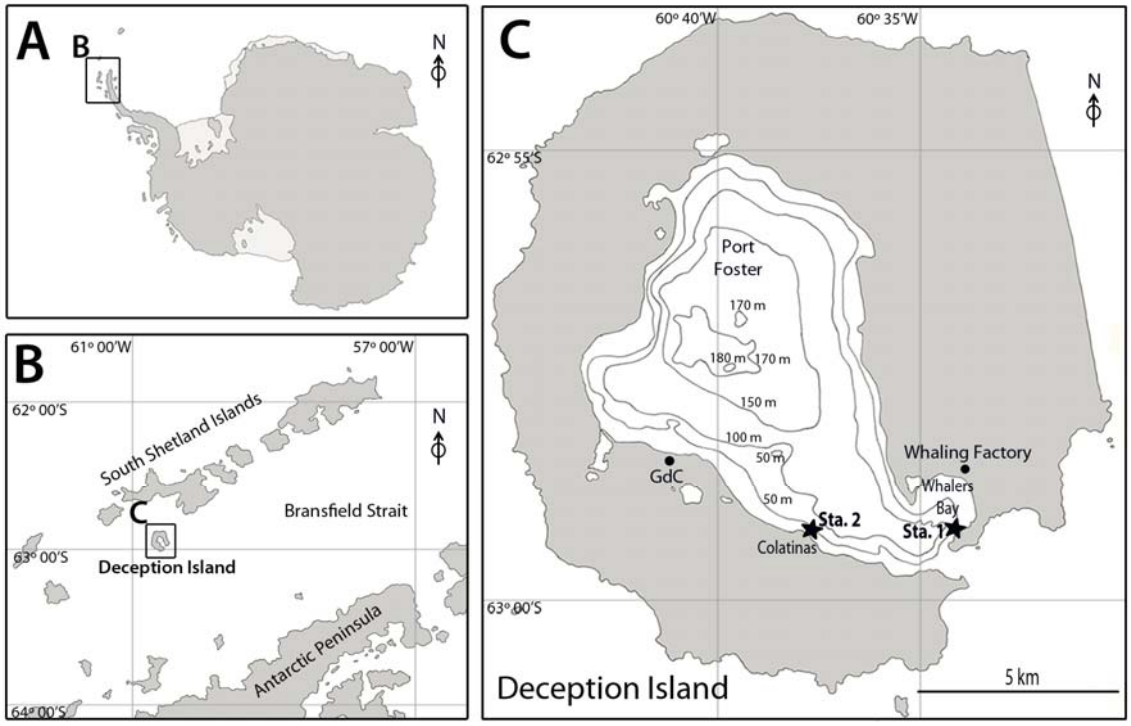

Figure 1. A. General Map of Antarctica; **B.** South Shetland Islands, Bransfield Strait, and Antarctic Peninsula; **C.** Deception Island. GdC, "Gabriel de Castilla" Spanish Antarctic Base; Sta. 1, station where experiment was deployed (fresh bone); Sta. 2, additional bone collected via scuba-diving (old bone)

DNA analysis

Organisms for DNA sequencing were preserved in 95% ETOH and stored in -20ºC. Total genomic DNA was extracted from three ethanol-fixed specimens (paratype voucher number MCZ DNA106471) using the DNeasy kit (Qiagen, Valencia, CA), following manufacturer's instructions. The mitochondrial protein-encoding gene cytochrome *c* oxidase subunit I (COI) was amplified using the primer pair LCO1490/HCO2198 (Folmer *et al*. 1994) and AmpliTaq® 360 DNA Polymerase (Invitrogen, CA, USA). Thermal cycling was as follows: 94ºC/90s–(94ºC/45s–47ºC/60s–72ºC/60s)*45 cycles–72ºC/300s. Sequencing reactions were performed using ABIBigDye Terminator v3.0 (Applied Biosystems) and the products were analyzed using an ABI Prism® 3730 Genetic Analyzer (Applied Biosystems).

Systematic Account

Family Cirratulidae Ryckholt, 1851

Genus *Cirratulus* Lamarck, 1818

Genus Diagnosis (from Blake 1996). Prostomium wedge-shaped, elongate or blunt, usually with eyes; peristomium with 2–3 annulations. Two or more grooved tentacular filaments arising from a single anterior segment. Branchiae first present from same chaetiger as tentacular filaments, occurring singly, continuing over most of body to posterior end. Parapodial rami well separated. Chaetae including capillaries and acicular spines.

Cirratulus balaenophilus sp. nov. Figures 2–4

Material examined. Port Foster, Deception Island, South Shetland Islands, Antarctica; 62º 59.33' S; 60º 33.45' W, 21 m, associated with a minke whale (*Balaenoptera acutorostrata*) caudal vertebra. Collected by S. Taboada, J. Cristobo, and C. Avila, January 25, 2010. Holotype (CRBA-9616) and four paratypes (CRBA-9617; CRBA-9618; CRBA-9619; CRBA-9620) complete and well preserved. Additional material seven specimens preserved in 10% formalin and transferred to 70% ETOH, three used for SEM; 10 specimens preserved in 95% ETOH.

Description. A moderate-sized species; holotype complete, 14 mm long, 0.6 mm wide across both thorax and abdomen, for about 100 chaetigers (Figure 2A). Largest paratype complete, 7.2 mm long and 0.5 mm wide across both thorax and abdomen, for about 69 chaetigers (Figure 2B). Remaining paratypes all complete juveniles, 2.6–3.6 mm long, 0.2–0.3 mm wide across both thorax and abdomen, with 40–45 chaetigers. Thoracic region not expanded, composed of 11–15 crowded chaetigers, lacking dorsal and ventral grooves. Juveniles with about six crowded thoracic chaetigers. Cross-section of thoracic region rounded both dorsal and ventrally. In life, body light yellow-orange with conspicuous dorsal red blood vessel anteriorly; tentacles pale yellow (Figure 2B). After preservation specimens opaque white, lacking all pigmentation; dorsal blood vessel remains visible (Figure 2A).

Prostomium as wide as long, anteriorly rounded; eyes absent; peristomium longer than wide with three prominent annulations viewed both dorsal and ventrally (Figures 3A–B). Pair of circular nuchal organs located posterior and lateral to the mouth, lacking pigmentation (Figures 3B, 4C–D). Dorsal tentacles arising from chaetiger 1, arranged in two groups, each with up to four separate tentacles forming an arc (Figure 3A); first branchiae arising just dorsal to notochaete on chaetiger 1 (Figures 3A–B, 4A–B). Second pair of branchiae dorsal to notochaetae on chaetiger 2, in line with first pair; subsequent branchiae close to notochaeta throughout. Branchiae thick in anteriormost chaetigers decreasing in thickness posteriorly.

Noto- and neurochaetae arise close together throughout, shifted ventrally in posterior segments. Each podial lobe bearing long simple capillaries lacking serrations; 6–9 capillaries per fascicle anteriorly arranged in two rows; decreasing in posterior region to 2–3 capillaries in single row. Noto- and neurochaetae similar in length

throughout, appearing smooth under the light microscope, with splayed fibrils observed in SEM pictures (Figure 4E).

Thoracic segments with well-developed parapodia (Fig. 3B, 4B); reduced to low tori posteriorly. Thoracic-abdominal transition indistinct. Abdominal segments slightly less crowded, never moniliform. Posterior end weakly tapered, dorsally rounded and ventrally flattened (Figure 2C). Pygidium ventral, simple rounded lobe above terminal anus (Figure 3C).

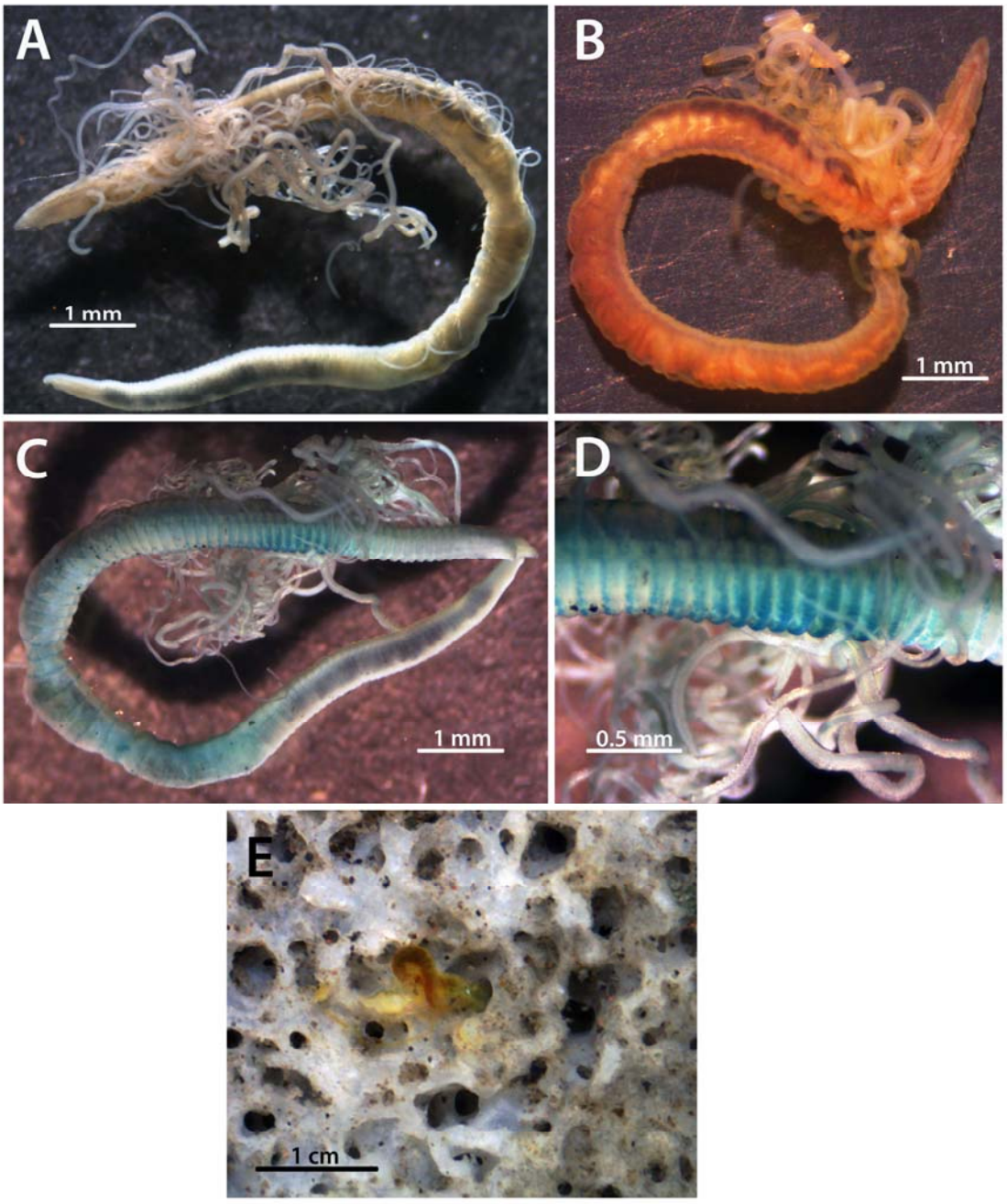

Figure 2. *Cirratulus balaenophilus* **sp. nov. A.** Preserved holotype (CRBA-9616); **B.** Living adult paratype (CRBA-9617); **C.** Holotype stained with Methyl Green; **D.** Holotype mid-anterior region stained with Methyl Green; **E.** Living specimen crawling in the opening of one of the galleries in the bone matrix

Methyl Green staining. Methyl Green staining observed only in adults; conspicuous ventral staining of chaetigers 10–20. Remaining chaetigers of first half of body with thin band on posterior half of segment, incomplete ventrally (Figures 2C–D).

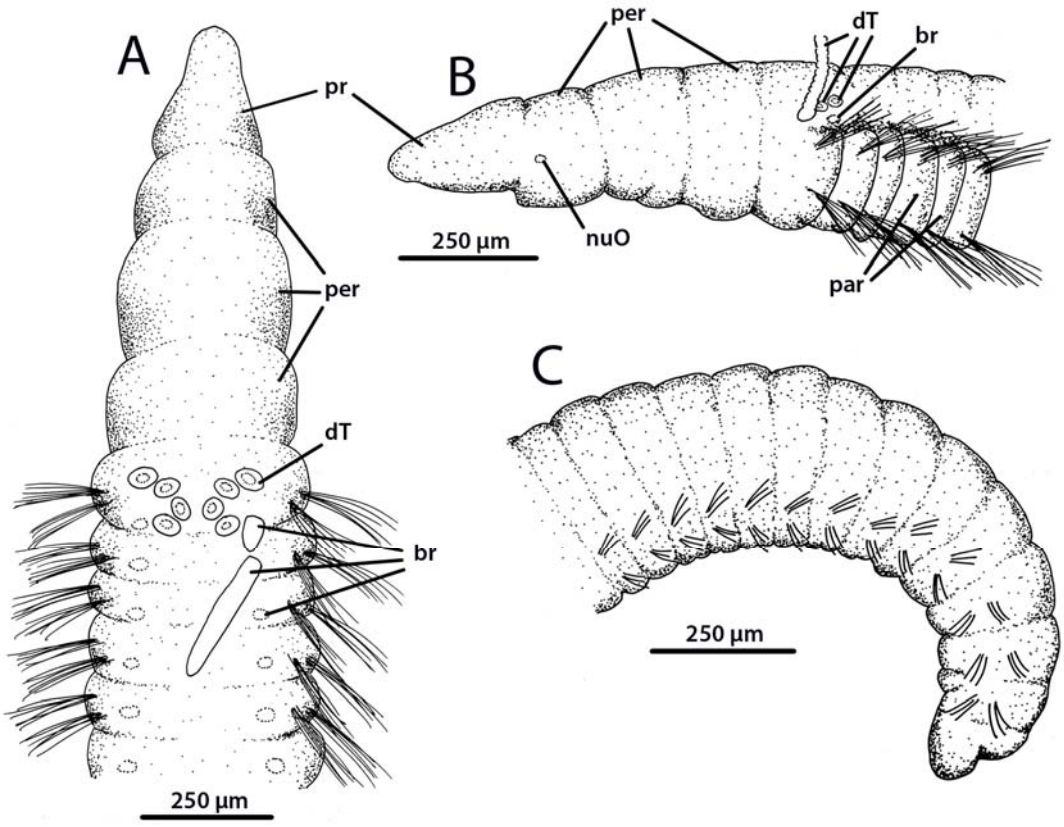

Figure 3. *Cirratulus balaenophilus* **sp. nov. A.** Anterior region dorsal view (holotype; CRBA-9616); **B.** Anterior region, lateral view (adult paratype; CRBA-9617); **C.** Posterior region, lateral view (adult paratype; CRBA-9617). br, branchiae; dT, dorsal tentacle; nuO, nuchal organ; par, parapodia; per, peristomium; pr, prostomium

DNA analysis. The cytochrome *c* oxidase subunit I (COI) sequence was obtained from the sequencing vouchers (MCZ 106471) and is published on GenBank (JQ048545). The 28S sequence was also attempted without success.

Distribution. *Cirratulus balaenophilus* **sp. nov.** is known only from Port Foster, Deception Island in the South Shetland Islands, Antarctica.

Habitat and Ecology. As oxygen was depleted from the water in which the bone was kept, the yellowish tentacles of *C. balaenophilus* **sp. nov.** were noticed in the galleries of the trabecular bone tissue (Figure 2E). These organisms apparently lived inside these natural cavities and did not appear to bore into the bone. This species may live only in fresh whale bones since it did not occur in an older vertebra with no smell of sulphide and with no apparent remaining organic matter that was collected from a similar depth in a nearby area (Figure 1C; Sta. 2). It is important to point out that this old bone, presumably dating back to the whaling factory that operated in Whalers Bay

in the early 20th century, hosted other polychaete species that were also found in the experimental fresh bone (authors' unpublished data). Thus, we may hypothesize that *C. balaenophilus* **sp. nov.** relies on the food supply that the fresh bone provides. No information about reproduction can be inferred from the specimens collected due to lack of ovigerous specimens.

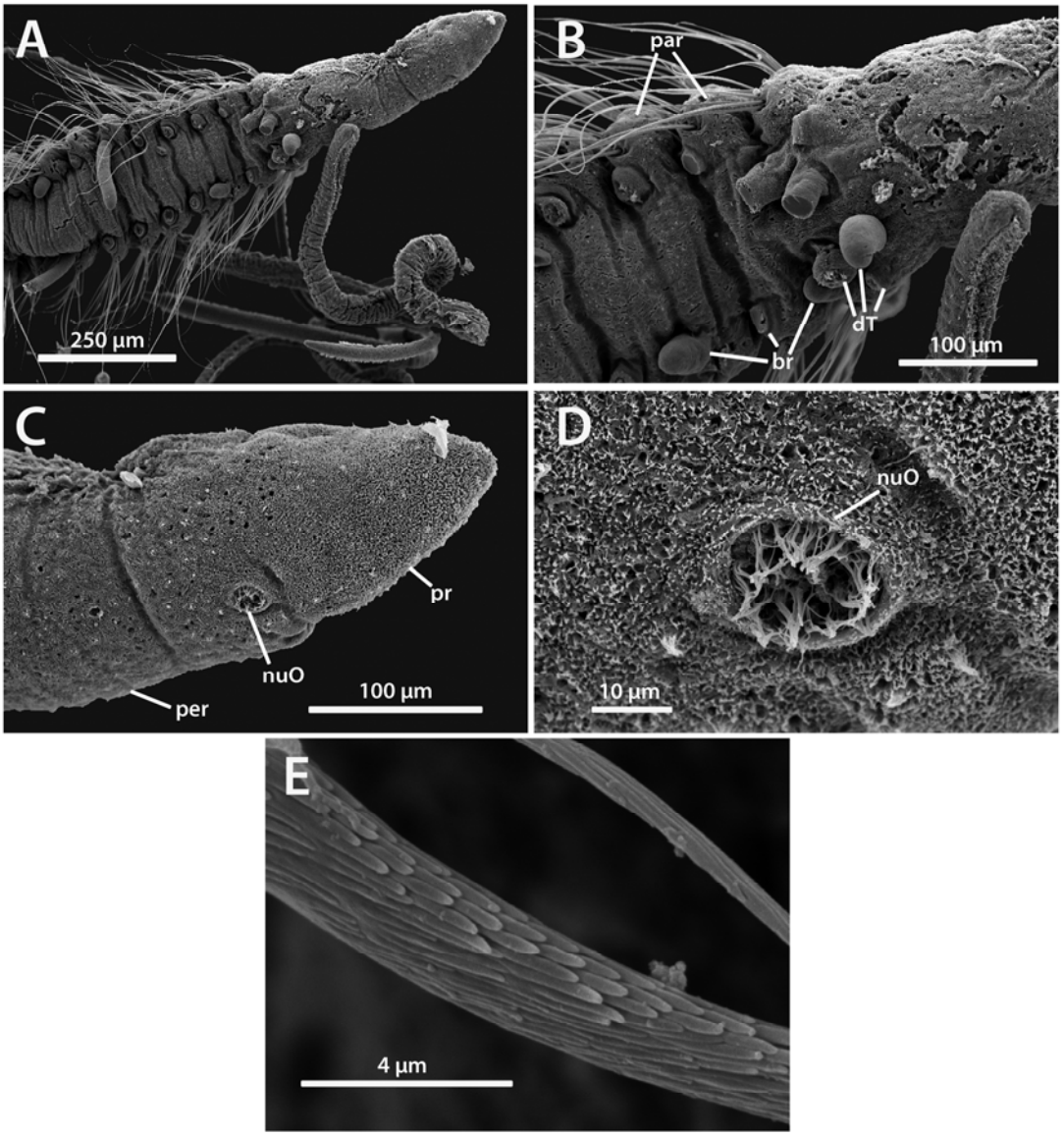

Figure 4. *Cirratulus balaenophilus* **sp. nov.** SEM micrographs. **A.** Thoracic region; **B.** Detail of anterior region showing the general arrangement of dorsal tentacles and first branchiae; **C.** Anterior region showing the nuchal organ; **D.** Detail of the nuchal organ; **E.** Detail of splayed fibrils in the capillary chaeta from second notopodia. br, branchiae; dT, dorsal tentacle; nuO, nuchal organ; par, parapodia; per, peristomium; pr, prostomium

Remarks. The absence of spines, the number and arrangement of the dorsal tentacles, and the lack of eyes characterize *Cirratulus balaenophilus* **sp. nov.** Of the six species of *Cirratulus* occurring in the Southern Ocean and adjacent waters, only *C. nuchalis* (Ehlers, 1907) and *C. parafiliformis* Hartmann-Schröder & Rosenfeldt, 1989 are also reported to lack spines (Table 1). *C. nuchalis* was originally described from the harbor of Auckland, New Zealand, and differs from *C. balaenophilus* **sp. nov.** in the prostomial shape (rounded rather than triangular), color in life (purple as opposed to light yellow-orange), the number of chaetigers in adults (375 versus 40–100), and the very long branchiae that is its most characteristic feature.

On the other hand, *C. parafiliformis* was originally described from an area near Deception Island (Admiralty Bay, King George Island), although from deeper waters (133–458 m). That species, as described, differs from *C. balaenophilus* **sp. nov.** in prostomial shape (bluntly conical versus triangular), the number of dorsal tentacles (5–6 pairs rather than 3–4), in having capillary chaetae of different sizes, as well as in the color after preservation (dark brown-purple instead of white) (Table 1). As part of a separate study, one of us (JAB) examined 43 paratypes (ZMH-19622) of *C. parafiliformis* deposited at the Zoologisches Museum der Universität Hamburg and can confirm that *C. parafiliformis* is indeed a different species than *C. balaenophilus* **sp. nov**. The body of *C. parafiliformis* is relatively robust; the thoracic region consists of numerous crowded segments; abdominal segments are generally narrow and more elongate, but not moniliform. The body is flesh-colored in alcohol; some specimens have a dusky black pigmentation on the dorsum, sides, and ventrum of the first 5–10 chaetigers. The prostomium is triangular in outline, tapering to a narrow anterior end; eyes are absent. There are three peristomial annulations as in *C. balaenophilus* **sp. nov.**, but the entire head region is compressed and thicker. Dorsal tentacles occur anterior to chaetiger 1 and number 5–7 in each of two groups. All chaetae are capillaries and are arranged in spreading fascicles with the chaetae of anterior segments long and silky. The pygidium is a simple ring surrounding the anus without appendages. Methyl Green imparts a distinctive “mask” to the head region, with each of the three peristomial annulations staining heavily with a clear dorsal unstained area between the first and second annulations and smaller clear areas laterally; the tip of the prostomium does not stain; anterior chaetigers retain stain intersegmentally mainly on the lateral and ventral surfaces.

Regarding the presence or absence of eyes, most species of *Cirratulus* occurring in shallow waters tend to have eyes (*e.g. C. cirratus sensu* Hartman, 1966 and *C. gilchristi* Day, 1961). However, species such as *C. balaenophilus* **sp. nov.**, *C. nuchalis*, and *C. patagonicus* (Kinberg, 1866), also shallow waters dwellers, lack eyes.

Etymology. *Cirratulus balaenophilus* **sp. nov.** is named after its original collection from a whale bone as well as from having been collected from the area of Whalers Bay in Deception Island. *Balaenophilus* is a Latin-Greek compound word meaning “liking whales” (*balaena* = whale, *philus* = like).

Table 1. Comparative list of characters for *Cirratulus* species found in the Southern Ocean and adjacent waters

Species	Area Depth range	Prostomium shape	Eyes	Num. Chaetigers	Tentacles location (num. pairs)	Capillaries remarks	Spines	Color after preservation	Data source
Cirratulus cirratus[1] (O.F. Müller, 1776)	Cosmopolitan. Intertidal to 845 m	bluntly conical	yes	93–130	chaetiger 1 (7 p.)	dorsal longer than ventral	yes	deep purple-pale	Hartman 1966, 1967; Carrasco 1977
Cirratulus concinnus Ehlers, 1908	Agulhas Bank (South Africa). 117 m	conical, ventrally flattened	no	77–80	perist.-chaetiger 1 (1–2 p.)	long throughout	yes	—	Ehlers 1908
Cirratulus gilchristi Day, 1961	Saldanha Bay (South Africa). 8–12 m	broadly rounded	yes	98	perist.-chaetiger 1 (8 p.)	nothing remarkable	yes	pale yellow	Day 1961
Cirratulus nuchalis (Ehlers, 1907)	Auckland (New Zealand). Shallow waters	rounded	no	375	—	shiny	no	red-brown	Ehlers 1907
Cirratulus parafiliformis Hartmann-Schröder & Rosenfeldt, 1989	Admiralty Bay (Antarctica). 133–458 m	bluntly conical	no	75	perist.-chaetiger 1 (5–6 p.)	longest 3 times the shortest	no	dark brown-purple	Hartmann-Schröder & Rosenfeldt, 1989
Cirratulus patagonicus (Kinberg, 1866)	Straits of Magellan. Shallow waters	rounded, short	no	185	chaetiger 1 (4 p.)	nothing remarkable	yes	—	Kinberg 1866; Hartman 1948, 1966
Cirratulus balaenophilus **sp. nov.**	Deception Island (Antarctica). 21 m	triangular, pointed, short	no	40–100	chaetiger 1 (3–4 p.)	nothing remarkable	no	white	This report

[1]Type species for the genus.

Discussion

To the best of our knowledge, *Cirratulus balaenophilus* **sp. nov.** is the first cirratulid to be described solely from whale bone remains, although it is not the first cirratulid to be documented from whale falls. Bennett *et al.* (1994) reported *Monticellina tesselata* (Hartman, 1960) (as *Tharyx tesselata*) from a whale skeleton in Santa Catalina Basin (USA) from about 1,200 m; this species was later reported in high densities near another whale carcass in the San Diego Trough (USA) at a similar depth (Smith *et al*. 2002). Goffredi *et al.* (2004) recorded a single unidentified cirratulid from a whale carcass in the Monterey Canyon (>2,800 m depth), and Fujiwara *et al.* (2007) reported an abundance of unidentified cirratulids in sperm whale falls in *ca.* 250 m depth off Cape Nomamisaki, Japan.

It is important to note that *C. balaenophilus* **sp. nov.** occurred only in the fresh whale vertebra experimentally implanted on the sea floor, but not in the single older bone examined from a nearby area at a similar depth (Figure 1C). A detailed survey should be conducted in the surrounding shallow-water sediments and also in other older whale vertebrae remains (presumably deployed decades ago during the whaling factory activity) in order to confirm the wider occurrence of this species.

With the available information, we postulate *C. balaenophilus* **sp. nov.** to be a shallow-water Antarctic opportunistic species that may thrive on natural (*e.g.* whale remains) or anthropogenically organic-enriched environments. Whale falls that sink to the sea floor constitute massive supplies of food as well as a long-term habitat for many different benthic organisms. These inputs of organic matter that arrive in an otherwise food-limited environment promote the occurrence and thriving of different opportunistic species both in deep- and shallow-water environments (Smith & Baco 2003, Wiklund *et al*. 2009a,b). Opportunistic species of cirratulids have been reported in the literature associated with organically enriched and polluted areas in temperate regions (*e.g.* Pearson & Rosenberg 1978, Elías *et al*. 2006), but also in nutrient rich and ice-scouring disturbed areas in Antarctica (Lenihan *et al*. 1995, Conlan *et al*. 2004, 2010).

The experimental bone from Deception Island yielded a small population of *Cirratulus balaenophilus* **sp. nov.** (n=25). What are these cirratulids feeding on? In terms of trophic requirements, cirratulids are thought to be surface deposit-feeders that use their grooved dorsal tentacles for food collection (Fauchald & Jumars 1979). Although no direct feeding observations or fecal pellet analyses were conducted as part of this study, based on the possible food sources, we speculate that *C. balaenophilus* **sp. nov.** could be grazing directly on bacterial mats observed to occur on some parts of the fresh bone. Bacterial grazing has been suggested as the feeding strategy of cirratulids occurring in high abundance associated with mat-forming sulfur bacteria in deep-water seeps and oxygen minimum zones (Levin 2003, Robinson *et al.* 2004); polychaetes from other families have been reported to feed on bacterial mats growing on whale falls (*e.g.* Glover *et al.* 2005, Wiklund *et al*. 2009a,b).

Cirratulids are traditionally divided into two main groups: bitentaculates and multitentaculates. Among multitentaculates the genus *Cirratulus* is characterized by the presence of multiple dorsal tentacles arising from a single anterior segment, as well as the presence of acicular spines (Blake 1996). Our decision to place *C. balaenophilus* **sp. nov.** in the genus *Cirratulus* although it lacks spines in both adult and juvenile forms is based on the emphasis given to the dorsal tentacles (synapomorphic character defining the group) rather than the spines. Characters such as the first appearance of acicular spines, commonly used as species-level characters, have been observed to be highly variable among cirratulids and have often been related to growth (Blake 1996). Other species of *Cirratulus* in the Southern Ocean and adjacent waters also lack spines (*C. nuchalis* and *C. parafiliformis*; Table 1). Further studies combining morphological characters and molecular data (very scarce so far to conduct significant phylogenetic reconstructions of the genus) should be conducted to investigate possible relationships between the species in the group as well as at the family level.

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Chapter 5

Two new Antarctic *Ophryotrocha* (Annelida: Dorvilleidae) described from shallow-water whale bones

Photos by S. Taboada

Chapter 5

Two new Antarctic *Ophryotrocha* (Annelida: Dorvilleidae) described from shallow-water whale bones

Abstract. Two new species of *Ophryotrocha* are described from the shallow Antarctic waters of Deception Island (South Shetland Islands). *Ophryotrocha* **sp. nov.** 1 and *O.* **sp. nov.** 2 are originally described from a minke whale (*Balaenoptera acutorostrata*) fresh caudal vertebra experimentally deployed for about a year, as well as from an unknown whale vertebra presumably dating back to the early 20th century. *Ophryotrocha* **sp. nov.** 2, found in relative high abundance in the fresh bone, is hypothesized to be an opportunistic species in the context of Antarctic shallow-water organically-enriched environments. On the other hand, *Ophryotrocha* **sp. nov.** 1 appears to be the same species as the unnamed *Palpiphitime* sp., near *lobifera* formerly reported from a nearby area. Phylogenetic analyses based on the nuclear gene H3 and the mitochondrial genes COI and 16S, using MrBayes and Maximum Likelihood analyses, show that *Ophryotrocha* **sp. nov.** 2 is close to *Iphitime hartmanae* and is included in the 'hartmanni' clade, while *Ophryotrocha* **sp. nov.** 1 falls in the 'lobifera' clade. Apart from discussing the phylogenetic position of both species, remarks about their feeding preferences and ecology are also given. Our findings seem to suggest that members of the genus *Ophryotrocha* are important members of organically-enriched Southern Ocean environments, as has been reported for this clade in other geographic areas.

Introduction

Invertebrate communities associated with whale carcasses at the seafloor ('whale-falls') were initially discovered at a whale-carcass found in the eastern Pacific at 1,200 m depth (Smith *et al*. 1989). Since this accidental discovery, several studies have followed describing the fauna that thrives on these specialized substrates, and their ecology and evolution (Baco & Smith 2003, Smith & Baco 2003, Smith 2006). To date, several works on different aspects of the biology, ecology, taxonomy, and phylogeny of polychaetes associated with whale-falls have been carried out using natural or experimentally-implanted whale carcasses. These studies have investigated the northeastern and northwestern Pacific and the north Atlantic, at depths between 30 to about 3,000 m (*e.g.* Bennet *et al*. 1994, Rouse *et al*. 2004, Dahlgren *et al*. 2006, Fujiwara *et al*. 2007, Vrijenhoek *et al*. 2009, Wiklund *et al*. 2009b,c, Lundsten *et al*. 2010).

Sunken whale-falls constitute massive inputs of organic matter that can sustain invertebrate communities for years thanks to the slow degradation rate of the lipids and proteins that fill the bones (Smith & Baco 2003). Once the flesh from carcasses is consumed by scavengers, sulphophilic chemoautotrophic bacteria can dominate these particular ecosystems making the organic matter retained in the bones available for different macroinvertebrates (Smith 1992, Deming *et al*. 1997, Treude *et al*. 2009). Most of the invertebrates in these specialized habitats are opportunistic species that thrive in the low-oxygen conditions and elevated sulfide concentrations occurring in the bones (Smith & Baco 2003). Some of them take advantage on the feeding resources that bones offer (*e.g.* filamentous sulphophilic bacteria; Wiklund *et al*. 2009c), and are also provided shelter by the bone crevices and cavities in the trabecular matrix. Examples for opportunistic species occurring in whale-falls are found in the literature in different polychaete families. Such is the case of the polynoid *Bathykurila guaymasensis* Pettibone, 1989, collected from a deep-water experimentally implanted whale carcass in the southern California coast, or the chrysopetalid *Vigtorniella ardabilia* Wiklund, Glover, Johannessen & Dahlgren, 2009, collected from a shallow-water implanted whale-fall in the Swedish coast (Glover *et al*. 2005, Wiklund *et al*. 2009c). The family Dorvilleidae, and particularly members of the genus *Ophryotrocha*, are one of the most represented groups among polychaetes associated with whale-falls. Within *Ophryotrocha*, nine new species have recently been reported from shallow and deep-water whale remains off the Swedish and Californian coasts (Wiklund *et al*. 2009a,b). In its phylogenetic context, previous molecular analyses using 16S and cytochrome *c* oxidase I (COI) sequences agree on two main clades, the 'hartmanni' clade and the 'labronica' clade (Dahlgren *et al*. 2001, Heggøy *et al*. 2007). A third clade was suggested by Paxton (2009), the 'lobifera' clade containing some species that were formerly described as *Palpiphitime*.

To date, only invertebrate communities occurring in whale-falls from the northern hemisphere have been studied. However, communities associated with whale-falls are likely to naturally exist in any marine area, with chances to find naturally sunken whale remains being higher in areas with high whale populations. One such area is the Western Antarctic Peninsula (comprising the South Shetland Islands),

where several cetacean species meet for breeding and feeding (Friedlander *et al*. 2006). With the aim of describing the polychaete fauna associated with whale-falls in the Southern Ocean, we experimentally deployed a fresh whale bone in the shallow waters of Port Foster (Deception Island, South Shetland Islands). The experiment consisted of a minke whale (*Balaenoptera acutorostrata* Lacépède) caudal vertebra implanted on the sea floor in the area of Whalers Bay in January 2009. Another whale bone from unknown origin was also collected from a nearby shallow-water area in Port Foster. After retrieval and examination of both bones (January 2010), it was concluded that the bones hosted at least five undescribed polychaete species from the families Cirratulidae, Terebellidae, Siboglinidae, and Dorvilleidae, the most abundant being two new dorvilleids from the genus *Ophryotrocha*. In the present study we formally describe the first two *Ophryotrocha* occurring in whale remains in the Southern Ocean. Apart from the morphological description, we also provide the phylogenetic relationships of the new dorvilleids using one nuclear (H3) and two mitochondrial (16S and COI) markers in an analysis containing 40 terminal taxa. We also comment on their apparent ecology and feeding behavior.

Material and Methods

Sample collection

Specimens of *Ophryotrocha* **sp. nov.** 1 and *O.* **sp. nov.** 2 were collected from two whale bones in Port Foster, Deception Island (South Shetland Islands, Antarctica). The first bone, a minke whale (*Balaenoptera acutorostrata*) caudal vertebra, was obtained from a juvenile carcass found in the Cantabric Sea (Asturias, Spain) in May 2008. After de-fleshing the vertebra it was frozen to -20ºC and shipped to Deception Island. The vertebra, firmly attached to a heavy metallic grid by means of steel cables, was experimentally implanted on the seabed on January 2, 2009 in the area of Whalers Bay, 21 m depth, 62º 59.33' S; 60º 33.45' W (Figure 1B; Sta. 1). The experimental mooring was kept in the water using an acoustic release (IXSEA OCEANO 500) connected to a large piece of ballast and a buoy, and was recovered on January 25, 2010 activating the acoustic release with a telecommand unit (IXSEA TT300 Mors). The other vertebra, presumably dating back to the Norwegian-Chilean whaling factory that operated in Whalers Bay in the early 20th century (Dibbern 2010), was collected via scuba-diving in front of Colatinas' area at 15 m depth, January 11, 2010, 62º 59.482' S; 60° 37.095' W (Figure 1B; Sta. 2). After retrieval, both bones were brought to the laboratory at the "Gabriel de Castilla" Spanish Antarctic Base (Deception Island), where they were placed in two separate aquaria containing 0.2-µm filtered seawater, and kept at ambient temperature (0 to 5ºC). No additional oxygenation was supplied to the aquaria forcing the system to go into anoxic conditions. Following several days of observation, specimens of *Ophryotrocha* **sp. nov.** 1 and *O.* **sp. nov.** 2 were noticed crawling inside holes in the bone matrix; they were then collected with a Pasteur pipette and transferred to a Petri dish with 0.2-µm filtered seawater. Prior to preservation, animals were relaxed in 7% $MgCl_2$ in fresh water, and photographed alive with a camera (Invenio 5S 5MPixel CMOS) mounted on a Zeiss Stemi 2000-C stereomicroscope.

Additionally, two specimens of two undescribed *Ophryotrocha* (*Ophryotrocha* sp. A and *O.* sp. B) were also collected from the bone at Station 2 (Figure 1B; Sta. 2).

Morphological analysis

Ophryotrocha **sp. nov.** 1 and *O.* **sp. nov.** 2 organisms were preserved for scanning electron microscopy (SEM), DNA analysis and standard morphology. Specimens for SEM were fixed in 3% glutaraldehyde in 0.1 mol l^{-1} PBS with 0.3 mol l^{-1} sucrose (pH 7.8), and stored in -20ºC. Samples were then washed with cacodylate buffer. Postfixation was carried out for 60 min in 1% osmium tetraoxide, followed by a distilled water wash. Specimens were subsequently dehydrated in a graded series of alcohol, critical point dried, mounted, gold-coated, and imaged using a Philips XL-30 FEG (Natural History Museum of London) as well as a Hitachi H-4100FE (University of Barcelona) scanning electron microscope. Organisms for DNA sequencing were preserved in 95% ETOH and stored in -20ºC. Specimens for standard morphology were fixed in 10% buffered formalin in seawater for 24 h, then transferred to 70%

ETOH. Jaws from several ethanol-fixed specimens were obtained after digesting anterior decapitated ends with a trypsin solution. Once the tissue was digested, the jaw elements were cleaned with distilled water and transferred to microscope slides. The live photographs, SEM, and light micrographs obtained were edited using Adobe Photoshop CS4, making the background black and enhancing contrast. Jaws light micrographs were obtained after stacking pictures with different focus.

Type material is deposited in the Natural History Museum of London, United Kingdom, and vouchers for the sequencing are deposited in the Museum of Comparative Zoology in Cambridge (MCZ), Harvard University, USA. All animals not deposited as type material or specimen vouchers are deposited in the first author's collection at the Department of Animal Biology, Faculty of Biology, University of Barcelona, Spain.

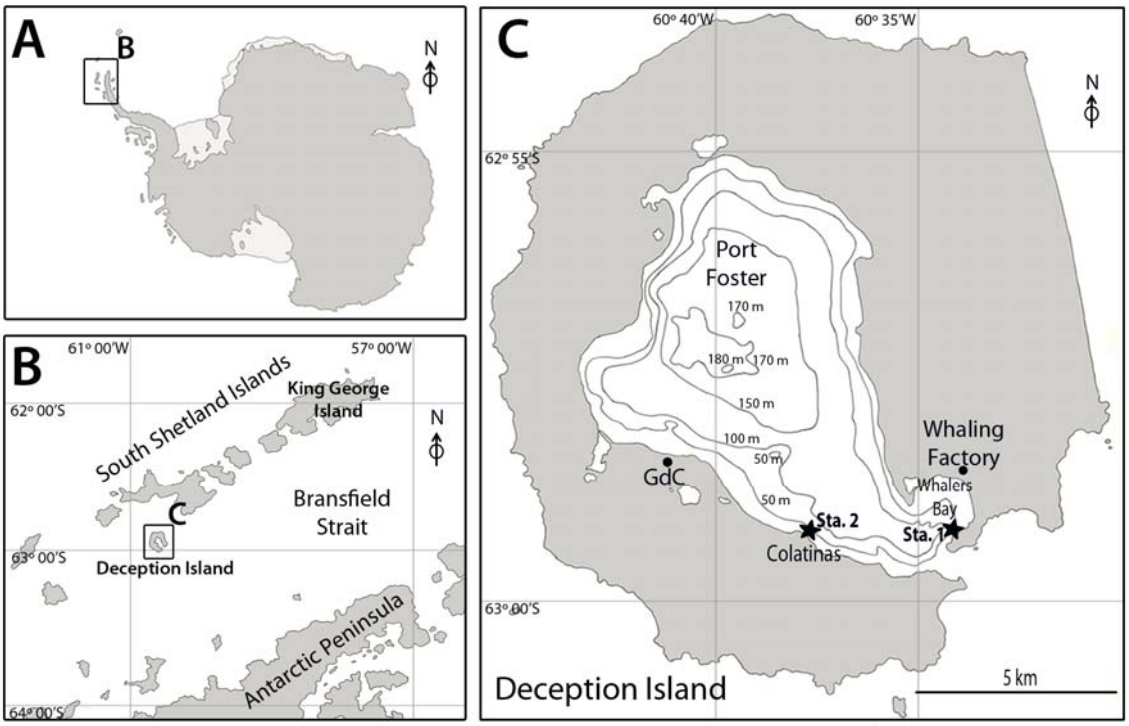

Figure 1. A. General map of Antarctica; **B.** South Shetland Islands, Bransfield Strait, and Antarctic Peninsula; **C.** Deception Island. GdC, "Gabriel de Castilla" Spanish Antarctic Base; Sta. 1, station where the experiment was deployed (fresh bone); Sta. 2, station where the additional bone was collected scuba-diving (old bone)

Molecular analysis

The molecular phylogenetic analyses were made with datasets from the sequences 16S, cytochrome *c* oxidase subunit I (COI), and H3. In total, 40 terminal taxa were used in the analyses, including 30 species from the genus *Ophryotrocha*, nine species from other genera within Dorvilleidae, and rooted using *Eunice pennata* (O. F. Müller, 1776) (Table 1). Total genomic DNA was extracted from 10 ethanol-fixed specimens of each of the two species using the DNeasy kit (Qiagen), following the protocol described

in the manual provided by the manufacturer. About 500 bp of the 16S, 650 bp of COI, and 330 bp of H3 were amplified using the primers listed in Table 2. PCR mixtures and temperature profiles used are listed in Table 3. Sequencing was performed on an ABI 3730XL DNA Analyser (Applied Biosystems). Apart from the *Ophryotrocha* **sp. nov.** 1 and *O.* **sp. nov.** 2 specimens, sequences of the genes 16S, COI, and H3 were also obtained from a single individual of the undescribed species *Ophryotrocha* sp. A.

Overlapping sequence fragments were merged into consensus sequences using Geneious (Drummond *et al*. 2010) and aligned using MAFFT (Katoh *et al*. 2002) for 16S, and MUSCLE (Edgar 2004) for COI and H3, both alignment programs provided as plug-ins in Geneious and used with default settings. Alignments will be available at TreeBase, http://www.treebase.org. Bayesian phylogenetic analyses (BA) were conducted with MrBayes 3.1.2 (Ronquist & Huelsenbeck 2003). Analyses were run three times for each dataset with four chains for 2,000,000 generations; 500,000 generations were discarded as burn-in. The treefiles were tested with AWTY (Are We There Yet) (Nylander *et al*. 2008) in order to see that the analyses had reached a stationary phase. The evolutionary models used for the molecular data in BA were obtained by running the datasets in MrModelTest (Nylander 2004), and for 16S the optional model was GTR+I+G. For COI and H3 the data was partitioned into codon positions, and position 1 and 2 followed GTR+I+G, while HKY+G was used for position 3. For H3, position 1 and 3 followed GTR+G, while GTR+I+G was used for position 2.

Table 1. Taxa included in the molecular analyses with NCBI GenBank accession numbers

Terminal taxa	16S	COI	H3
Dorvillea erucaeformis (Malmgren, 1865)	AY838827	AY838868	—
Dorvillea rubrovittata (Grube, 1855)	GQ415457	CRSdorv	GQ415490
Dorvillea similis (Crossland, 1924)	DQ317915	DQ317857	—
Eunice pennata (O.F. Müller, 1776)	AF321418	AY838870	DQ779731
Exallopus jumarsi Blake, 1985	CRSdorv	CRSdorv	—
Iphitime hartmanae Kirkegaard, 1977	GQ415458	GQ415472	GQ415491
Ophryotrocha adherens Paavo *et al*., 2000	AF321421	CRSdorv	CRSdorv
O. alborana Paxton & Åkesson, 2011	AF321422	GQ415473	GQ415492
O. birgittae Paxton & Åkesson, 2011	AF321426	EF464539	—
O. costlowi Paxton & Åkesson, 2010	CRSdorv	CRSdorv	CRSdorv
O. craigsmithi Wiklund *et al*., 2009	GQ415459	GQ415474	GQ415493
O. diadema Åkesson, 1976	AF321425	CRSdorv	CRSdorv
O. eutrophila Wiklund *et al*., 2009	GQ415460	GQ415475	GQ415494
O. geryonicola (Esmark, 1874)	GQ415461	GQ415476	GQ415495
O. globopalpata Blake & Hilbig, 1990	GQ415462	GQ415477	GQ415496
O. gracilis Huth, 1933	AF321424	EF464545	GQ415497
O. hartmanni Huth, 1933	AF321419	EF464546	CRSdorv
O. japonica Paxton & Åkesson, 2010	GQ415463	GQ415478	GQ415498
O. labronica La Greca & Bacci, 1962	AF321429	GQ415479	GQ415499
O. lobifera Oug, 1978	GQ415464	GQ415481	GQ415500
O. longidentata Josefson, 1975	GQ415471	GQ415482	GQ415501

Table 1. (Continued)

Terminal taxa	16S	COI	H3
O. macrovifera Paxton & Åkesson, 2010	AF321430	CRSdorv	CRSdorv
O. maculata Åkesson, 1973	GQ415465	GQ415483	CRSdorv
O. notoglandulata Pfannenstiel, 1972	AF321431	EF464542	CRSdorv
O. permanae Paxton & Åkesson, 2010	AF321432	GQ415484	GQ415502
O. puerilis Claparède & Mecznikow, 1869	GQ415466	GQ415485	GQ415503
O. robusta Paxton & Åkesson, 2010	AF321433	EF464547	CRSdorv
O. rubra Paxton & Åkesson, 2010	GQ415468	GQ415487	GQ415505
O. scutellus Wiklund *et al*., 2009	GQ415469	GQ415488	GQ415506
O. shieldsi Paxton & Davey, 2010	HM181932	HM181931	CRSdorv
O. socialis Ockelmann & Åkesson, 1990	AF321420	CRSdorv	CRSdorv
O. vellae Paxton & Åkesson, 2010	AF321434	EF464537	—
O. vivipara Banse, 1963	CRSdorv	CRSdorv	—
O. **sp. nov.** 1	this study	this study	this study
O. **sp. nov.** 2	this study	this study	this study
O. sp. A	this study	this study	this study
Parougia albomaculata (Åkesson & Rice, 1992)	AF380115	EF464550	CRSdorv
Parougia bermudensis (Åkesson & Rice, 1992)	CRSdorv	CRSdorv	CRSdorv
Parougia eliasoni (Oug, 1978)	GQ415470	GQ415489	GQ415507
Protodorvillea kefersteini (McIntosh, 1869)	DQ779634	AY598738	DQ779759

Table 2. PCR and sequencing primers

Primer	Sequence 5'–3'	References
16SarL	CGCCTGTTTATCAAAAACAT	Palumbi (1996)
ann16Sf	GCGGTATCCTGACCGTRCWAAGGTA	Sjölin *et al*. (2005)
16SbrH	CCGGTCTGAACTCAGATCACGT	Palumbi (1996)
H3f	ATGGCTCGTACCAAGCAGACVGC	Colgan *et al*. (2000)
H3r	ATATCCTTRGGCATRATRGTGAC	Colgan *et al*. (2000)
LCO1490	GGTCAACAAATCATAAAGATATTGG	Folmer *et al*. (1994)
COI-E	TATACTTCTGGGTGTCCGAAGAATCA	Bely & Wray (2004)
COI-7	ACNAAYCAYAARGAYATYGGNAC(f)	Shimayama *et al*. (1990)
COI-D	TCNGGRTGNCCRAANARYCARAA(r)	Kojima *et al*. (1997)

Table 3. PCR temperature profiles and mixtures

Fragment	Species	PCR program	PCR mixture
16SarL/16SbrH	*O.* **sp. nov.** 1	94ºC/180s-(94ºC/30s-44ºC/30s-65ºC/180s)*45cycles-65ºC/420s	PCRmix1[a]
ann16Sf /16SbrH	*O.* **sp. nov.** 2	95ºC/180s-(94ºC/30s-48ºC/30s-72ºC/90s)*39cycles-72ºC/300s	PCRmix2[b]
ann16Sf /16SbrH	*O.* sp. A	95ºC/180s-(94ºC/30s-48ºC/30s-72ºC/90s)*39cycles-72ºC/300s	PCRmix2[b]
H3f/H3r	*O.* **sp. nov.** 1	95ºC/180s-(94ºC/30s-48ºC/30s-72ºC/90s)*39cycles-72ºC/300s	PCRmix2[b]
H3f/H3r	*O.* **sp. nov.** 2	94ºC/180s-(94ºC/30s-42ºC/30s-65ºC/180s)*45cycles-65ºC/420s	PCRmix1[a]
H3f/H3r	*O.* sp. A	94ºC/180s-(94ºC/30s-42ºC/30s-65ºC/180s)*45cycles-65ºC/420s	PCRmix1[a]
LCO1490/COI-E	*O.* **sp. nov.** 1	94ºC/180s-(94ºC/30s-45ºC/30s-65ºC/180s)*49cycles-65ºC/420s	PCRmix3[c]
COI-7/COI-D	*O.* **sp. nov.** 2	95ºC/180s-(94ºC/30s-45ºC/30s-72ºC/90s)*39cycles-72ºC/300s	PCRmix2[b]
LCO1490/COI-E	*O.* sp. A	94ºC/180s-(94ºC/30s-45ºC/30s-65ºC/180s)*49cycles-65ºC/420s	PCRmix3[c]

[a]17 µl ddH_2O, 0.2 µl each primer (10 µM), 0.1 AmpliTaq® 360 DNA Polymerase (Invitrogen, CA, USA), 2 µl PCR buffer (10x), 0.4 µl dNTP's, 2 µl DNA template; [b]21 µl ddH_2O, 1 µl each primer (10 µM), puReTaq Ready-To-Go PCR Beads (GE Helthcare), 2 µl DNA template; [c]19 µl ddH_2O, 1 µl each primer (10 µM), 0.3 Hot Master Taq DNA Polymerase (5 Prime, Hamburg, DE), 2.5 µl PCR buffer (10x), 0.5 µl dNTP's, 1 µl DNA template

Results

Ophryotrocha sp. nov. 1

Material examined. Port Foster, Deception Island, South Shetland Islands, Antarctica, from two stations: Station 1 (Figure 1B; Sta. 1; 62º 59.33' S; 60º 33.45' W), 21 m, eight specimens from a minke whale (*Balaenoptera acutorostrata*) caudal vertebra, January 25, 2010; Station 2 (Figure 1B; Sta. 2; 62º 59.482' S; 60° 37.095' W), 15 m, 28 specimens from an unknown whale vertebra, January 11, 2010. Holotype ('NHM-xxx1'), and two paratypes ('NHM-xxx2'; 'NHM-xxx3') preserved in 10% formalin, and transferred to 70% ETOH. Paratype 'NHM-xxx3' broken, used for parapodia dissection. Holotype 'NHM-xxx1' and paratype 'NHM-xxx2' collected from Station 2; paratype 'NHM-xxx3' collected from Station 1. Four specimens used for SEM, and 27 specimens preserved in 95% ETOH (MCZ DNA 106469) for DNA analysis. Two specimens preserved in RNA*later*. Material collected by S. Taboada, J. Cristobo, and C. Avila.

Description. Holotype 7.7 mm long, 0.5 mm wide in the peristomium, and 0.8 mm wide throughout. Paratype 'NHM-xxx2' 7.5 mm long, 0.44 mm wide in the peristomium, and 0.5 mm wide throughout. Both holotype and paratype for 38 chaetigers, but other ethanol-fixed specimens for 28–34 chaetigers. Body shape elongated, with uniform width throughout the body, slightly tapering at the posterior end. In life, body brown-yellowish (Figure 2A), with iridescent surface due to ciliation, becoming opaque white after preservation. No distinctive Methyl Green staining pattern.

Prostomium wider than longer with a surrounded disk-like end, dorso-ventrally flattened, tapering anteriorly. Pair of smooth, digitiform antennae inserted dorsally in the mid prostomium. Smooth, cylindrical paired palps inserted ventro-laterally, shorter than antennae, with large palpophores (Figures 2A, 3A–B). Pair of elongated slanted eyes, internal, light-reflecting, very close to each other in the living organism, invisible after preservation (Figure 2A). Mandibles L-shaped with cutting plates having 8–15 conical teeth and a medial, large tooth. P-type maxillae with apparently eight pairs of denticles. (Figures 2B–D); some specimens were moulting their jaws so both the old and the new set of maxillae were present (Figures 2B–C).

Two peristomial achaetous segments, shorter than prostomium. Cross section of the animal dorsally rounded, ventrally flattened. Well-defined ventral plates for each chaetiger. Prominent cushion-like dorsal and ventral lateral lobes. Parapodia uniramous distally lobated with short, rounded dorsal and ventral cirri, bearing 4–5 supraacicular serrated simple chaetae, and 4–5 subacicular compound falcigers with serrated blades (Figure 3D). Simple chaetae with splayed fibrils and a terminal denticle; blades of compound chaetae with double serration rows and a terminal denticle (Figures 2E–F). Some parapodia appear to have subacicular retractable lobes with simple chaetae.

Pygidium bearing terminal anus, paired conical pygidial cirri about the size as antenna, inserted laterally; unpaired appendage absent (Figure 3C).

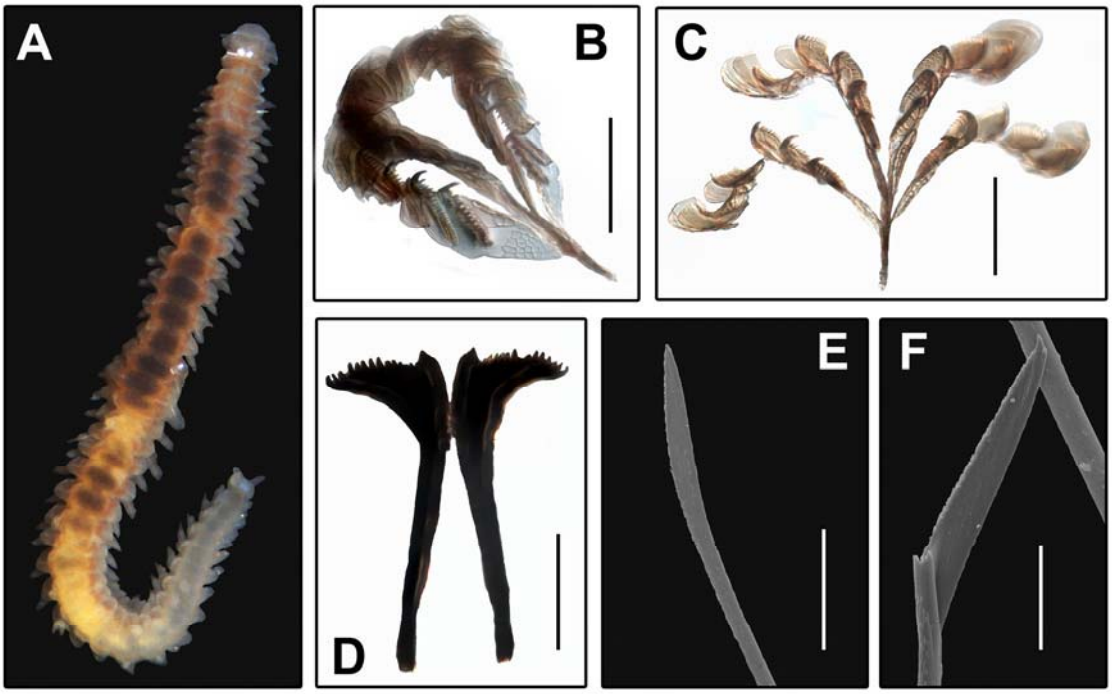

Figure 2. *Ophryotrocha* **sp. nov.** 1. **A.** Living adult paratype ('NHM-xxx2'); **B.** Light micrograph of P-type maxillae moulting; **C.** Light micrograph of P-type maxillae moulting; **D.** Light micrograph of mandibles; **E.** SEM micrograph of simple chaetae from anterior region; **F.** SEM micrograph of compound falciger from anterior region. Scale bars: **B**–**D** =100 µm; **E** =20 µm; **F** =10 µm

Habitat and ecology. *Ophryotrocha* **sp. nov.** 1 is known from Port Foster, Deception Island (South Shetland Islands, Antarctica) at depths ranging 15–21 m. This species seems to have preference for whale bones, since it occurred in the trabecular matrix of an experimentally implanted minke whale vertebra in the area of Whalers Bay (Figure 1B; Sta. 1), as well as in an unknown whale vertebra found on the sea floor close to Colatinas' area (Figure 1B; Sta. 2). Both bones presented a different degree of organic matter content: the bone at Station 1 (fresh-bone experimentally deployed for about a year) gave off smell of sulfide and some filamentous bacterial mats were present at some parts in the bone; the bone from Station 2 (presumably dating back to the whaling factory that operated in Whalers Bay in the early 20th century) had no smell of sulfide, and showed no apparent remaining organic matter or any signal of filamentous bacterial mats. These organisms do not appear to bore into the bone.

Remarks. *Ophryotrocha* **sp. nov.** 1 characterizes by having a pair of dorsal antennae and a pair of ventral palps shorter than antennae, with large palpophores. It also has prominent cushion-like lateral dorsal and ventral lobes, and uniramous parapodia distally lobated with short, rounded dorsal and ventral cirri. Mandibles are L-shaped with cutting plates having numerous conical teeth, and P-type maxillae with apparently eight pairs of denticles. All these characters and others related to the number of chaetigers as well as the features of both simple and compound chaetae, seem to fit with the description of the unnamed *Palpiphitime* sp., near *lobifera* (Oug, 1978) given by Orensanz (1990). The localities and depths where the species described by Orensanz was collected, reinforce the believe that *Palpiphitime* sp., near *lobifera* and

O. **sp. nov.** 1 are in fact the same species (Table 4). Regarding the clade where *O.* **sp. nov.** 1 falls in the phylogenetic tree (Figure 4), the 'lobifera' clade (clade C), *O. lobifera* is the most similar to *O.* **sp. nov.** 1. Unlike *O. lobifera*, *O.* **sp. nov.**1 lacks K-type maxillae and both dorsal and ventral cirri, and acicular lobes are shorter, though this could be a preservation artifact. Among the other species in the 'lobifera' clade, *O. shieldsi* is the only that occurs in a relatively nearby region (shallow-water fish farms from Tasmania). As opposed to *O.* **sp. nov.**1, *O. shieldsi* has digitate dorsal and ventral cirri and K-type maxillae. *Ophryotrocha craigsmithi*, originally described from an experimentally deployed minke whale carcass and from the sediment beneath a fish farm in Norway, differs from *O.* **sp. nov.**1 in having lamellae-like dorsal lateral lobes, cirriform dorsal and ventral cirri, and no eyes. Three other members of the 'lobifera' clade not included in the phylogenetic analysis (*Palpiphitime lipovskyae* Paxton, 2009, *O. platykephale* Blake, 1985 and *O. wubaolingi* Miura, 1997) also differ from *O.* **sp. nov.**1 in the shape of the lateral lobes and the form of the dorsal and ventral cirri (Table 4).

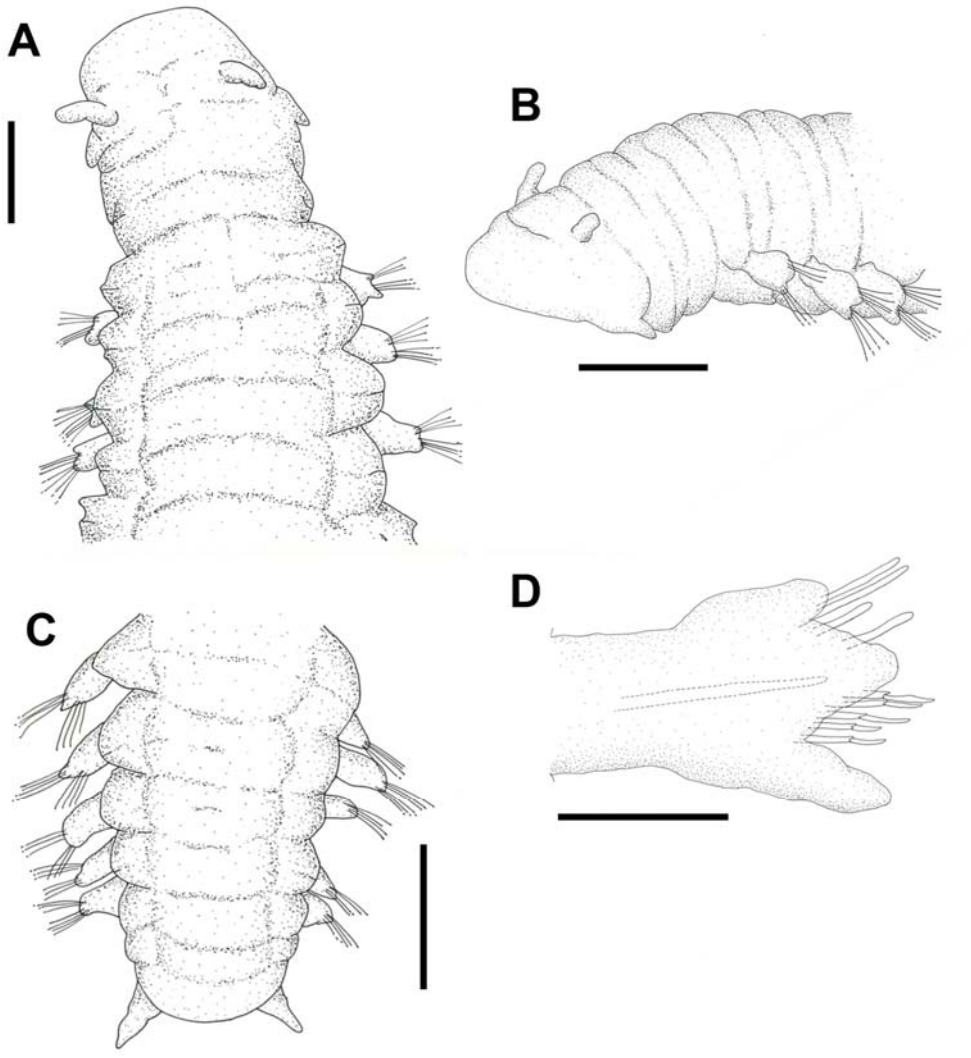

Figure 3. *Ophryotrocha* **sp. nov.** 1. **A.** Anterior region, dorsal view (holotype); **B.** Anterior region, lateral view (holotype); **C.** Posterior region, dorsal view (paratype); **D.** Parapodium from chaetiger 10 (paratype). Scale bars: **A**–**C** =250 µm; **D** =100 µm

Table 4. Comparative list of selected characters for members of the 'lobifera' clade

Species	Area Depth Range	Lateral lobes	Dorsal cirri	Ventral cirri	K-type maxillae	Eyes	Data source
Ophryotrocha craigsmithi	Sweden, minke whale carcass, 125m. Norway, beneath fish farm, 150 m	lamellae-like dorsal lobes	cirriform	cirriform	absent	absent	Wiklund *et al*. 2009b
Ophryotrocha lobifera	Norway, black mud with H_2S, 50 m; minke whale carcass, 125 m	cushion-like triangular	conical	conical	present	present	Oug 1978; Wiklund *et al*. 2009b
Ophryotrocha platykephale	Guayamas Basin, hydrothermal vent, 2000–2030 m	short, digitiform dorsal lobe; foliaceous ventral lobe	digitiform becoming distally bifid	short, retractile	absent	absent	Blake 1985; Solis-Weiss & Hilbig 1992
Ophryotrocha shieldsi	Tasmania (Australia), underneath fish farm, 20 m	ovate cushion-like dorsal lobe, digitate to triangular ventral lobe	digitate	digitate	present	present	Paxton & Davey 2010
Ophryotrocha wubaolingi	Kagoshima Bay (Japan), around submarine fumaroles, 200 m	papilliform dorsal lobe; conical ventral lobe	papilliform	absent	present	?	Miura 1997
Palpiphitime lipovskyae	British Columbia (Canada), near fish farm, 215 m	lamellae-like dorsal lobe; digitate ventral lobe	digitate	digitate	present	?	Paxton 2009
Palpiphitime. sp., near *lobifera*	Anvers Is. (Antarctica), 12 m. South Georgia Is. (Antarctica), 20 m	cushion-like	short, rounded	short, rounded	absent	?	Orensanz 1990
Ophryotrocha **sp. nov.** 1	Deception Island (Antarctica), whale bones, 15–21 m	cushion-like	short, rounded	short, rounded	absent	present	This study

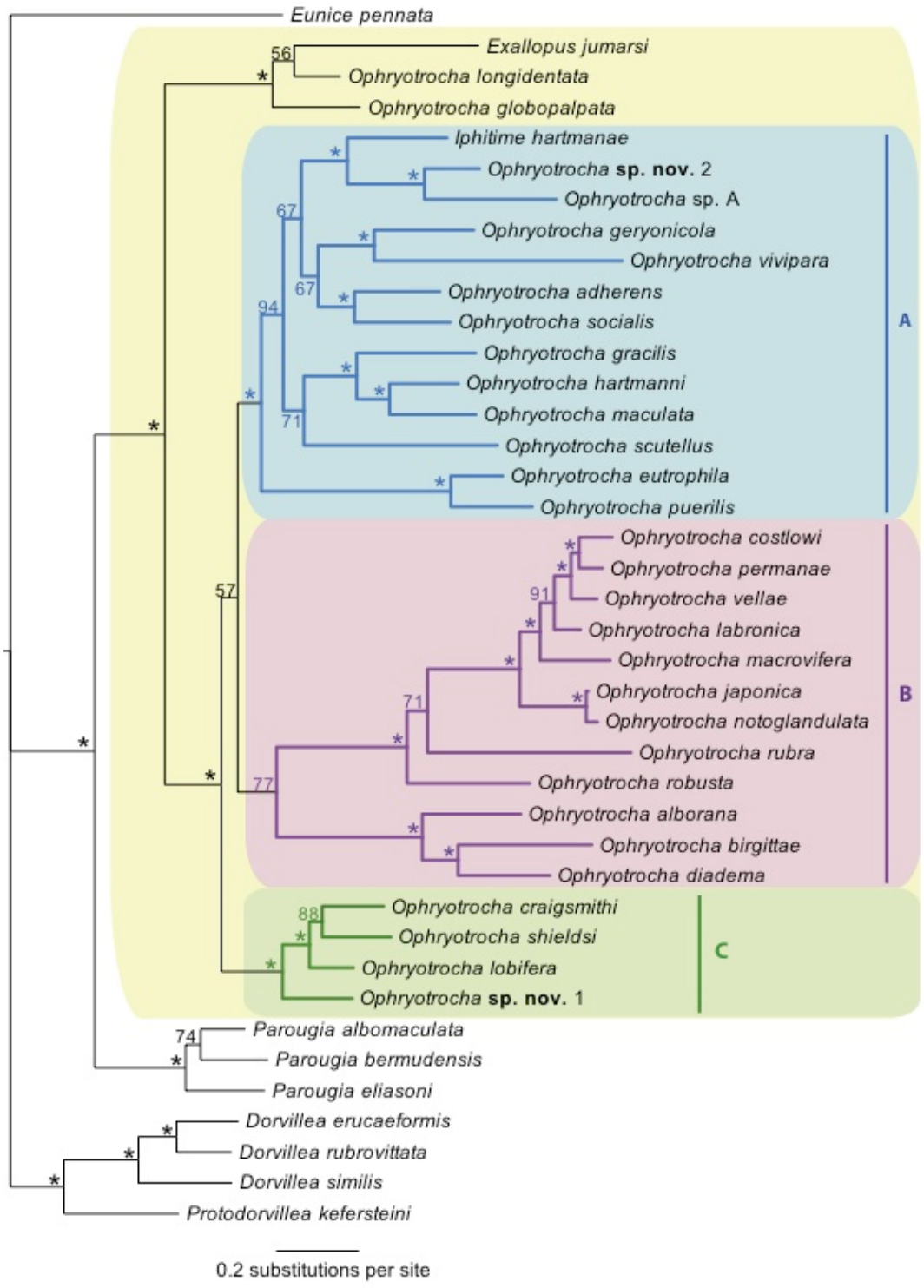

Figure 4. Phylogenetic analyses of a combined dataset of 16S, COI, and H3. Majority rule consensus tree from the Bayesian analyses with posterior probability values after analyses in MrBayes; * >95% support value. A, 'hartmanni' clade; B, 'labronica' clade; C 'lobifera' clade

Ophryotrocha sp. nov. 2

Material examined. Port Foster, Deception Island, South Shetland Islands, Antarctica, from two stations: Station 1 (Figure 1B; Sta. 1; 62º 59.33' S; 60º 33.45' W), 21 m, 110 specimens from a minke whale (*Balaenoptera acutorostrata*) caudal vertebra, January 25, 2010; Station 2 (Figure 1B; Sta. 2; 62º 59.482' S; 60º 37.095' W), 15 m, five specimens from an unknown whale vertebra, January 11, 2010. Holotype ('NHM-xxx4'), and six paratypes ('NHM-xxx5'; 'NHM-xxx6'; 'NHM-xxx7'; 'NHM-xxx8'; 'NHM-xxx9'; 'NHM-xx10') preserved in 10% formalin and transferred to 70% ETOH, all of them collected from Station 1. Paratype 'NHM-xxx7' broken, used for parapodia dissection. A total of 11 specimens used for SEM and 92 specimens preserved in 95% ETOH (MCZ DNA 106470) for DNA analysis. Five specimens preserved in RNA*later*. Material collected by S. Taboada, J. Cristobo, and C. Avila.

Description. Holotype 4.6 mm long, 0.4 mm wide in the peristomium, and 0.6 mm wide throughout. Paratypes ranging from 3.8–4.5 mm long (one ethanol-fixed specimen reached 7.8 mm), 0.3–0.4 mm wide in the peristomium, and 0.4–0.5 mm wide throughout. Holotype and paratypes for 21 chaetigers, but other ethanol-fixed specimens for 17–25 chaetigers. Body shape elongated, with uniform width throughout the body, slightly tapering at the posterior end. Last posterior segment bearing pygidial cirri slightly wider than previous segments. In life, body transparent, with iridescent surface due to ciliation, becoming opaque white after preservation (Figure 5A). Some specimens stain with Methyl Green forming distinct pattern throughout the body (Figure 5B).

Prostomium bluntly triangular, dorso-ventrally flattened, tapering anteriorly. Pair of smooth, robust, triangular antennae inserted dorsally in the mid prostomium (Figures 6A–B). In life antennae with cylindrical shape, longer than fixed antennae but significantly shorter than pygidial cirri (Figure 5A). No palps present. Pair of small internal light-reflecting eyes, well separated from each other in the living organism, invisible after preservation (Figure 5A). Mandibles rod-like, distally V-shaped with anterior dentition; apophyses extending the median lateral edge of the cutting plates (Figure 5C). P-type maxillae with apparently eight denticles; K-type maxillae with apparently seven denticles (Figures 5D–E).

Two peristomial achaetous segments about the same length and width as prostomium. First two chaetigers increasing width respect to peristomial segments, and subsequent chaetigers about the same size. Cross section of the animal dorsally rounded, ventrally slightly flattened. Well-defined ventral plates for each chaetiger (Figure 6C). Parapodia uniramous with globular dorsal and postchaetal lobes (Figure 6D), bearing 4–6 supraacicular serrated simple chaetae distally curved, and 4–6 subacicular compound falcigers with serrated blades and shafts distally bifid. Both simple and compound chaetae with double serration rows and a terminal denticle (Figures 5F–G).

Pygidium bearing terminal anus, paired club-shaped pygidial cirri longer than antennae, inserted laterally; unpaired appendage absent (Figures 6A, C).

Mature females with eggs from chaetiger 4–7 to the end of the body. Only one egg mass observed numbering 55 eggs, with egg diameters between 220–268 µm, laid

on a thin transparent covering (Figure 5H), becoming translucent after preservation. No data available on the presence of sperm.

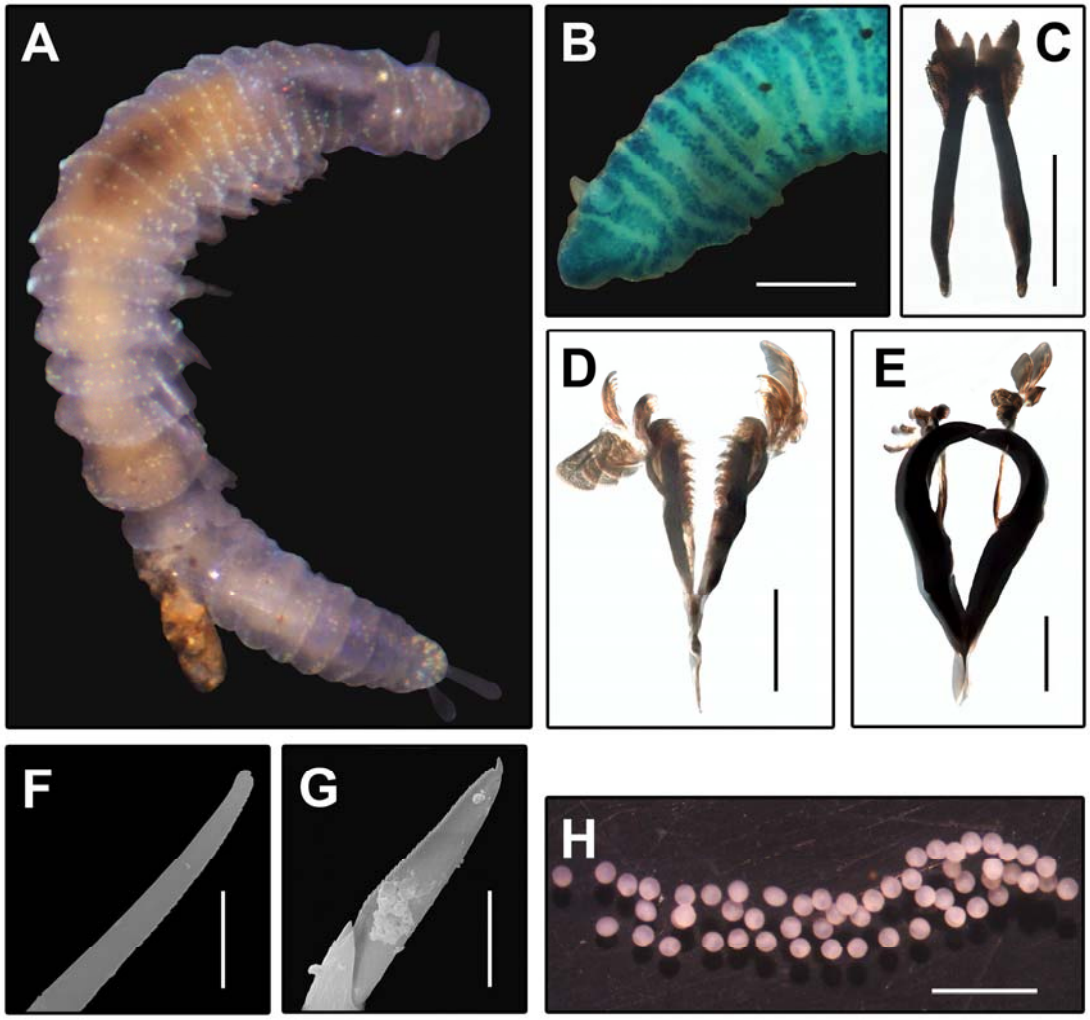

Figure 5. *Ophryotrocha* **sp. nov. 2**. **A.** Living adult; **B.** Preserved paratype ('NHM-xxx8') stained in Methyl Green, anterior region, lateral view; **C.** Light micrograph of mandibles; **D.** Light micrograph of P-type maxillae, dorsal view; **E.** Light micrograph of K-type maxillae, ventral view; **F.** SEM micrograph of simple chaetae from chaetiger 2; **G.** SEM micrograph of compound falciger from chaetiger 10; **H.** Egg mass in life. Scale bars: **B** =250 µm; **C**–**E** =100 µm; **F**–**G** =7.5 µm; **H** =1 mm

Habitat and ecology. *Ophryotrocha* **sp. nov.** 2 is known from Port Foster, Deception Island (South Shetland Islands, Antarctica) at depths ranging 15–21 m. Similarly as in *O.* **sp. nov.** 1, this species also seems to live in association to whale bones since it was collected from an experimentally implanted minke whale vertebra in the area of Whalers Bay (Figure 1B; Sta. 1), and also from an unknown whale vertebra found on the sea floor close to Colatinas' area (Figure 1B; Sta. 2). As with *O.* **sp. nov.** 1, *O.* **sp. nov.** 2 specimens do not appear to bore into the bone; they may live inside the cavities in the trabecular matrix.

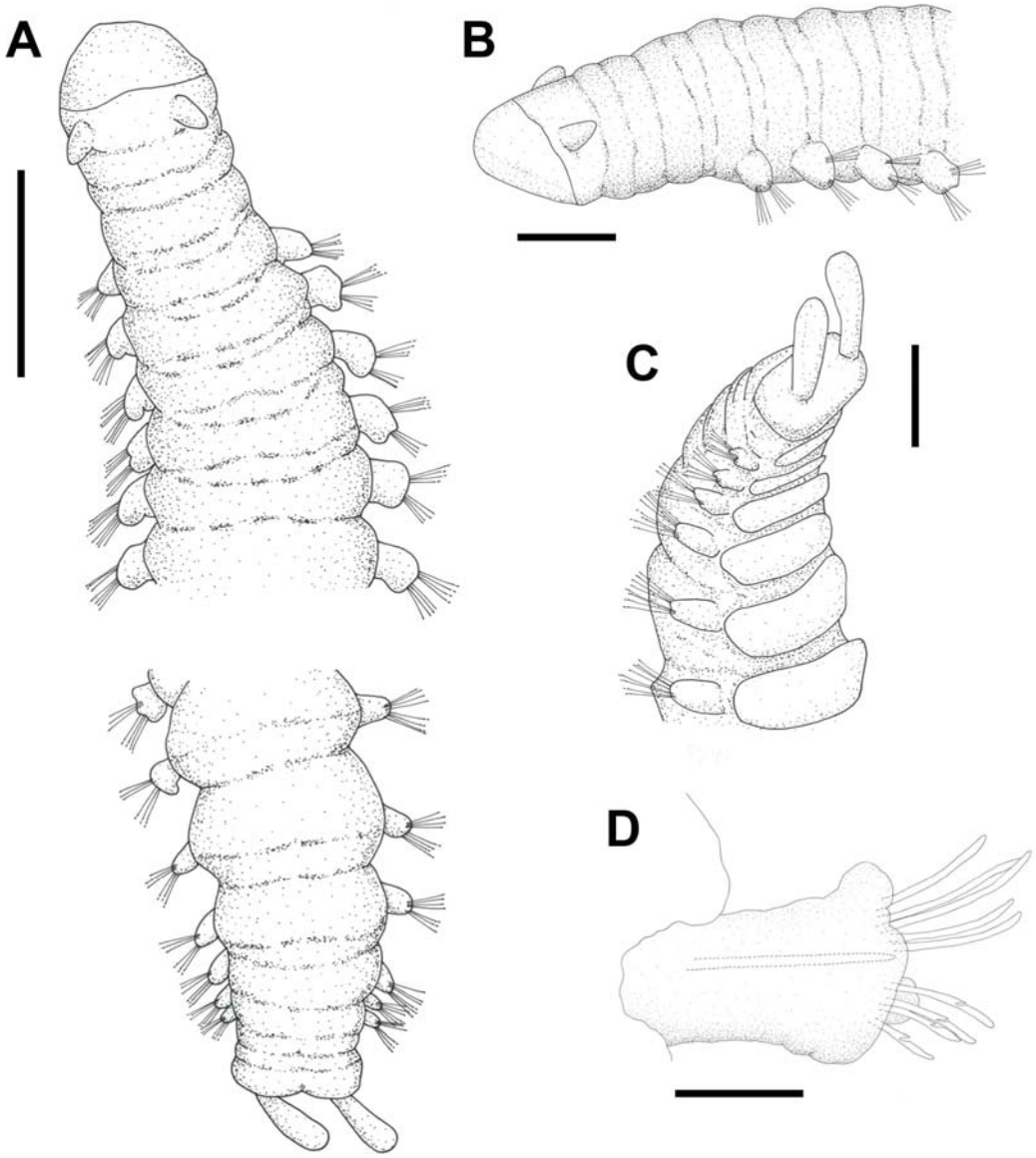

Figure 6. *Ophryotrocha* **sp. nov.** 2. **A.** Entire animal, dorsal view (holotype); **B.** Anterior region, lateral view (holotype); **C.** Posterior region, ventro-lateral view (holotype); **D.** Parapodium from chaetiger 7 (paratype NHM-xxx7). Scale bars: **A** =500 µm; **B**–**C** =250 µm; **D** =100 µm

Remarks. *Ophryotrocha* **sp. nov.** 2 differs from *O. notialis* (Ehlers, 1908) in that it lacks the slender simple chaeta projecting from a ventral retractile lobe. As opposed to *O. notialis*, *O.* **sp. nov.** 2 has two long and conspicuous club-shaped pygidial cirri, becoming the most prominent feature for this species. When comparing *O.* **sp. nov.** 2 with *O. claparedei* Studer, 1878*,* the other *Ophryotrocha* originally described from the Southern Ocean, it has to be considered that its original description was only based on observations made on living specimens collected from algae at the Kerguelen Island (sub-Antarctic). Studer (1878) described a worm having pyriform prostomium with two purplish eyespots and spiniger compound chaetae, as opposed to the bluntly triangular prostomium, with two bright small eyes, and falciger compound chaetae observed in *O.* **sp. nov.** 2. As concluded by Orensanz (1990), *O. claparedei* seems to be only known

from its original record although it has been erroneously reported several times virtually from every Antarctic and sub-Antarctic area. *Ophryotrocha* **sp. nov.** 2 clusters together with *Iphitime hartmanae* (Figure 4). This species is a parasitic worm that lives attached to the tail of two common species of crabs in the Oslo Fjord, Norway. Unlike *O.* **sp. nov.** 2, *I. hartmanae* has branchiae, dorsal cirri completely covering the dorsum of the animal, and lacks compound falcigers. As for the rest of members in the 'hartmanni' clade (Figure 4; clade A), *O.* **sp. nov.** 2 differs from them in the presence of long club-shaped cirri and the absence of pygidial unpaired appendage. Other characters such as the presence/absence of palps, K-type maxillae and eyes also vary among these species (Table 5).

Ophryotrocha sp. A

Material examined. Port Foster, Deception Island, South Shetland Islands, Antarctica, Station 2 (Figure 1B; Sta. 2; 62º 59.482' S; 60º 37.095' W), 15 m, one specimen from an unknown whale vertebra, January 11, 2010.

Remarks. *Ophryotrocha* sp. A resembles *O.* **sp. nov.** 1 but, as opposed to it, has long pygidial cirri similar to those in *O.* **sp. nov.** 2. The analysis of the sequences for the genes 16S, COI, and H3 confirmed that *O.* sp. A differs from the two described species in this study, though it is sister to *O.* **sp. nov.** 2 (Figure 4).

Ophryotrocha sp. B

Material examined. Port Foster, Deception Island, South Shetland Islands, Antarctica, Station 2 (Figure 1B; Sta. 2; 62º 59.482' S; 60º 37.095' W), 15 m, one specimen from an unknown whale vertebra, January 11, 2010.

Remarks. *Ophryotrocha* sp. B resembles *O.* **sp. nov.** 1 but clearly differs in having dorso-lateral processes appearing on the last third region of the animal, becoming larger posteriorly. Similar structures have been described in the males of *O. cosmetandra* Oug, 1990 as well as in *Mammiphitime tridentata* Orensanz, 1990.

Molecular analysis

The combined alignment consisted of 1,592 characters, of which 16S had 557 characters, COI had 684 characters, and H3 351 characters. The three Bayesian analyses (BA) converged on similar log-likelihood values, mean values for all parameters, and clade probabilities (Figure 4). The 50%-majority rule consensus tree from the BA supports 37 nodes, of which 26 with clade credibilities at 95% or above. There is strong support for a monophyletic *Ophryotrocha* containing *Exallopus jumarsi* and *Iphitime hartmanae*. The new species *O.* **sp. nov.** 1 falls basally within the 'lobifera' clade (clade C), whereas both the new species *O.* **sp. nov.** 2 and the undescribed species *O.* sp. A fall within the 'hartmanni' clade (clade A) as sister to *I. hartmanae* (Figure 4).

Table 5. Comparative list of characters for selected members of the 'hartmanni' clade

Species	Area Depth Range	Palps	K-type maxillae	Pygidial Cirri	Eyes	Data source
Ophryotrocha adherens	Hawaii (USA), 70 m	present	present	two ovate cirri, small unpaired appendage	present	Paavo *et al*. 2000
Ophryotrocha eutrophyla	Sweden, minke whale carcass, 125m	present	present	two cirri, unpaired appendage	absent	Wiklund *et al*. 2009b
Ophryotrocha hartmanni	Mediterranean & North Atlantic, shallow-waters	absent	present	two cirri	absent	Huth 1933
Ophryotrocha maculata	Sweden, 25 m	present as ciliated pads	present	two slender cirri, unpaired appendage	present	Åkesson 1973
Ophryotrocha puerilis puerilis	Mediterranean, shallow-waters	present	present	two cirri, unpaired appendage	present	Paxton & Åkesson 2007
Ophryotrocha scutellus	Sweden, minke whale carcass, 125m. Norway, beneath fish farm, 104 m	present	absent	two long cirri, nub-like unpaired appendage	absent	Wiklund *et al*. 2009b
Ophryotrocha socialis	Denmark, shallow-waters	present as ciliated pads	absent	two cirri, unpaired appendage	present	Ockelmann & Åkesson 1990
Ophryotrocha vivipara	San Juan Archipelago (USA), 22 m	present	absent	two cirri, inconspicuous unpaired appendage	present	Banse 1963
Ophryortrocha geryonicola	Skagerak (Denmark), on the gills of *Geryon tridens*, 190–300 m	present	present	two cirri, short unpaired appendage	absent	Pfannenstiel *et al*. 1982
Iphitime hartmanae	Norway, on the tail of *Hyas araneus* and *H. coarctatus*	absent	present	two short conical cirri	absent	Kirkegaard 1977
Ophryotrocha **sp. nov.** 2	Deception Island (Antarctica), whale bones, 15–21 m	absent	present	long club-shaped cirri	present	This study

Discussion

The present study, with the description of two new shallow-water *Ophryotrocha*, represents a substantial increase for the Antarctic waters in the number of described species in the genus. So far, the only two described *Ophryotrocha* occurring in the Southern Ocean were *O. claparedei* and *O. notialis*, aside from other deep-water still undescribed species (Blake & Narayanaswamy 2004, Hilbig 2004), and some unnamed species formerly included in the currently unaccepted family Iphitimidae (Orensanz 1990). Other than our findings in the bones from Deception Island, it should be pointed out that at least eight new deep-water congeneric species, associated to experimentally deployed whale bones in the area of the South Shetlands Islands and the Weddell Sea, have recently been discovered (Wiklund *et al*. in prep.). Thus, the current and near-in-the-future descriptions of new *Ophryotrocha* species will confirm this group as an important clade at nutrient rich habitats also in Antarctic waters, similarly to other geographic areas (Thornhill *et al*. 2009). Then, in accordance with Wiklund *et al*. (2009c), these findings support the hypothesis that, when new suitable sites are investigated (*e.g.* organic-enriched environments as whale-falls), the species diversity within *Ophryotrocha* will keep on raising in the Southern Ocean as well as in other poorly studied geographic areas.

The discovery of *O.* **sp. nov.** 1 and *O.* **sp. nov.** 2 is remarkable since they occur in a region, the Western Antarctic Peninsula, comprising a series of islands whose benthic macrofauna has been extensively surveyed during the last decades (see Orensanz 1990, Barnes *et al*. 2008, Sicinski *et al*. 2011). Among the several studies conducted, apart from a few records from the Anvers Island shore and at moderated depths in the Bransfield Strait (Hartman 1967, Orensanz 1990), *O. notialis*, the only *Ophryotrocha* reported in the region, has chiefly been collected in the King George Island shore. Although there it occurs from 5 to 165 m depth (Sicinski 2000), it has mainly been reported as a sub-tidal early-colonizer (6–11 m), sometimes becoming the principal meio- and macrofauna polychaete member in areas disturbed by ice scouring (Bromberg *et al*. 2000, Petti *et al*. 2006). As for the also well surveyed Port Foster (Deception Island), bay where our experiments took place, no *Ophryotrocha* representative had been recorded so far (see Barnes *et al*. 2008, and references herein). In this case, however, it should be mentioned that most of the studies describing the polychaete assemblages in Port Foster have mainly focused on its deepest part (40–165 m), and also that whale bones have been largely overlooked.

Whale-falls that sink to the sea floor constitute massive substrates of organic enrichment that arrive to an otherwise food-limited environment. These huge and long lasting inputs of organic matter promote the colonization of different sulfide-tolerant opportunistic species occurring in high-density, low-diversity assemblages (Smith & Baco 2003). Other examples of opportunistic *Ophryotrocha* species occurring in high densities in whale bones have lately been reported. Such are the cases of *O. scutellus* and *O. craigsmithi*, found in a shallow-water whale carcass experimentally deployed off the Swedish coast (Wiklund *et al*. 2009c), or the six new *Ophryotrocha* collected from deep-water naturally occurring and implanted whale carcasses off the Californian coast (Wiklund *et al*. 2009a). In our study, although no evidence is present that *O.* **sp. nov.** 1

and *O.* **sp. nov.** 2 occurred in high densities, they showed distinct abundances in the two bones which may suggest a succession (Table 6). While *O.* **sp. nov.** 2 was the most abundant organism in the bone at Station 1 (fresh-bone with bacterial mats; one year deployed), it strongly decreased in abundance in the bone at Station 2 (old bone with no smell of sulfide and no apparent organic matter content; presumably several decades old). Conversely, *O.* **sp. nov.** 1 was the most abundant organism in the bone at Station 2 and was far less abundant in the bone at Station 1. Although a more extensive study should be conducted to confirm this tendency, we postulate that *O.* **sp. nov.** 2 is an early-colonizer, opportunistic species that may rely on the high levels of organic matter that fresh bones provide.

Table 6. Total and relative abundance of the polychaetes surveyed from the Deception Island whale vertebrae

	Total Abundance (% relative abundance)	
Species	Sta. 1	Sta. 2
Ophryotrocha **sp. nov.** 2	110 (68)	5 (10)
Cirratulus sp. nov.	25 (15)	—
Capitella cf *perarmata*	8 (5)	16 (31)
Ophryotrocha **sp. nov.** 1	8 (5)	28 (54)
Polygordius cf *antarctica*	2 (1)	—
Leitoscoloplos cf *kerguelenensis*	2 (1)	—
Ophryotrocha sp. A	—	1 (2)
Ophryotrocha sp. B	—	1 (2)
Polycirrus sp. nov.	1 (<1)	1 (2)
Apistobranchiidae sp.; *Capitella* sp.; Nereididae sp.; *Osedax* sp. nov.; Syllidae sp.; Terebellidae juv.	1 each (<1 each)	—

Except for a few cases, Antarctic shores almost completely lack the habitats where most opportunistic *Ophryotrocha* members inhabit, eutrophicated littoral zones (Thornhill *et al*. 2009). Several studies on the benthic assemblages taken in a highly perturbed area in front of McMurdo Station (Ross Sea) have reported high densities of *O. notialis*, an early successional species, co-occurring with other opportunistic species (Lenihan & Oliver 1995, Lenihan *et al*. 2003, Conlan *et al*. 2004, 2010). Apart from these rare examples in Antarctica on anthropogenically-enriched habitats, other natural sources of eutrophication could sustain populations of opportunistic littoral species. One of such natural sources could be the frequent and ecologically relevant number of carcasses from different species of birds, seals, and whales arriving to the sub-littoral Antarctic waters. Natural patches created after the combined effects of ice-scouring and the subsequent accumulation and decomposition of organic matter, could also promote the occurrence of opportunistic species. These patches, recently described by Powell *et al*. (2012) but previously observed by Richardson & Hedgpeth (1977), host

sulfur-oxidizing bacterial mats, fact that often correlates with the presence of opportunistic *Ophryotrocha* (see below).

In terms of trophic requirements, though no direct feeding observations, fecal pellet or stable isotope analyses were conducted as part of this study, we may suggest that *O.* **sp. nov.** 1 and *O.* **sp. nov.** 2 could rely part of their diet feeding on filamentous *Beggiatoa*-like bacterial mats that were present in some parts of the bone at Station 1. Some recently published studies conducted with other *Ophryotrocha* species support this hypothesis. Wiklund *et al*. (2009b) observed various *Ophryotrocha* from a shallow-water whale-fall grazing on filamentous bacterial mats (*Beggiatoa* spp.). Bacterial grazing has also been reported for polychaetes pertaining to other groups, such as the polynoid *Bathykurila guaymasensis*, recorded both in deep-water whale falls and hydrothermal vents (Glover *et al*. 2005), and the chrysopetalid *Vigtorniella ardabilia*, collected from shallow-water whale-falls and in sediment samples beneath fish farms (Wiklund *et al*. 2009c). These bacterial mats are also common where other *Ophryotrocha* representatives are found in high densities, *e.g.* wood falls (Wiklund *et al*. 2009a), the sediment beneath fish farms (Paxton 2009, Wiklund *et al*. 2009b, Paxton & Davies 2010), or areas influenced by sewage outfall (Conlan *et al*. 2010). This suggests a strong trophic relationship between communities dominated by filamentous bacteria and their grazing polychaetes. Other specialized environments such as the hydrothermal vent sediments of Middle Bay (northeastern Pacific Ocean) have been investigated in terms of macrobenthic trophic relationships (Levin *et al*. 2009). This study, based on the isotope signature of a common unidentified *Ophryotrocha*, suggested this species to be directly feeding on filamentous bacterial mats proliferating on the substrate.

In the phylogenetic analyses *O.* **sp. nov.** 2 as well as the undescribed *O.* sp. A are included in the 'hartmanni' clade (Figure 4; clade A) and they both fall within a well supported clade containing *Iphitime hartmanae*. Other authors (Høisæter & Samuelson 2006, Heggøy *et al*. 2007) have argued the genus *Iphitime* belongs within *Ophryotrocha*, although the inclusion in the phylogenetic analysis of the type species for *Iphitime* is needed to confirm this hypothesis. *Ophryotrocha* **sp. nov.** 1 falls within the 'lobifera' clade (Figure 4; clade C). The members of this clade, most of them originally described from organic-enriched environments such as fish-farms and whale-falls (see Table 4), share morphological characters such as biarticulated palps, dorsal and ventral lobes, both K-type and P-type jaws, and P-forceps with transverse serrated ridges (Paxton 2009). For *O.* **sp. nov.** 1, however, no K-type maxillae were observed after the examination of several specimens in our study.

Our contribution describing two new *Ophryotrocha* along with several others that will be released in the near future (Wiklund *et al*. in prep.; unpublished data from the authors), will certainly contribute to increase the knowledge of whale-fall communities in the Southern Ocean. These findings suggest that members of the genus *Ophryotrocha* play an important role in the Antarctic organically-enriched environments.

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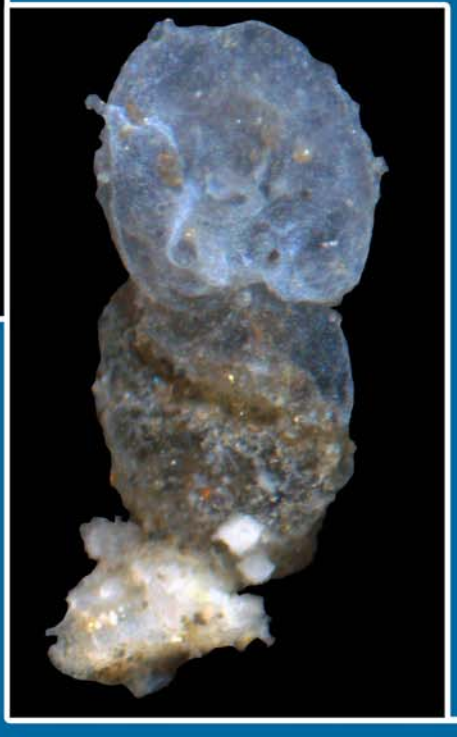
Chapter 6

The first *Osedax* (Annelida: Siboglinidae) described from the Southern Ocean



Photos by S. Taboada

Chapter 6

The first *Osedax* (Annelida: Siboglinidae) described from the Southern Ocean

Abstract. So far, members in the genus *Osedax*, commonly known as 'bone-eating worms', have only been reported from the northern hemisphere. Although they have only been found in the Pacific Ocean and the North Sea, these organisms are postulated to occur world-wide. Here we formally describe the first *Osedax* from the southern hemisphere, collected at an experimentally implanted whale bone from the shallow Antarctic waters of Deception Island (South Shetland Islands). This new species is characterized by its pale palps lacking pinnules, gelatinous hemispherical tube, and small size when compared with the previously reported *Osedax* operational taxonomic units (OTUs). Also, its presence in shallow waters (21 m depth) suggests that these organisms may play an important role in the bone degradation in the Antarctic shoreline context, where a broad list of vertebrates occur. Finally, we discuss the phylogenetic position of the new *Osedax* within its clade after analyses based on one nuclear (18S) and two mitochondrial (16S and COI) markers.

Introduction

Whale-falls and the invertebrate and microbial marine communities they host, are currently one of the most extraordinary and poorly understood habitats in the world. After the accidental discovery of these communities at a whale-carcass found in the eastern Pacific (Smith *et al*. 1989), a series of studies followed investigating the invertebrate fauna associated to natural and experimentally-implanted whale carcasses (*e.g.* Baco & Smith 2003, Smith & Baco 2003, Smith 2006, Braby *et al*. 2007, Lundsten *et al*. 2010). One of the principal conclusions derived from these studies is that polychaete annelids dominate these assemblages, which exploit the huge feeding resources that bones offer.

Among the polychaetes that thrive in these ephemeral resources, members of the genus *Osedax*, commonly known as 'bone-eating worms', have lately attracted a great deal of attention by different authors. These recently discovered siboglinids were originally described associated to a whale carcass at 2,891 m depth from the Monterey Bay Canyon (Rouse *et al*. 2004). These organisms are unusual sessile annelids lacking mouth and gut, displaying a marked sexual dimorphism, with harems of paedomorphic dwarf males hosted within the lumen of the female's tube (Rouse *et al.* 2004, 2008, Worsaae & Rouse 2010). Females of these animals live anchored to bones thanks to a ramified root system, obtaining nutrition via a symbiosis with heterotrophic bacteria that degrade organic compounds sequestered in the bone (Goffredi *et al*. 2005, 2007). Nutrition in these organisms, however, is not restricted to nutrient-rich cetacean bones since bones from other mammals, birds and fish have also proved to be suitable substrates (Jones *et al.* 2008, Kiel *et al.* 2010, Rouse *et al.* 2011). As for the reproductive strategy in *Osedax*, at least two species spawn lecithotrophic trocophore larvae, strategy suggested to allow these organisms dispersal and colonization of new appropriate substrates (Rouse *et al.* 2009). So far, the 25 *Osedax* operational taxonomic units (OTUs), considering named and undescribed species, occur in the Pacific as well as in the North Atlantic. They cover a wide bathymetric range (30 to 2,891 m), although the bulk of the genus has been described from deep waters (Vrijenhoek *et al*. 2009).

Despite the postulates that these organisms live world-wide (Glover *et al*. 2005), its occurrence in Antarctic waters has not been documented to date. With the aim of investigating the presence of *Osedax* species in the Southern Ocean, we experimentally implanted a fresh whale vertebra during one year in Port Foster, Deception Island (South Shetland Islands). Here we report the presence and the morphological description of *O.* **sp. nov.** 'Deception', the first Antarctic *Osedax* which is the also the shallowest OTU described so far. We also discuss its phylogenetic position within the frame of its clade, based on one nuclear (18S) and two mitochondrial (16S and COI) markers.

Material and Methods

Sample collection

The only specimen of *Osedax* **sp. nov.** 'Deception' was collected from a juvenile minke whale (*Balaenoptera acutorostrata*) caudal vertebra in Port Foster, Deception Island (South Shetland Islands, Antarctica). The bone was obtained from a juvenile beached carcass found in Asturias (Cantabric Sea, Spain) in May 2008. Vertebra was de-fleshed, frozen to -20ºC and shipped to Deception Island. There, the vertebra was experimentally implanted on the sea floor on January 2, 2009 in the area of Whalers Bay, 21 m depth, 62º 59.33' S; 60º 33.45' W (Figure 1; Sta. 1). The experimental mooring was kept in the water using an acoustic release (IXSEA OCEANO 500) connected to a large piece of ballast and a buoy, and was recovered on January 25, 2010 activating the acoustic release with a telecommand unit (IXSEA TT300 Mors). After retrieval, the bone was brought to the laboratory at the "Gabriel de Castilla" Spanish Antarctic Base (Deception Island), where it was placed in an aquarium containing 0.2-µm filtered seawater, and kept at ambient temperature (0 to 5ºC), with no additional oxygenation. Following some days of observation, a rounded tube with a living specimen of *O.* **sp. nov.** 'Deception' was noticed inside a 1 cm diameter hole in the bone. Prior to preservation, the animal was relaxed in 7% MgCl in fresh water, and photographed *in situ* (Figures 2A–B). Pictures from the living animal and its tube were also taken after removing it from the bone (Figures 2C–D). All pictures were obtained using a camera (Invenio 5S 5MPixel CMOS) adapted to a stereomicroscope (Zeiss Stemi 2000-C) and a light microscope (Zeiss PrimoStar). Photographs were edited using Adobe Photoshop CS4, making the background black and enhancing contrast.

Morphological and DNA analysis

The specimen was preserved in 95% ETOH and stored in -20ºC for DNA and standard morphology analysis. After preservation, pictures to measure the animal were taken using the camera adapted to the stereomicroscope and the light microscope mentioned above.

The molecular phylogenetic analyses were made with datasets from the sequences 18S, 16S and cytochrome *c* oxidase subunit I (COI). In total, 46 terminal taxa were included in the analyses, 26 from *Osedax*, 17 from other genera within Siboglinidae, and three outgroup taxa of which a spionid, *Malacoceros fuliginosus*, was used as root. In the Sabellidae outgroup, 18S and 16S from *Sabella pavonina* was used together with COI from *Sabella spallanzanii*. In the Oweniidae outgroup, 18S and COI from *Owenia fusiformis* was used together with 16S from *Myriochele* sp. Extraction of DNA from a piece of root was done with DNAeasy Tissue Kit (Qiagen) following the protocol supplied by the manufacturer. About 1800 bp of 18S, 500 bp of 16S, and 600 bp of COI were amplified. PCR mixtures contained ddH2O, 1 µl of each primer (10µM), 2 µl template DNA, and puReTaq Ready-To-Go PCR Beads (GE Healthcare) in a mixture of total 25 µl. The temperature profile was as follows: 96ºC/240s–(94ºC/30s–48ºC/30s–72ºC/60s)*45cycles–72ºC/480s. PCR products were purified with the

E.Z.N.A. Cycle-Pure Kit (Omega Bio-tek). Sequencing was performed by the Macrogen Sequencing System in Korea, on an ABI 3730XL DNA Analyser (Applied Biosystems), using the same primers as in Glover *et al*. (2005).

Type material is deposited in the Centre of Biodiversity Resources (CRBA, formerly Museum of Zoology) from the Faculty of Biology, University of Barcelona, Spain (CRBA-9621).

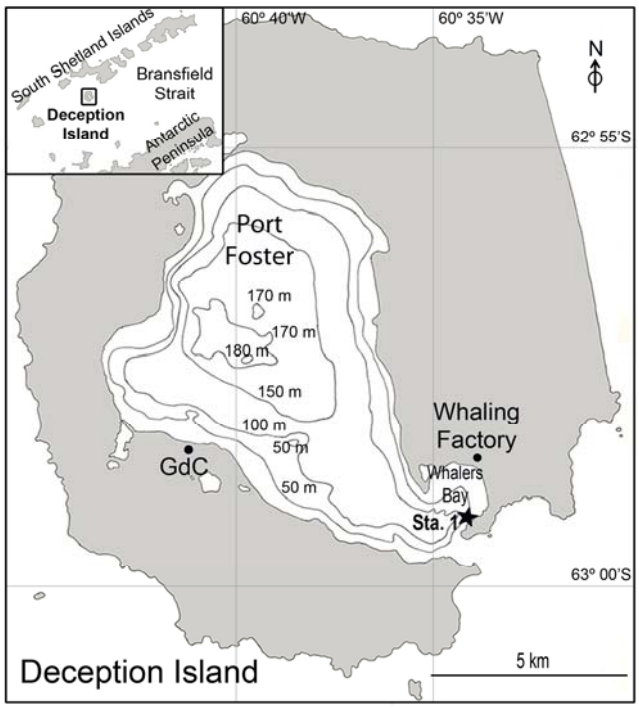


Figure 1. Map of Deception Island showing the sampling station (Sta. 1) where the experiment was implanted. GdC, "Gabriel de Castilla" Spanish Antarctic Base

Results

Material examined. Port Foster, Deception Island, South Shetland Islands, Antarctica, 62º 59.33' S; 60º 33.45' W, area of Whalers Bay, 21 m, from a minke whale (*Balaenoptera acutorostrata*) caudal vertebra (1 specimen) (Figure 1; Sta. 1). Holotype, mature adult female removed from its original tube also kept, (CRBA-9621), preserved in 95% ETOH stored at -20ºC. Material collected by S. Taboada, J. Cristobo, and C. Avila; January 25, 2010.

Description. Holotype, live specimen as four pale-translucent palps emerging from a hemispherical mucous tube (Figures 2A–B). Tube consisting in two hemispherical distinct parts: anterior or water-exposed part, transparent; posterior or inner-bone part, light-brown opaque (Figure 2C). Trunk region 0.6 mm long, 0.3 mm wide, whitish in live. Mouth and gut absent. Four smooth palps with no pinnules (Figure 2E), of equal length about 0.6 mm for about 50 µm wide (measures after preservation). After removing the animal from the bone, it detached palps from the base. No oviduct observed and no trace of any male. Lobulated ovisac 0.7 mm long, 0.8 mm wide, greenish in live. Palps, trunk, and ovisac becoming opaque white after preservation. Several spherical eggs (about 40) ranging 70–80 µm diameter, some of them released from ovisac after the specimen removal (Figure 2D).

Remarks. *Osedax* **sp. nov.** 'Deception' is the shallowest and smallest species collected so far. This species lacks pinnules in the palps, a character that has already been documented in six still undescribed OTUs (Table 1). However, *O.* **sp. nov.** 'Deception' differs from all them in the size (the smallest OTUs with no pinnules, *O.* nude-palp-C, *O.* nude-palp-D, and *O.* nude-palp-E, are 10 times larger than *O.* **sp. nov.** 'Deception'), in the color of the palps (pale-translucent instead of red), as well as in the bathymetric range where they occur (shallow water as opposed to more than 1,000 m depth). *Osedax* **sp. nov.** 'Deception' seems to have a tube resembling that of *O. frankpressi* Rouse, Goffredi & Vrijenhoek, 2004 and *O. mucofloris* Glover, Källström, Smith & Dahlgren, 2005, although both species have palps bearing pinnules and the palps coloration is diverse (Table 1).

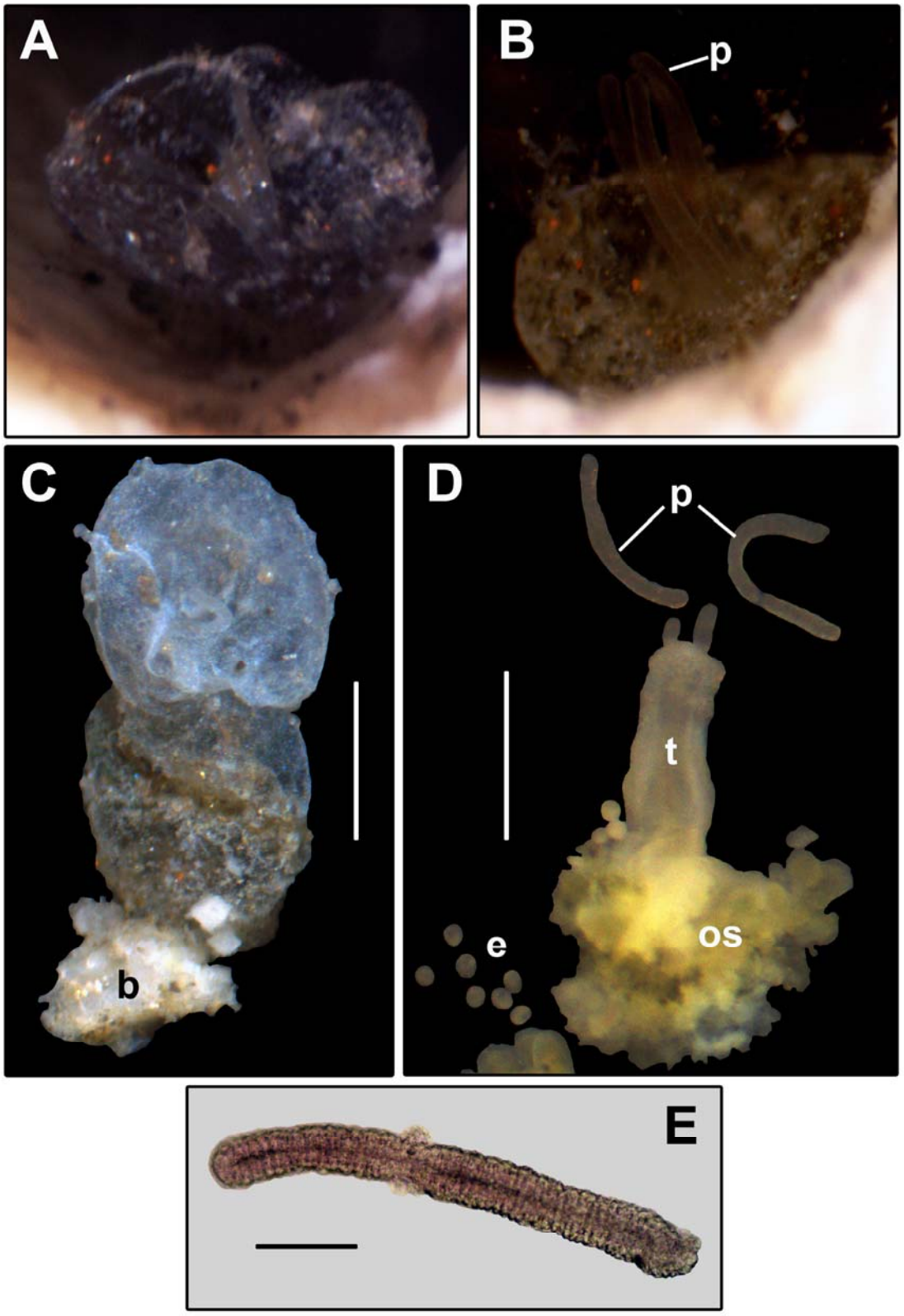


Figure 2. *Osedax* **sp. nov.** 'Deception'. **A.** Tube attached to the bone, specimen with palps retracted; **B.** Same as before but palps projecting out from the tube; **C.** Tube after removing the animal from the bone; **D.** Living specimen; **E.** Piece of detached nude palp under the light microscope. Scale bar: **C** =1 mm; **D** =0.5 mm; **E** =100 µm. b, bone; e, eggs; os, ovisac; p, palps; t, trunk

Discussion

Osedax **sp. nov.** 'Deception' is the shallowest species described in the genus, beating the former record by the North Sea *O. mucofloris* reported for 30 m depth (Dahlgren *et al*. 2006). Our finding also gives support to the idea that these organisms occur world-wide (Glover *et al.* 2005), since this is the first report of an *Osedax* member for the southern hemisphere. The type locality of *O.* **sp. nov.** 'Deception', Port Foster, Deception Island's bay (South Shetland Islands), is an enclosed drowned volcano caldera with a maximum depth of 180 m, only connected to the open ocean (the Bransfield Sea) by a narrow and shallow opening with a very limited water exchange (Lenn *et al*. 2003). Whether colonization of the implanted bone by *O.* **sp. nov.** 'Deception' came from outside the bay or from stable populations that may thrive inside Port Foster remains unknown. In this sense, it is worth mentioning that whale bones constitute a relatively common hard substrate in Deception Island that has been systematically overlooked for years. These bones, very frequent and conspicuous at Whalers Bay shallow-waters (authors' personal observations), have its origin in the Norwegian-Chilean whaling factory that operated in the area in the early 20th century (Dibbern 2010).

The first two *Osedax* species were described occurring in naturally implanted whale-fall remains from deep waters off the Monterey Bay Canyon (Rouse *et al.* 2004). Since then, 23 other OTUs have been discovered, with the majority of them occurring down to 385 m (Table 1). Only two species, *O. mucofloris* and *O. japonicus* Fujikura, Fujiwara & Kawato, 2006, have been collected in shallow-water environments (30 and 224 m depth, respectively). Several reasons may explain the predominant deep-water distribution of these organisms. On the one hand, there has been a clear biased effort surveying deep waters rather than near-shore environments (Table 1). Also, shallow-waters seem to have inherent characteristics that turn into difficulties for the colonization of bones by *Osedax* (Dahlgren *et al.* 2006, Smith 2006). As opposed to deep-water environments, high rates of sedimentation linked to sporadic episodes of fluvial sediment transport, can be frequent at shallow near-shore areas, and can ultimately affect the settlement of these sedentary organisms. This is especially relevant in Port Foster, since both seasonal fluvial sediment transport during the summer period (as a consequence of ice melting), and aeolian processes that entrain gravel and sand, remarkably contribute to increase the turbidity in the bay (Gray *et al*. 2003). Apart from these abiotic factors, others such as the presence of active and abundant scavengers can also affect the colonization of bones. The shallow-water benthos of Whalers Bay is dominated by a few and abundant scavenger species (Barnes *et al*. 2008; author's personal observations): the echinoderms *Sterechinus neumayeri*, *Ophionotus victoriae*, and *Odontaster validus*, the nemertean *Parborlasia corrugatus*, and the amphipod *Cheirimedon femoratus*. *Odontaster validus* and *P. corrugatus* are also recognized as two voracious predators which prey on a wide range of items (Dearborn 1965, McClintock *et al*. 1994). We then hypothesize that the only specimen from *O.* **sp. nov.** 'Deception' that developed in the experimentally implanted bone, succeeded because it settled and colonized one of the holes in the bone, being thus protected from abiotic disturbances and predation pressure of common scavengers and predators in the area.

Table 1. Comparative list of characters of *Osedax* OTUs

Taxa	Depth (m)	Size[a]	Color palps	Pinnules	Tube shape	References
O. rubiplumus	1820–2893	59	red	yes	rigid, cylindrical	Rouse *et al*. 2004
O. frankpressi	1820–2893	23	red, striped	yes	gelatinous, hemispherical	Rouse *et al*. 2004
O. mucofloris	30–125	14	white to pink	yes	gelatinous, hemispherical	Glover *et al*. 2005
O. japonicus	224–250	4–18	pink/red	yes	gelatinous, cylindrical	Fujikura *et al.* 2006
O. roseus	633–1820	24	red, striped	yes	transparent, cylindrical	Rouse *et al*. 2008
spiral	2893	25	—	—	?	Braby *et al.* 2007
yellow collar	385	18	pale	yes	?	Braby *et al.* 2007
orange collar	385–1018	18	pale	yes	?	Braby *et al.* 2007
nude-palp-A	1820	25	red	no	?	Jones *et al.* 2008
nude-palp-B	2893	25	red	no	?	Jones *et al.* 2008
nude-palp-C	1018	12	red	no	?	Rouse *et al.* 2009
nude-palp-D	1018–1820	12	red	no	?	Vrijenhoek *et al.* 2009
nude-palp-E	1018	12	red	no	?	Vrijenhoek *et al.* 2009
nude-palp-F	2893	18	red	no	?	Vrijenhoek *et al.* 2009
white collar	1018	6	red, striped	yes	?	Vrijenhoek *et al.* 2009
yellow patch	633–1018	5	pale	yes	?	Vrijenhoek *et al.* 2009
green palp	1820	3	red/green	?	?	Vrijenhoek *et al.* 2009
Sagami 1–8	—	—	—	—	—	Unpublished results[b]
sp. nov. 'Deception'	21	1.2	pale	no	gelatinous, hemispherical	This report

[a]Maximum length of trunk and crown (mm) after preservation; [b]Only nucleotide sequences available at the National Centre for Biotechnology Information (www.ncbi.nlm.nih.gov)

The phylogenetic analyses indicate that *O.* **sp. nov.** 'Deception' is sister to clade I, which contains taxa bearing pinnules in the palps (Figure 3). It is noteworthy that despite *O.* **sp. nov.** 'Deception' has palps devoid of pinnules, it does not fall in the well-supported clade II (nude-palp OTUs) formerly described by Vrijenhoek *et al*. (2009). Additional specimens should be investigated in order to cover possible intraspecific morphological variations and also to deepen into the phylogenetic conclusions.

The discovery of *O.* **sp. nov.** 'Deception' draws a new and promising perspective in the study of these organisms inhabiting near-shore Antarctic waters. So far, several bone substrates have proved their suitability hosting these particular animals. Apart from whale bones (investigated in the present study as well as in most of the studies conducted previously), cattle, bird, and even fish bones are potential substrates that can sustain *Osedax* (Jones *et al.* 2008, Kiel *et al.* 2010, Rouse *et al.* 2011). Thus, we predict that, despite the colonizing difficulties discussed above, chances to find *Osedax* in shallow waters may be high in the Southern Ocean, since there is a broad potential list of species that frequent the Antarctic shoreline (*e.g.* cetaceans, pinnepedes, penguins) whose bones could be used as a suitable substrate. Future studies will be addressed to confirm this hypothesis.

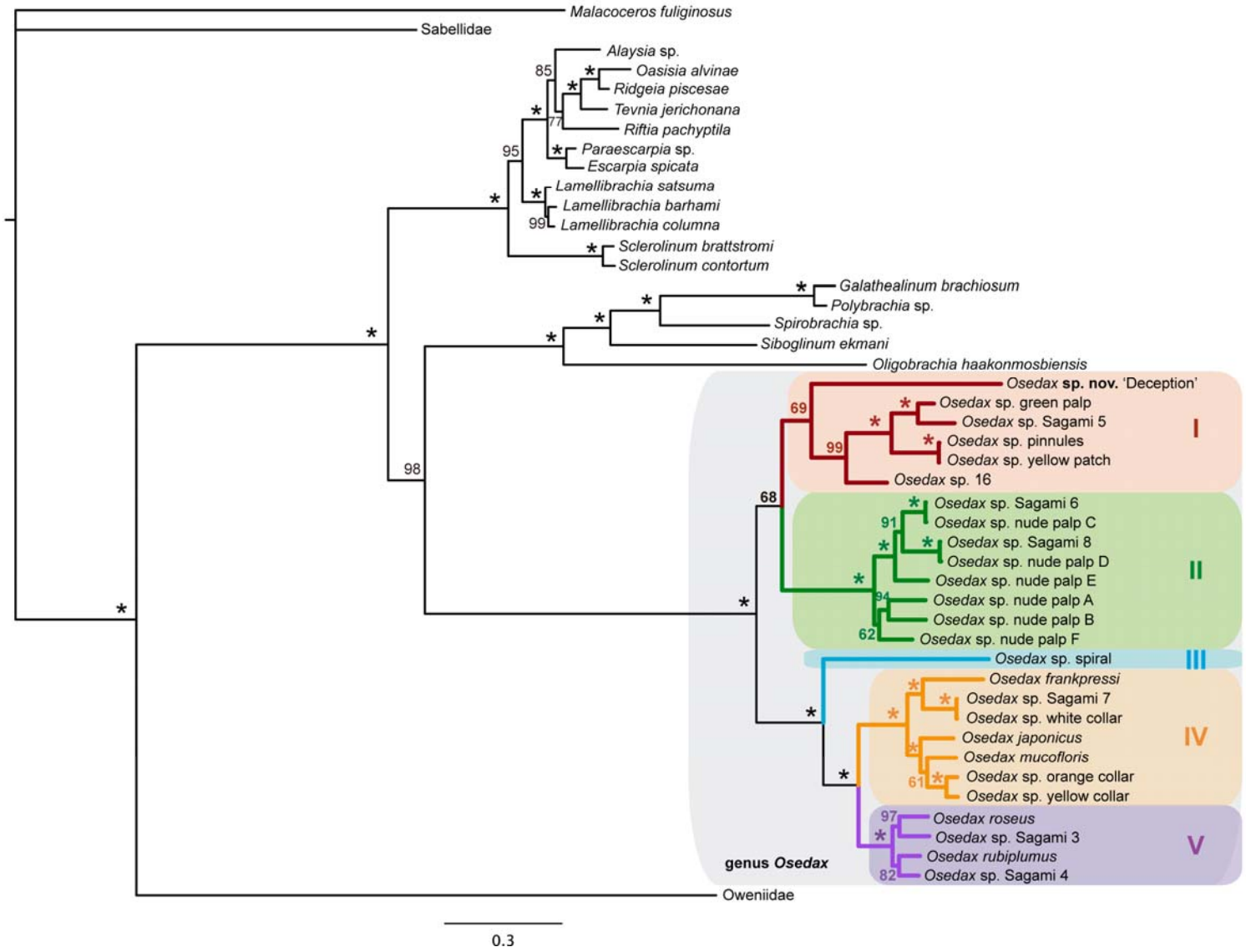


Figure 3. Phylogenetic analyses of a combined dataset of 16S, COI, and H3. Majority rule consensus tree from the Bayesian analyses with posterior probability values after analyses in MrBayes; *indicates support value of 95% or above

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General Discussion and Conclusions

Photo by S. Taboada

General Discussion

The studies presented in this PhD dissertation are focused on Antarctic marine benthic invertebrates. The three different approaches here considered (chemical ecology, bioactivity, and biodiversity) need to be taken separately, and this will be done following the order of the list of chapters. Within this general discussion I will comment some of the most significant achievements for each of the chapters without deepen too much in the most particular aspects, since they are thoroughly discussed in the respective papers.

Chemical ecology of marine benthic organisms in Antarctic and sub-Antarctic waters (Papers I-II)

Compared with tropical and temperate ecosystems, SO marine natural products have been scarcely studied, in part due to the remoteness and the inherent climatologic difficulties to sample in Antarctic waters (Lebar *et al*. 2007, **Paper I**). Also, former arguments considering the SO as impoverished in both terms of biodiversity and chemodiversity (challenged by Amsler *et al*. 2000a) did not allow the interests on chemical ecology to grow in this region. Despite these and other difficulties, over the last years, chemical studies on marine benthic invertebrates (predominantly shallow-water) have expanded mostly investigating organisms from the McMurdo Sound (Ross Sea) and the Western Antarctic Peninsula, and to a lesser extent from the deep-waters of the Weddell Sea (see McClintock *et al*. 2010, **Paper I**).

The information reviewed in **Paper I** provides an overview of what is known (up to May 2007) on the chemical ecology of SO marine organisms. From the nearly 300 natural products described from these waters, we include the information on the chemical structure, location in the organism, origin, bioactivity, and ecological role(s). Although insufficiently studied, several laboratory experiments using sympatric species have demonstrated that natural products are involved in mediating ecological relationships in many different groups of Antarctic organisms. Ecologically relevant experimentation greatly contributes to enhance the knowledge on the ecosystem chemical interactions, and this approach is particularly important in the SO where most of the communities seem to be ruled by biological factors (Dayton *et al*. 1974, Arntz *et al*. 1994). Below, I highlight the major conclusions achieved in the review. Firstly, I briefly comment some aspects for every taxonomic group making special emphasis on what is known about the ecological roles that natural products play. The most important

contributions published posterior to May 2007 are included in the discussion, except for the information included in **Paper II** that is discussed in a separate section.

- Macroalgae dominate shallow marine communities on hard substrates along the Antarctic continent. This group of organisms represents the most important source for natural products in Antarctic waters with more than 90 species investigated. Although ecological information on some macroalgal natural products is already available, mainly focusing on feeding deterrence assays using sympatric potential herbivores (*e.g.* Amsler *et al*. 2002, Huang *et al*. 2006), the ecological role of many of the described compounds still remains unknown.

- Sponges are a very speciose group in Antarctic waters and, along with cnidarians and bryozoans, play an important role structuring the benthic communities (Dayton *et al*. 1974, Clarke & Johnston 2003, Brandt *et al*. 2007a). Despite being one of the major targets of chemical investigations in the SO and the group with the highest number of examples investigating the ecological functions of their natural products (see **Paper I** and references herein), a lot of work still remains to be done. Recently, three studies using ecologically relevant approaches have increased remarkably the information available for Antarctic sponges: Amsler *et al*. (2009) evaluated the effects of sponge extracts on a sympatric amphipod; Peters *et al.* (2009) investigated the palatability of several shallow-water sponges against the sea star *Odontaster validus*; and more recently Peters *et al*. (2010) analyzed the bioactivity displayed by extracts of a similar array of sponges against sympatric microorganisms.

- As previously underlined, cnidarians and bryozoans constitute two important groups in the SO benthic communities. However, both groups have been scarcely investigated and largely ignored in chemical ecology studies, leading to just 8 cnidarians and 10 bryozoans chemically studied. So far, only 3 shallow-water soft-corals and one deep-water gorgonian have been used in antipredatory tests against *O. validus* (Slattery & McClintock 1995, Iken & Baker 2003).

- Molluscs are also a very diverse group in the SO waters (Clarke & Johnston 2003, De Broyer *et al*. 2011). However, although some Antarctic molluscs have been studied in greater detail (*e.g. Austrodoris kerguelenensis, Bathydoris hodgsoni*; see discussion in **Paper I**), many species still remain to be further investigated. In addition, more accurate investigations should be conducted in terms of histological localization of the chemical defensive compounds as it has been done in Mollusca from other latitudes (Wägele *et al*. 2006).

- The research conducted with Antarctic echinoderms suggests that bioactive metabolites are very common in a large number of species, research that has particularly focused on saponin-related compounds [see discussion in **Paper I**; more recently the papers by Antonov *et al*. (2008, 2009, 2011) have increased

the number of known compounds of this nature]. Chemical studies have investigated 36 echinoderm species (including a recently studied holothurian posterior to **Paper I**; Antonov *et al*. 2009) chiefly focusing on sea stars, some of them proving feeding deterrence properties against *O. validus* (McClintock *et al*. 2003, 2006). Although echinoderms seem to be more studied than other groups, relevant ecological experiments are lacking.

- Up to 2007, only 7 tunicates had been chemically investigated in the SO and just 2 of them had been used in ecologically relevant experiments (*e.g.* McClintock & Baker 1997b, McClintock *et al*. 2004). However, two recent studies investigating several shallow-water solitary and colonial species (Koplovitz *et al*. 2009, 2011), as well as another study on two deep-water species from the genus *Aplidium* (Núñez-Pons *et al*. 2010), have increased considerably the knowledge in the group. Interestingly, some results have confirmed the complementary role that acidic tunics may play in some species deterring potential sympatric sea star predators (McClintock *et al*. 2004, Koplovitz *et al*. 2009).

- As for the rest of the groups investigated in Antarctic waters, only the nemertean *Parborlasia corrugatus*, the brachiopod *Liothyrella uva*, and the crustacean *Glyptonotus antarcticus*, have been studied in ecologically relevant experiments (Heine *et al*. 1991, McClintock *et al*. 1993, 2003).

The review in **Paper I** demonstrates that Antarctic benthic organisms are a rich and diverse source of natural products, with great interest from both ecological and pharmacological viewpoints. However, the knowledge on natural products in the SO is still far for being complete and thus far from being compared on equal terms with other geographical areas. Suffice it to say that from the more than 22,000 marine natural compounds described up to 2011 (MarinLit database) just *ca.* 300 were described from Antarctic waters.

Similarly as what happens for tropical and temperate waters, predation has been the most extensively explored ecological mechanism. These results, however, appear to be insufficient. It is thus necessary to increase the number of ecologically relevant experiments and to develop more realistic assays including field experiments. Apart from the research on predator-prey interactions, other mechanisms such as competition or antifouling activity, among others, should be explored too, since secondary metabolites may play different defensive functions within the ecosystem (Paul 1992). Further studies should also be directed to identify and locate the molecules responsible for the ecological activities (*e.g.* Núñez-Pons *et al*. 2010) as well as investigating on the origin of natural products (König *et al*. 2006).

For the SO chemical ecology, the existing gap of information will only be filled by increasing the number of species investigated across the different phyla as well as by exploring new areas that still remain unknown. However, all this information needs to be integrated into a broader and more complex framework including, through interdisciplinary approaches, the physical and biological characteristics of the

environment where organisms occur (Hay 1996, Paul *et al*. 2011). Only when all these different sources of information will be obtained and integrated we will be able to understand how the communities in the SO work. When this will be achieved, it will be then possible to predict, for instance, how climatic changes may affect these communities (Pörtner *et al*. 2007).

Paper II is an original contribution in the chemical ecology field. In this study we deepen in the predator-prey interactions of a wide number of marine benthic invertebrate species (55) from 9 different phyla against a common sympatric predator, the circumpolar sea star *O. validus*. Two main aspects make **Paper II** remarkable when compared with earlier literature: (i) it deals with deep-water marine invertebrates (most of them investigated for the first time in the literature); and (ii) the areas where the organisms investigated were collected (eastern Weddell Sea and Bouvet Island) are two poorly known areas in terms of chemical ecology studies.

As it is mentioned in **Paper II**, comparisons with previous chemical ecology contributions in the SO are difficult. In spite of that, our results greatly contribute to increase the knowledge in the antipredatory field in groups such as Porifera, Cnidaria, Bryozoa, Mollusca, Chordata, Echinodermata, and to a lesser extent Annelida (see discussion in **Paper II**). Also remarkable are some of the results obtained after testing the Optimal Defense Theory (ODT; Rhoades 1979). According to this theory, potential preys under the pressure of sea star predation should allocate defensive metabolites in their most exposed tissues, owing to the sea stars extraoral feeding mode. In our survey, a total of 25 species were dissected into parts and further analyzed under the light of the ODT. Of the 7 dissected sponges, *Cinachyra barbata* and *Tedania oxeata* accumulated chemical defenses in their outermost parts. Of the 4 holothurians dissected into parts, only the tentacles of *Ekmocucumis steineri* showed significant feeding repellence against *O. validus*; this defensive strategy seems to be explained by the holothurian feeding habits (Gutt 1991). As for molluscs, some results from the 5 species dissected into parts, seem to stress the role that acid secretions from the mantle may play in deterring potential predators, a protective mechanism that has already been suggested for some ascidians with acid tunic (McClintock *et al*. 2004, Koplovitz *et al*. 2009). Apart from the comments related to the ODT, a last consideration should also be given for the polychaete *Polyeunoa laevis*, a species commonly occurring in symbiotic association with gorgonians from the genus *Thouarella* (Pettibone 1969; authors' personal observations). Our results seem to indicate that a chemically-based commensalistic relationship may exist between the polychaete and two of the gorgonians where it occurred, similarly as what has recently been reported for an octocoral and its amphipod host in the Japanese coast (Kumagai 2008).

As a summary for **Paper II**, our results show that more than half (53%) of the deep-water Antarctic and sub-Antarctic benthic marine invertebrates tested are chemically protected against predation from *O. validus*. This confirms that chemical defenses in marine sessile and sluggish invertebrates play an important role in predator-prey interactions in these ecosystems. However, as stated in **Paper I**, other than in antipredatory interactions, secondary metabolites may fulfill other ecological

roles in the ecosystem context that should also be investigated (Paul 1992). In this sense, it is worth mentioning that our research group is intensively working to progress on this holistic approach. In the frame of the ECOQUIM and ACTIQUIM projects our group has been working on establishing different sources of ecological activity comprising defense against macro- and micropredators, toxicity towards small-sized organisms and larvae, cytotoxicity, and antifouling activity, leading to a preliminary model integrating all the chemically-mediated interactions in the Antarctic benthos (Figuerola *et al*. 2012).

Bioactivity: Antitumoral potential in Antarctic and sub-Antarctic waters (Paper III)

Over the last years, marine pharmacology has experienced a renaissance with the recent release of various marine-derived compounds (Molinski *et al.* 2009), and also because several of the future anticancer drugs currently in clinical and pre-clinical trials have their origin in marine organisms (Newman & Cragg 2004, Simmons *et al*. 2005, Mayer & Gustafson 2008). The majority of these natural products have been originally described from tropical and temperate waters, areas that have focused the major prospecting efforts so far (see Blunt *et al*. 2011 and previous reviews). However, as proved in **Paper III**, antitumoral activity in benthic organisms appears to be a very promising research field specially when prospecting remote and unknown areas such as Antarctic and sub-Antarctic waters. This is particularly relevant in the SO since its waters have been almost isolated for several million years leading to a high degree of endemicity for some groups (Brandt & Gutt 2011).

Paper III represents the largest pharmacological study ever carried out in Antarctic and sub-Antarctic waters. Despite the bias after a qualitative sampling, the majority of active antitumoral results were recorded from strict sessile invertebrates (sponges, cnidarians, and tunicates) that in turn were the most represented groups in number of assayed species. Our results are in agreement with what has been described for other geographic areas, where sessile and sluggish organisms provide the highest proportion of cytotoxic compounds (Schmitz *et al*. 1993, Munro *et al*.1999). Only bryozoans, the second group in number of species tested within our survey, appear not to follow this tendency. Despite the relatively high diversity of bryozoans in the SO as well as in the rest of the seas, this group has been scarcely investigated for natural products (Sharp *et al*. 2007, **Paper I**). Nevertheless, there are remarkable examples for this group in other areas. Such is the case of bryostatin 1, isolated from *Bugula neritina*, one of the strongest naturally-derived antitumoral compounds known (Pettit *et al*. 1982).

Undoubtedly, the most remarkable results within our survey are the ones obtained for *Aplidium cyaneum*. Some of the new alkaloids isolated from this species (aplycianins A-F) displayed a strong antitumoral and antimitotic activity (Reyes *et al*. 2008) and were patented by PharmaMar SA. Interestingly, another example in the genus *Aplidium* (*A. falklandicum*), confirms this genus as a potential resource for antitumoral compounds in Antarctic waters, as previously recognized in other areas (McKee *et al.* 1998, Tourneau *et al*. 2007). Apart from these two noteworthy examples, it is important to highlight the importance of Chordata as the phylum with the highest number of species displaying antitumoral activity in our experiments. Other than tunicates, several other species from the phyla Porifera, Cnidaria, Echinodermata, and Annelida also showed relevant antitumoral effects, and a comprehensive discussion is given for all of them in **Paper III**.

In our study, the two *Latrunculia brevis* specimens collected from two different sampling stations displayed a similar antitumoral activity. It is common that individuals from the same species possess similar activity regardless of the geographical area, as it is has previously reported, for instance, for the ascidian *Ecteinascidia turbinata* (Munro *et al*. 1987). However, we also found species that showed antitumoral activity in one sampling station and did not display any antitumoral effect in the rest of the stations where they were collected (see **Paper III**). Whether this situation is common or rare in nature is still to be established, and it could be related, among other reasons, to the presence of symbionts (König *et al*. 2006). We suggest, therefore, that it is important to bioprospect different areas even when sampling similar or the same species, since unexpected results may be obtained.

One of the major achievements for **Paper III** is that it greatly contributes to increase the pharmacological information for the SO area (eastern Weddell Sea and South Shetland Islands) and another poorly known area such as the Bouvet Island (sub-Antarctic). As far as we know, the only previous comparable study was conducted by Blunt *et al*. (1990) in the shallow-waters of the Ross Sea. Remarkably, in their study, although using a considerably smaller number of species, the main active phyla are coincident with our results. Another major achievement for our study is that most of the species assayed were collected from deep-water, as opposed to the few previous studies on antitumoral activity conducted with Antarctic organisms. Samples showing antitumoral activity in our survey were predominantly found at depths ranging 250–500 m in the eastern Weddell Sea and Bouvet Island, whereas the active samples from the South Shetland Islands were found shallower than 100 m depth. However, no conclusion can be reached since during our investigation there was not an homogeneous sampling effort across the bathymetric range. Similarly, the antitumoral activity found in the three different surveyed areas proportionally correlated with the sampling effort for each area (eastern Weddell Sea>South Shetland Islands>Bouvet Island).

Results discussed in **Paper III** uncover the high potential of antitumoral pharmacology in both Antarctic and sub-Antarctic waters. These results are in agreement with the diverse array of natural products described so far for the SO region (Lebar *et al.* 2007, **Paper I**), which is in part correlated with the high biodiversity of sessile and sluggish benthic suspension feeders described for these waters (Dayton *et al*. 1974, Clarke & Johnston 2003, Brandt *et al*. 2007a). Our results should encourage

others to continue prospecting in poorly known areas such the ones here surveyed and also focus on the deep water organisms since these organisms, due to the extreme environmental conditions they suffer, have higher probabilities to develop structurally unique metabolites (Skropeta 2008).

Biodiversity: new polychaetes associated to whale bones (Papers IV-VI)

Despite the extraordinary scientific efforts to know the polychaete benthic fauna Western Antarctic Peninsula in the last decades, leading to a relatively complete background (see Barnes *et al*. 2008, Sicinski *et al*. 2011), still new and interesting organisms are being discovered (**Papers IV-VI**). In our case, these new discoveries are closely related to the study of previously overlooked substrates such as whale bones, substrates that have lately captured a great interest in other geographic areas (*e.g*. Rouse *et al*. 2004). The study of the marine invertebrate communities associated to whale-falls is predicted to be even more intriguing in areas such as the SO, not only owing to the important role that natural whale remains may play in this context (areas such as the Western Antarctic Peninsula are highly haunted by several species of whales; Friedlander *et al*. 2006), but also because the SO has remained nearly isolated for several million years (Scher & Martin 2006, Lagabrielle *et al*. 2009). Thus, research on these particular invertebrate communities offers an excellent opportunity to establish interesting comparisons with communities from other areas.

Results presented in **Papers IV-VI** are the first obtained from an experimentally implanted whale bone in Antarctica. Just to briefly remind some important experimental data, organisms described in these papers were collected from a fresh whale bone experimentally deployed in Whalers Bay (Deception Island) and also from an old bone collected from nearby area.

Despite the fact that the three new polychaetes in **Papers IV-V** (*Cirratulus balaenophilus*, *Ophryotrocha* **sp. nov.** 1, and *O.* **sp. nov.** 2) are originally described from whale remains, they are not suggested to be whale bone endemics. Owing to the relatively high abundance reported for *O.* **sp. nov.** 2 and *C. balaenophilus* in the fresh bone from Whalers Bay, both species are proposed to be shallow-water opportunistic species. Thus, other than associated to fresh whale bones, we hypothesize that these species may also be found in other shallow-water, organic-enriched environments from the South Shetland Islands, similarly to what has already been observed for other species in the McMurdo Sound area (Ross Sea): benthic assemblages taken in a highly perturbed area in front of the McMurdo Station have reported high densities of opportunistic polychaetes (Lenihan & Oliver 1995, Lenihan *et al*. 2003, Conlan *et al*. 2004). Apart from these anthropogenically organic-enriched areas, other shallow-water

environments could also host these opportunistic polychaetes. One of such environments are the natural patches created in the benthos after the combined effects of ice-scouring and the subsequent accumulation and decomposition of organic matter. These patches, recently described by Powell *et al*. (2012) but previously observed by Richardson & Hedgpeth (1977), host sulfur-oxidizing bacterial mats and could therefore promote the occurrence of *O.* **sp. nov.** 2 and/or *C. balaenophilus* (see below). In this sense, it is important to note that the presence of bacterial mats often correlates with the presence of opportunistic *Ophryotrocha* (*e.g.* Wiklund *et al*. 2009a,b).

Regarding the trophic requirements of the species described in **Papers IV-V**, although no direct feeding observations or fecal pellets analyses were conducted for any of them, we hypothesize that *C. balaenophilus*, *O.* **sp. nov.** 1, and *O.* **sp. nov.** 2 could rely at least part of their diet feeding on the filamentous bacteria that were observed in the fresh bone. This feeding strategy has also been observed in different polychaetes occurring in high abundances in other whale-falls (Glover *et al.* 2005, Wiklund *et al*. 2009b,c).

As for the new *Osedax* described in **Paper VI** some important remarks should be given. Our results confirm the presence in the SO (and thus in the southern hemisphere) of these organisms that so far have only been described in the northern hemisphere. It is highly remarkable that our new *Osedax* is the shallowest in the genus beating the former record by the North Sea *O. mucofloris*, reported for 30 m depth (Dahlgren *et al*. 2006). The bulk of previous studies reporting the presence of *Osedax* have mainly focused on deep water rather than near-shore environments (see Vrijenhoek *et al.* 2009 and references herein), which is in part explained by the fact that some inherent factors of shallow-water environments difficult the bone colonization by *Osedax* (Dahlgren *et al.* 2006, Smith 2006). The description of the new *Osedax* from Deception Island, however, opens a new perspective in the study of these organisms inhabiting the SO shallow waters.

Our results in **Papers IV-VI** confirm the study of SO communities associated to whale bones as a very promising research field. Research on these communities will certainly expand over the next years since other similar experiments are currently ongoing (A.G. Glover & T.G. Dahlgren pers. comm.; author's data). Further, in the near future, the great importance that the genus *Ophryotrocha* play in the SO whale-falls context will be confirmed with the description of several new deep-water species (H. Wiklund pers. comm.). Other than whale-falls, it is important to remind that a wide array of vertebrates live (and die) in the Antarctic shorelines (*e.g.* pinnipeds, penguins), which means that there is considerable potential amount of bones accumulating in the marine benthos. Since some of the species originally described from whale remains are known to occur also in other type of bones (Jones *et al.* 2008, Kiel *et al.* 2010, Rouse *et al*. 2011), we suggest that invertebrate communities developing in SO bones may play a more important ecological role than previously expected. We predict that, in the near future, most of the processes and patterns involved in these communities will be revealed and this will help to understand how the inputs of organic matter captured in the bones are recycled into the Antarctic trophic web.

Final Conclusions

The final conclusions in the present PhD dissertation are summarized below in a brief and concise manner.

- Antarctic organisms, although scarcely investigated when compared with tropical and temperate areas, are rich and diverse in marine natural products. The ecological roles of the different compounds have been scarcely studied in the majority of groups.

- Deep-water Antarctic and sub-Antarctic marine benthic invertebrates are chemically protected against the sea star *Odontaster validus*, a common and sympatric predator with circumpolar distribution. Some of the investigated benthic organisms locate their defensive secondary metabolites in their most exposed tissues, which agrees with the postulates of the Optimal Defense Theory.

- Antarctic and sub-Antarctic marine benthic invertebrates have a high antitumoral potential. The most remarkable results are those provided by the colonial ascidian *Aplidium cyaneum*.

- Invertebrate communities associated to whale remains play an important role in the Southern Ocean. The new species found in our experiment indicate that these overlooked substrates deserve further investigations. The description of two new *Ophryotrocha* suggests this is an important clade in organic-enriched Southern Ocean environments. *Cirratulus balaenophilus* sp. nov. is also suggested to live associated to nutrient-rich environments. With the description of a new *Osedax* species it is verified that these organisms also occur in the southern hemisphere.

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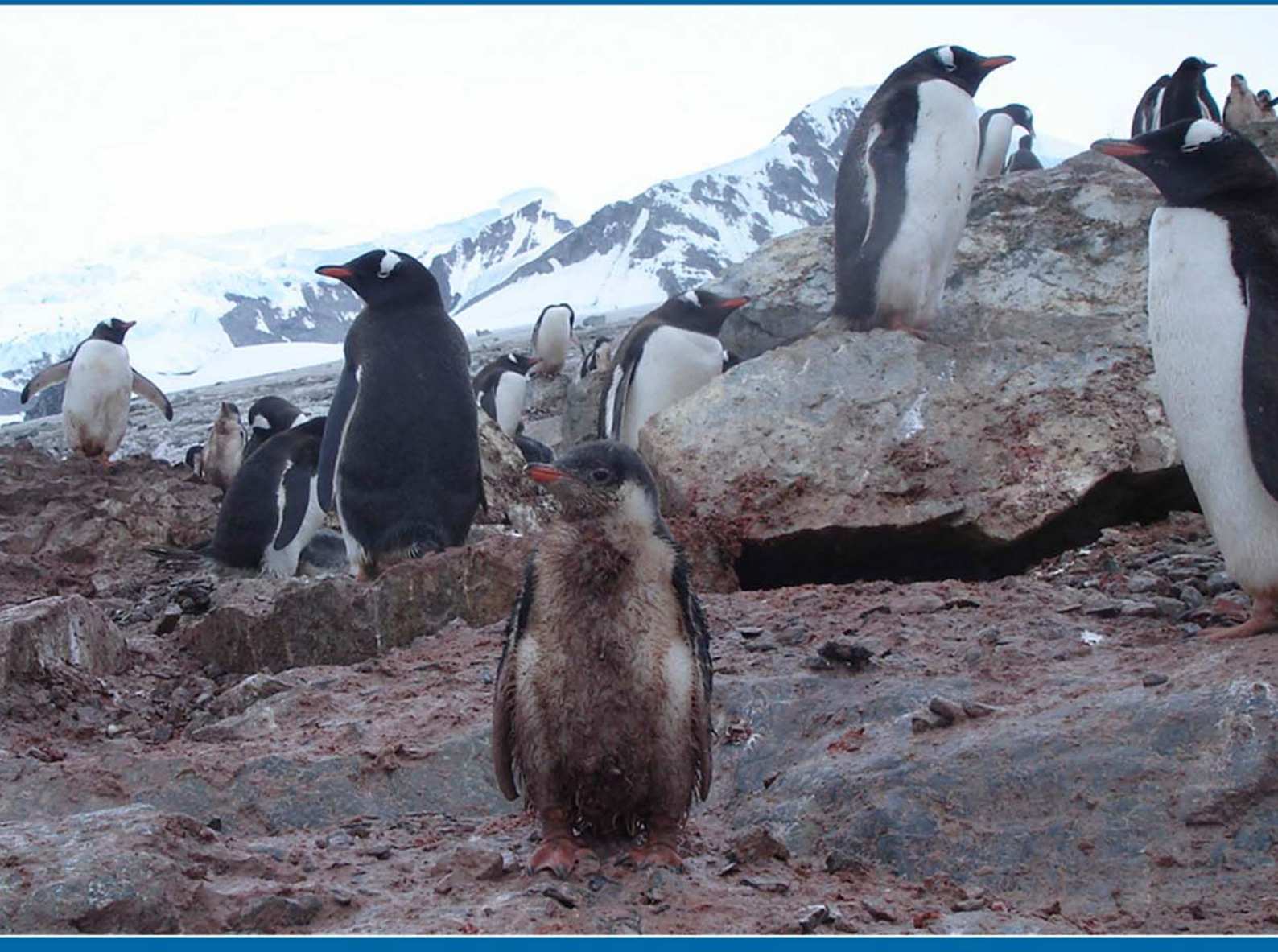

Photo by S. Taboada

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Resumen

Photo by S. Taboada

Introducción General

Los invertebrados bentónicos del Océano Austral

La Antártida da cobijo a una fauna terrestre y marina única en la Tierra. Las costas de este continente están bañadas por el Océano Austral (OA), cuyas aguas de cerca de 35 millones de km^2 (se trata del penúltimo océano en extensión después del Océano Ártico) han sido sometidas a las más extremas condiciones durante millones de años. Debido a su localización en el polo sur, el OA es un océano marcadamente estacional. No obstante, las particulares características actuales de este océano no están únicamente explicadas por esta extrema estacionalidad. Como sucede en cualquier otra área del planeta, la fauna que aquí encontramos está influenciada por una combinación de factores evolutivos con efectos a largo y corto plazo, así como por factores ecológicos. A una escala de tiempo mayor, la fauna existente refleja la influencia de los movimientos de placas tectónicas, los cambios climáticos, los cambios oceanográficos, las invasiones y los eventos de radiación/extinción (Arntz *et al*. 1994, Clarke & Johnston 2003). En una escala menor de tiempo, los organismos están sometidos a factores ecológicos tales como la depredación, la competencia, las características del hábitat y la disponibilidad de alimento (Dayton *et al*. 1994, Arntz *et al*. 1994, Amsler *et al*. 2001a, Clarke & Johnston 2003, Barnes & Conlan 2007). Todos estos factores han contribuido a conformar la fauna de invertebrados marinos bentónicos que actualmente existe, fauna muy bien adaptada a las duras condiciones que predominan en el OA (Brandt & Gutt 2011).

Un océano prácticamente aislado

Algunos factores participan activamente en el aislamiento del OA de las masas de agua que lo rodean. Uno de estos factores es la temperatura del agua del mar, más fría que en ningún otro lugar de la Tierra, habiendo además permanecido relativamente constante a lo largo de millones de años (Zachos *et al*. 2001, Pörtner *et al*. 2007). El OA comprende las aguas al sur del Frente Polar Antártico o Convergencia Antártica (Figura 1), una franja de agua bien definida que marca la zona más al norte hasta donde extiende el agua superficial fría y densa que no se puede mezclar con las masas de agua circundantes, significativamente más calientes y menos densas (Moore *et al*. 1999). La temperatura del agua puede variar entre el punto de congelación para el agua marina (-1.8ºC) en el Mar de Weddell y el Mar de Ross, y los +2.0ºC que el agua alcanza en las aguas del Este de la Antártida (Brandt & Gutt 2011),

aunque estos valores para aguas superficiales pueden ser más elevados en otras áreas (Barnes *et al*. 2006).

A pesar de los valores relativamente constantes y bajos que la temperatura del agua ha mantenido durante un prolongado espacio de tiempo, esto no impidió la evolución de una rica y especializada fauna bentónica (Clarke 1988, Arntz *et al*. 1994). De hecho, en estas aguas se desarrollaron invertebrados marinos altamente estenotermos en comparación con especies de otras áreas geográficas (Pörtner *et al*. 2007). Una de las consecuencias del enfriamiento de las aguas de la Antártida fue el brusco cambio de biodiversidad sufrido en los ecosistemas de aguas poco profundas, incluyendo la pérdida (o migración fuera de las aguas del OA) de varios grupos taxonómicos dentro de los bivalvos, los peces teleósteos y los decápodos, debido principalmente a limitaciones fisiológicas (Clarke & Johnston 1996, Crame 2000, Aronson & Blake 2001, Thatje *et al*. 2005a). Este hecho desencadenó un cambio gradual en la estructura de las comunidades someras del bentos antártico con severas y duraderas consecuencias ecológicas. Así, en ausencia de depredadores durófagos (capaces de romper esqueletos) tales como peces y decápodos, otros organismos de desplazamiento lento (predominantemente equinodermos) ocuparon su nicho ecológico, llegando a ejercer una presión de depredación tan intensa como la observada en otras áreas geográficas (Dearborn 1977, McClintock 1994). En resumen, todos estos cambios dieron lugar a unas comunidades de aguas someras con un marcado carácter arcaico (similar a las comunidades Paleozoicas aunque con una composición específica no necesariamente antigua o primitiva) parecido al que tienen las comunidades de profundidad, con un claro predominio de invertebrados suspensívoros (Aronson *et al*. 1997, Aronson & Blake 2001, Gili *et al*. 2006).

Gran parte del OA se encuentra sobre el bentos profundo. El OA tiene asimismo una plataforma continental relativamente pequeña e inusualmente profunda como resultado del efecto erosivo de las placas de hielo y del hundimiento del continente producido por la enorme carga que el hielo ejerce sobre éste. Las plataformas continentales en otros lugares del planeta tienen alrededor de 100–200 m de profundidad con una anchura de 75 km, mientras que las plataformas continentales antárticas alcanzan una media de 450 m de profundidad (aunque en algunas zonas pueden sobrepasar los 1,000 m) y promedian una anchura de 125 km (ver Clarke & Johnston 2003). Estas plataformas continentales, anormalmente profundas y anchas, parecen estar zoogeográficamente aisladas de los mares adyacentes gracias al efecto de la Corriente Circumpolar Antártica (CCA), elemento crucial en la historia geológica de la Antártida así como para la fauna marina antártica actual (Crame 1999). A pesar de que existe una controversia acerca del período en que se abrió el Paso del Drake y el subsecuente establecimiento de la CCA, algunas estimaciones recientes confirman que este fenómeno pudo suceder hace ~38–28 Ma ó 29–22 Ma (Scher & Martin 2006, Lagabrielle *et al*. 2009), coincidiendo probablemente con los inicios de las glaciaciones antárticas y el enfriamiento del agua del mar (Barker & Thomas 2004, Katz *et al*. 2011). En la actualidad, esta corriente marina que discurre en el sentido de las agujas del reloj y está producida total o parcialmente por los fuertes vientos de la zona, contribuye enormemente a la distribución circumpolar observada en muchos organismos bentónicos (Arntz *et al*. 1997, Gutt *et al*. 2004). Aparte de esto, la CCA, considerada como el sistema de corrientes oceánicas más grande que existe en la

Tierra, está íntimamente relacionada con el clima del planeta a través de lo que se conoce como la Circulación Termohalina. Así, se exportan masas de aguas profundas (especialmente de los Mares de Weddell y de Ross) a la mayor parte de las zonas de profundidad del resto de océanos del mundo (Orsi *et al*. 1999). De esta manera, a diferencia de lo que sucede para la plataforma continental, la fauna antártica de profundidad puede migrar libremente hacia dentro y hacia fuera de las llanuras abisales del OA haciendo así más probables las conexiones entre faunas de diferentes cuencas (Brandt *et al*. 2007a,b, Brandt & Gutt 2011).

Organismos bentónicos marcadamente euribáticos y endémicos

Aunque se conocen bien los cambios que provocó el clima en la biodiversidad a lo largo de la escala geológica, las consecuencias de los cambios medioambientales debidos a las oscilaciones climáticas producidas por las variaciones orbitales (ciclos de Milankovitch) son aún poco conocidas (Clarke *et al*. 2004, Thatje *et al*. 2005b). Brey *et al*. (1996) demostraron que gran parte de los taxones bentónicos examinados (bivalvos, gasterópodos, anfípodos y decápodos, pero también poliquetos, asteroideos y ofiuorideos) tienen un rango batimétrico mayor que el de sus relativos de una zona mucho más estudiada como Europa. A pesar de que es probable que los rangos batimétricos estén infraestimados debido a la poca información que se tiene de muchas de las especies, los altos niveles euribáticos parecen estar explicados por la historia paleoclimática de la Antártida (Galéron *et al*. 1992, Clarke *et al*. 2004, Thatje *et al*. 2005b). Durante el Pleistoceno, períodos de gran extensión de la placa de hielo y bajo nivel del mar (período glacial) alternaron con períodos de poca extensión de la placa y altos niveles del mar (período interglacial). Se cree que estos ciclos glaciales-interglaciales pudieron ser la causa de que muchos invertebrados bentónicos antárticos desarrollaran un marcado carácter euribático. En los períodos de extensión de la placa de hielo, la fauna de la plataforma continental se pudo haber extinguido o se pudo ver forzada a trasladarse a refugios en aguas más profundas, mientras que durante el retroceso de la placa en el período interglacial, la plataforma continental defaunada pudo haber sido recolonizada por fauna del talud continental (Clarke *et al*. 2004). Esta hipótesis ha sido puesta en duda por Thatje *et al*. (2005b). Estos autores sugieren que es poco probable que el talud continental pudiera convertirse en un refugio para la fauna después del aumento de la placa de hielo, y argumentan que la supervivencia de las comunidades bentónicas fue únicamente posible en las aguas de profundidad o en refugios de la plataforma continental, como resultado de un diacronismo en la extensión máxima de la placa de hielo.

Estas alternancias glaciales-interglaciales pueden también estar detrás del alto nivel de endemismos (60–90%) para la fauna bentónica de la plataforma continental (Brandt & Gutt 2011), un hecho que confirma al OA como una zona evolutiva en sí misma (Linse *et al*. 2006). Los valores de endemicidad observados en diferentes taxones pueden estar reflejando cambios medioambientes del pasado así como prolongados aislamientos de otras zonas biogeográficas. Si cambios

medioambientales tales como el avance y retroceso de la placa de hielo coincidieron con fenómenos de aislamiento, la especiación alopátrica pudo haberse visto favorecida causando fenómenos de radiación adaptativa y endemicidad (Arntz *et al*. 1997, Thatje *et al*. 2005b, Brandt & Gutt 2011). La radiación de grupos tales como los picnogónidos, los poliquetos, los holoturoideos y los anfípodos (con una representación en estas aguas del 17.5%, 12.2%, 9.2% y 8.3% del global de especies, respectivamente) ha contribuido a que estos grupos tengan aquí una elevada diversidad. Por otro lado, los fenómenos de avance y retroceso de la placa de hielo pudieron también haber sido la causa de extinciones como en el caso de los decápodos, los cirrípedos o los bivalvos (Clarke & Johnston 2003).

Una particular cadena trófica bajo el hielo

La presencia de hielo marino, una característica aparente y común en la superficie marina de ambos polos, varía ostensiblemente en el OA a lo largo del año debido a la marcada estacionalidad del régimen lumínico. Durante el máximo invernal, 21 millones de km^2 de su área están cubiertos por hielo (una superficie mayor que la del propio continente antártico, 13 millones de km^2; Figura 2), mientras que solamente entre 4–7 millones de km^2 están cubiertos durante el mínimo de verano (Clarke & Johnston 2003, Brandt & Gutt 2011). Este periódico avance y retroceso de la cubierta de hielo crea uno de los más grandes y dinámicos ecosistemas de la Tierra (Brierley & Thomas 2002), que se apoya en la extraordinaria producción primaria de bacterias y sobretodo algas (diatomeas pinnadas en su mayoría) que crecen asociadas al hielo. A medida que el hielo empieza a derretirse y la radiación solar incrementa durante la primavera, “blooms” fitoplanctónicos (varias veces más productivos que los de mar abierto) desencadenan una respuesta en cascada en los niveles tróficos superiores. Es así como se produce un crecimiento espectacular del krill antártico (*Euphasia superba*), tanto en abundancia como en biomasa, y este euphausiáceo se convierte en la principal fuente de alimento para muchos organismos de gran tamaño tales como peces, aves marinas y mamíferos marinos. Para completar la red trófica del OA es preciso mencionar las interacciones columna de agua-bentos, el llamado acoplamiento bento-pelágico (revisado por Smith *et al*. 2006). Tras los enormes “blooms” fitoplanctónicos que se dan en la capa fótica en el periodo de primavera-verano, parte de esta materia orgánica es procesada por la comunidad microbiana (bacterias, protozoos y virus) en la columna de agua (Thompson *et al*. 2010), mientras que el resto se exporta al fondo del mar. Estos vastos pulsos de células algales muertas, fitodetritus y pellets fecales del zooplancton afectan de forma directa a los organismos bentónicos estimulando la aparición de una fauna muy rica y diversa de invertebrados suspensívoros. Estos inputs de materia orgánica, espaciados en el espacio y en el tiempo, son utilizados tanto por organismos suspensívoros de aguas someras como por organismos de aguas profundas, que se alimentan a lo largo del año gracias a fenómenos advectivos y de resuspensión (Gili *et al*. 2001). Además, el material orgánico depositado y acumulado en el sedimento marino es mineralizado mediante la

red trófica microbiana (Mincks *et al*. 2005). El último paso para cerrar la cadena trófica del OA comprende los procesos que conectan la fauna bentónica con el compartimento pelágico. Gracias a las corrientes de profundidad, los micronutrientes regenerados en el fondo marino llegan a la capa fótica donde serán incorporados de nuevo al sistema por organismos autótrofos (*e.g.* Sedwick *et al*. 2000).

Situación actual

Recientemente se ha estimado que el número de especies que habitan el bentos del OA supera las 7,000 (De Broyer *et al*. 2011), lo cuál representa un aumento muy considerable (casi el doble) respecto al número de especies conocidas desde que se hiciera una de las últimas revisiones sobre biodiversidad bentónica (Clarke & Johnston 2003). Este hecho confirma que la biodiversidad en el bentos del OA es mayor de lo que en un principio se esperaba, a pesar de que un número muy grande de áreas (*i.e.* océano profundo, zonas bajo las placas de hielo flotantes, zonas intermareales) siguen sin ser exploradas o han sido exploradas muy vagamente (Griffiths 2010). En este sentido, unos resultados más que destacables obtenidos de recientes estudios de la fauna de profundidad del Mar de Weddell y del Mar de Scotia (incluyendo una nueva comunidad de fuentes hidrotermales endémica) cuestionan la hipótesis que postula una riqueza específica baja para el OA profundo (Brandt *et al*. 2007a,b, Rogers *et al*. 2012).

En los últimos años se ha confirmado que, a diferencia de lo que le sucede a la fauna terrestre, la fauna marina del bentos antártico no sigue una clina latitudinal (Arntz & Gili 2001, Arntz *et al*. 2005). La curva latitudinal con forma de campana parece ser válida únicamente para unos pocos grupos, mientras que muchos otros, como los picnogónidos o los isópodos de profundidad, incluso incrementan su presencia en aguas del OA (Clarke & Johnston 2003, Brandt *et al*. 2007b); en consecuencia, se debería adoptar más bien el concepto de distribución asimétrica para muchos taxones (Arntz *et al*. 2005). Entre los diferentes organismos del bentos antártico, el grupo de los poliquetos parece ser uno de los mejor representados, aunque tanto isópodos como anfípodos presentan también un número muy elevado de especies (Clarke & Johnston 2003, Brandt *et al*. 2007a,b). No obstante, una de las características más destacables de la fauna bentónica antártica es que, en la mayoría de ambientes, predominan ricas y diversas comunidades de organismos suspensívoros (tanto sésiles como de movimientos lentos). Estas comunidades están sobretodo favorecidas en la plataforma continental, como resultado de una combinación entre un sedimento “blando” de origen glacial y la disponibilidad de alimento gracias a fenómenos advectivos y de resuspensión producidos por corrientes de profundidad (Clarke 1996, Gili *et al*. 2001, Gutt 2007). Los organismos suspensívoros suelen conformar estructuras tridimensionales (Dayton *et al*. 1974, Clarke & Johnston 2003, Gili *et al*. 2006, Brandt *et al*. 2007a) con una importante representación de fauna epibiótica que generalmente utiliza como substrato a grandes esponjas, briozoos y cnidarios (Gutt & Schickan 1998) (Figura 3).

En el OA encontramos comunidades estructuradas de suspensívoros en parte debido a lo altamente predecible y relativamente constante que es el medio físico donde se encuentran. Hay que decir que estas comunidades no se encuentran en muchas áreas de poca profundidad y en muchas zonas de la plataforma continental, puesto que la fauna en estos lugares está fuertemente afectada por fenómenos de abrasión del fondo causados por icebergs y por fenómenos de hielos anclados ("anchor ice"), dos de los mayores agentes naturales de perturbación para la fauna bentónica de la Antártida (Barnes & Conlan 2007). En consecuencia, las comunidades de suspensívoros que se encuentran lejos de la influencia de factores de perturbación parecen vivir en ambientes extremadamente constantes. En estos ambientes las relaciones bióticas parecen predominar y mecanismos tales como la depredación o la competencia juegan un papel esencial en la estructuración de las comunidades bentónicas (Dayton *et al*. 1974, Arntz *et al*. 1994). Estos organismos suspensívoros han prosperado en estos ecosistemas gracias a haber desarrollado mecanismos no solo contra la depredación y la competencia, sino también por disponer de medios que inhiben el asentamiento y el recubrimiento por otros organismos (*e.g.* Dayton *et al*. 1974, Amsler *et al*. 2000b, Peters *et al*. 2009, Núñez-Pons *et al*. 2010, Koplovitz *et al*. 2011). Por consiguiente, aparte de defensas estructurales y/o comportamentales, muchas de estas especies han desarrollado metabolitos secundarios defensivos para asegurar su supervivencia. El rol que estos productos naturales juegan en el contexto ecológico del OA es uno de los principales temas de investigación que se tratan en esta Tesis Doctoral. En este sentido, se aporta una revisión sobre la ecología química en el OA (**Artículo I**) y se hace una contribución experimental en la que se usan extractos químicos de organismos bentónicos en tests antidepredación (**Artículo II**).

Aparte de estas dos contribuciones en el campo de la ecología química, se llevó a cabo un estudio más aplicado en el que se investigó el potencial farmacológico de invertebrados marinos del bentos antárctico y sub-antártico (**Artículo III**). Tanto el **Artículo II** como el **Artículo III** contribuyen muy significativamente a aumentar el conocimiento sobre la bioactividad de organismos bentónicos de la Antártida.

Ecología química de organismos marinos bentónicos antárticos y sub-antárticos

Los organismos marinos viven bajo la presión y las limitaciones físicas y biológicas propias de los ecosistemas que habitan. Para asegurarse la supervivencia, estos organismos han desarrollado, a lo largo de la evolución, diferentes mecanismos que incluyen estrategias comportamentales, físicas y/o químicas. En las últimas décadas, diversos productos naturales de origen marino se han descrito de un amplio número de organismos, la mayoría de los cuales proceden de aguas templadas y tropicales (ver Blunt *et al*. 2011 y revisiones anteriores), llegando a alcanzar los *ca.* 22,000 compuestos que se conocen en la actualidad (MarinLit database 2011). No obstante, a

pesar de este elevado y creciente número de metabolitos secundarios, se carece en muchos casos de la información acerca del papel ecológico que estos productos desempeñan dentro del ecosistema.

En términos comparativos, los productos naturales marinos han sido muy poco estudiados en el OA en parte debido a las dificultades para muestrear en estas aguas, pero también debido a anteriores argumentos que predecían una baja biodiversidad y en consecuencia una baja quimiodiversidad para sus organismos (Lebar *et al*. 2007). Independientemente de estas dificultades y de argumentos erróneos en lo que a quimiodiversidad se refiere (cuestionado por Amsler *et al*. 2000a), en los últimos años, el estudio de los productos naturales en el OA ha recibido mucha atención y el conocimiento recabado se ha incluido ya en algunas revisiones (McClintock & Baker 1997a, Amsler *et al*. 2001a,b). Dado que tras estas revisiones se han publicado una gran cantidad de trabajos, existía una necesidad de actualizar e integrar toda la información generada hasta la fecha en el campo de la química de los organismos antárticos. Con esta intención llevamos a cabo una revisión que pretendía compilar toda esta información, hasta Mayo de 2007, prestando especial atención tanto a las características químicas como al papel ecológico de los compuestos naturales descritos (**Artículo I**). Nuestra exhaustiva revisión fue publicada casi de manera contemporánea a la revisión de Lebar *et al*. (2007), quienes incluyeron la información de productos naturales de origen marino de organismos que se encuentran en los dos polos. Recientemente se ha publicado una revisión que cubre los trabajos sobre ecología química llevados a cabo en la Península Antártica Oeste (McClintock *et al*. 2010).

Como se ha comentado con anterioridad, gran parte de los fondos marinos antárticos parecen estar fuertemente influenciados por las relaciones bióticas (Dayton *et al*. 1974, Arntz *et al*. 1994). Como sucede para las zonas templadas y tropicales (*e.g.* Scheuer 1990, Paul 1992, Pawlik 1993, Hay 1996), las interacciones depredador-presa han captado gran parte de la atención en las aguas antárticas (ver McClintock & Baker 1997a, Amsler *et al*. 2001a, Lebar *et al*. 2007, McClintock *et al*. 2010, **Artículo I**). A diferencia de lo que sucede en regiones templadas y tropicales, asteroideos como *Odontaster validus* han reemplazado a los peces como potenciales superdepredadores ("top-predators") en las comunidades antárticas. De hecho, la presión de depredación causada por estos organismos ha demostrado ser tan intensa como la que se ha observado no solo en los ecosistemas templados sino también en los tropicales (Dearborn 1977, McClintock 1994). Así, a lo largo de los millones de años en que los ecosistemas antárticos han permanecido estables y aislados, la presión de depredación causada por estos depredadores simpátricos ha actuado como una fuerza de selección que ha llevado al desarrollo y adquisición de metabolitos secundarios defensivos en muchos invertebrados (*e.g.* McClintock & Baker 1997a, Amsler *et al*. 2001a,b, **Artículo I**). Este hecho es especialmente relevante cuando consideramos que los organismos suspensívoros predominan en el bentos antártico, ya que se conoce a muchos organismos con este modo de vida de otras áreas geográficas que han desarrollado estrategias defensivas químicas para sobrevivir (Paul *et al*. 2011).

Con la intención de ampliar el conocimiento en el campo de la actividad antidepredación en el contexto antártico y sub-antártico, se investigaron extractos

químicos de varias especies de invertebrados pertenecientes a diferentes phyla frente a *O. validus*, un depredador simpátrico muy común (**Artículo II**). Esta estrella de mar de distribución circumpolar ha sido utilizada previamente como organismo modelo para testar interacciones depredador-presa en varios trabajos tanto de otros grupos de investigación (*e.g.* Slattery & McClintock 1995, McClintock & Baker 1997b, Peters *et al*. 2009) como en nuestro propio grupo (Avila *et al*. 2000, Iken *et al*. 2002, Núñez-Pons *et al*. 2010) (Figura 4). En este sentido, el **Artículo II** representa un nuevo paso dentro de la investigación de nuestro grupo en lo que se refiere a relaciones antidepredación con significación ecológicamente relevante. Se trata de una aportación remarcable por dos motivos principales: (i) se investigan organismos recolectados de dos zonas pobremente estudiadas (este del Mar de Weddell e Isla de Bouvet) en lo que a estudios de ecología química se refiere; y (ii) se centra en organismos de profundidad, hasta la fecha muy poco estudiados.

Bioactividad: Potencial antitumoral en aguas antárticas y sub-antárticas

Aunque los organismos terrestres han sido tradicionalmente la fuente de recursos para nuevos compuestos anticancerígenos, en las últimas décadas la farmacología marina se ha convertido en un campo de investigación muy prometedor (Molinski *et al*. 2009). De hecho, varios de los futuros medicamentos anticancerígenos que se encuentran actualmente en fase clínica y preclínica son de origen marino (Newman & Cragg 2004, Simmons *et al*. 2005, Mayer & Gustafson 2008), con algunos ejemplos como Yondelis®, recientemente lanzado al mercado. Varios motivos parecen estar detrás de la interesante actividad antitumoral/citotóxica observada en muchos organismos marinos. Por un lado, los ambientes marinos son las mayores fuentes potenciales de biodiversidad en la Tierra, con algunos de sus ecosistemas con valores de diversidad incluso mayores que las selvas tropicales (Haefner 2003). Además, en los ambientes marinos encontramos un mayor número de phyla (algunos de ellos son de hecho exclusivamente marinos) en comparación con los hábitats terrestres (Clarke & Johnston 2003), lo que parece estar fuertemente correlacionado con la posibilidad de hallar nuevas clases de compuestos químicos que no se hallan en organismos terrestres (Devlin 1997, Munro *et al*. 1999). Finalmente, muchos organismos marinos son sésiles o de movimiento lento, lo que hace que necesiten defenderse de posibles depredadores y/o competidores, así como del asentamiento y el recubrimiento por parte de otros organismos. El desarrollo de defensas químicas (algunas de las cuales útiles en la lucha contra el cáncer) parece ser un mecanismo extendido y efectivo para estos organismos tanto en ambientes templados y tropicales como en la Antártida (*e.g.* Amsler *et al.* 2001a, Simmons *et al.* 2005, **Artículo I**, **III**).

Hasta la fecha, los mares templados y tropicales han sido los más estudiados en la búsqueda de nuevos productos naturales (ver Blunt *et al*. 2011 y anteriores revisiones). Comparado con estos mares, en el OA se han llevado a cabo muy pocos estudios sobre las propiedades antitumorales/citotóxicas de organismos marinos, siendo los organismos de zonas de poca profundidad los más estudiados (ver

discusión del **Artículo III**). Sin embargo, el OA parece ser un área muy prometedora en la búsqueda de nuevos fármacos ya que, como se ha comentado en la introducción general, es una región que ha permanecido prácticamente aislada durante varios millones de años, lo que ha provocado un grado de endemicidad extremadamente alto (Brandt & Gutt 2011). Además, en el aún poco conocido pero altamente biodiverso bentos antártico, predominan los organismos sésiles y de movimiento lento, los cuales se sabe que proveen la mayor proporción de compuestos con propiedades citotóxicas (Schmitz *et al*. 1993, Munro *et al*. 1999).

Aprovechando dos campañas antárticas que prospectaron tres áreas diferentes (este del Mar de Weddell, Islas Shetland del Sur e Isla de Bouvet), se llevó a cabo un estudio exhaustivo del potencial farmacológico de *ca.* 300 especies bentónicas antárticas y sub-antárticas (**Artículo III**). El trabajo, ensayando los efectos en tres líneas de células tumorales, se realizó en colaboración con la empresa farmacéutica PharmaMar SA, y los resultados obtenidos comprenden la mayor prospección farmacéutica que se haya hecho nunca en aguas antárticas y sub-antárticas.

Biodiversidad: nuevos poliquetos asociados a huesos de ballena

Los restos de ballena y las comunidades microbianas y de invertebrados que en ellos se desarrollan, son actualmente uno de los hábitats más extraordinarios y poco estudiados que se conocen. Tras el descubrimiento accidental de estas comunidades en una carcasa de ballena encontrada de forma natural en el este del Pacífico (Smith *et al*. 1989), diferentes estudios se han sucedido describiendo la fauna que prospera en estos substratos especializados. La mayoría de estos estudios se han centrado en el grupo de los poliquetos, debido al importante papel que juegan en estas comunidades en cuanto a abundancia y biodiversidad (Baco & Smith 2003, Smith & Baco 2003, Smith 2006). Estos estudios han investigado diferentes aspectos de la biología, ecología, taxonomía y filogenia de los invertebrados asociados a carcasas de ballena (tanto naturales como depositadas experimentalmente) con el propósito de describir y caracterizar la fauna que vive en estos substratos. Hasta la fecha, tan solo han sido investigadas las aguas del hemisferio norte (noreste y noroeste del Pacífico, y nord-Atlántico) a profundidades que van de los 30 hasta cerca de los 3,000 m (*e.g.* Bennet *et al*. 1994, Rouse *et al*. 2004, Dahlgren *et al*. 2006, Fujiwara *et al*. 2007, Lundsten *et al*. 2010).

Debido a la distribución global de las ballenas, las comunidades asociadas a sus huesos se espera que existan en cualquier área del planeta, si bien es cierto que las probabilidades de encontrar esta fauna debería ser mayor en áreas frecuentadas por ballenas, donde es más probable que se encuentren sus restos depositados en el bentos. Una de estas áreas es la Península Antártica Oeste (que incluye las Islas Shetland del Sur), donde diferentes especies de cetáceos se reúnen para alimentarse y reproducirse (Friedlander *et al*. 2006). Así pues, con el objetivo de llenar el vacío de conocimiento para el OA, se llevó a cabo un experimento pionero en aguas antárticas

utilizando huesos de ballena como substrato quimioatractivo para investigar sus invertebrados asociados. El experimento consistió en tres vértebras caudales descarnadas de rorcual aliblanco (*Balaenoptera acutorostrata*) implantadas en el fondo marino de Puerto Foster (Isla Decepción, Islas Shetland del Sur) en Enero de 2009. Las vértebras, firmemente sujetas a un elemento metálico por medio de cables de acero, se mantuvieron en el agua mediante un liberador acústico unido a un lastre y a una boya oceanográfica (Figura 5). Tras un año, solamente se pudo recuperar una de las vértebras. Las otras dos se perdieron presumiblemente tras el ataque de una foca leopardo, dado que los cables de acero que sujetaban estas vértebras parecían haber sido mordidos. Aparte de la vértebra recuperada, otro hueso de ballena (no fresco, viejo) de origen desconocido fue también recogido mediante inmersión con escafandra autónoma de una zona somera cercana dentro de Puerto Foster. Tras la recogida y examinado de ambos huesos (Enero de 2010) (Figura 6), se pudo concluir que, tal y como se esperaba, el grupo de los poliquetos era el taxón mejor representado, aunque fueron también hallados representantes del grupo de los crustáceos, platihelmintos, nemertinos y oligoquetos (resultados no publicados).

Vale la pena destacar que, aunque los huesos fueron recogidos en una zona, Puerto Foster, con una base faunística muy completa (ver Barnes *et al*. 2008), en ellos se hallaron al menos cinco nuevas especies de poliquetos de las familias Terebellidae, Cirratulidae (**Artículo IV**), Dorvilleidae (**Artículo V**) y Siboglinidae (**Artículo VI**).

Un nuevo cirratúlido descrito de un hueso de ballena de poca profundidad

Los cirratúlidos se dividen de manera general en bitentaculados y multitentaculados (Blake 1996). Dentro de los multitentaculados, el género *Cirratulus* es el que más especies comprende (más de 50 aceptadas actualmente), con seis de ellas descritas o registradas en el OA o en aguas adyacentes. En el grupo de los cirratúlidos se han encontrado especies oportunistas de áreas templadas asociadas a zonas contaminadas y ricas en materia orgánica (*e.g.* Pearson & Rosenberg 1978, Elías *et al*. 2006); también se han descrito en la Antártida en zonas eutrofizadas y en zonas perturbadas por el efecto abrasivo de los icebergs (Lenihan *et al*. 1995; Conlan *et al*. 2004, 2010). A pesar de que los cirratúlidos no son un grupo común sobre huesos de ballena, algunos estudios han documentado su presencia en asociación con otros poliquetos (Bennet *et al*. 1994, Smith *et al*. 2002, Fujiwara *et al.* 2007).

En el **Artículo IV**, se describe formalmente el primer cirratúlido originalmente descrito de restos de ballena. También se presenta la secuencia del gen citocromo *c* oxidasa I (COI), así como se dan algunas pinceladas sobre sus preferencias alimentarias y ecología.

Dos nuevas especies antárticas de *Ophryotrocha* descritas de huesos de ballena de poca profundidad

Los integrantes del género *Ophryotrocha* son pequeños gusanos bentónicos oportunistas que predominan en ambientes ricos en nutrientes tanto en los sedimentos de aguas someras como en los de aguas profundas (Thornhill *et al*. 2009). El género *Ophryotrocha*, uno de los más importantes en la familia Dorvilleidae, comprende unas 50 especies de las que únicamente dos han sido formalmente descritas de aguas del OA: *O. notialis* (Ehlers, 1908) y *O. claparedei* Studer, 1878. Entre las especies de poliquetos oportunistas que se han encontrado en huesos de ballena, el género *Ophryotrocha* es uno de los clados mejor representados. De hecho, nueve nuevas especies se han descrito recientemente en huesos de ballena tanto de poca como de mucha profundidad en las costas de Suecia y California (Wiklund *et al*. 2009a,b). En lo que respecta a su filogenia, anteriores análisis moleculares usando las secuencias del 16S y el COI apuntan a la existencia de dos clados principales, el clado 'hartmanni' y el clado 'labronica' (Dahlgren *et al*. 2001, Heggøy *et al*. 2007). Un tercer clado, el clado 'lobifera', que contiene algunas especies anteriormente incluidas en el género *Palpiphitime*, ha sido sugerido también por Paxton (2009).

En el **Artículo V** se describen formalmente dos nuevas especies del género *Ophryotrocha*, *O.* **sp. nov.** 1 y *O.* **sp. nov.** 2, y se dan algunos datos sobre sus preferencias alimentarias y su ecología. Se aporta también la información filogenética tras el análisis de los genes H3, COI y 16S.

Primer *Osedax* descrito en aguas antárticas

Los integrantes del género *Osedax* (Fam. Siboglinidae), comúnmente conocidos como ‘gusanos come-huesos’, son anélidos poco usuales que carecen de boca y digestivo. Tienen un marcado dimorfismo sexual donde los machos pedomórficos enanos viven en el lumen del tubo de la hembra (Rouse *et al*. 2004). Las hembras de estos organismos viven ancladas a los huesos gracias a un sistema enraizado y obtienen el alimento a través de una simbiosis con bacterias heterótrofas que degradan los compuestos orgánicos secuestrados en el hueso (Goffredi *et al*. 2005, 2007). Hasta la fecha, los 25 miembros taxonómicos que se conocen (unidades taxonómicas operacionales) del género *Osedax* tan solo se han hallado en el hemisferio norte (Océano Pacífico y Atlántico Norte). A pesar de que se han encontrado en un amplio rango batimétrico (entre los 30 y los 2,891 m), la mayoría de ellos se han descrito en aguas profundas. Curiosamente, estos organismos no solo se desarrollan sobre restos de ballena, donde han sido encontrados mayoritariamente, sino que también pueden vivir asociados a huesos de otros mamíferos, de pájaros y de peces (Jones *et al.* 2008, Kiel *et al.* 2010, Rouse *et al.* 2011).

Aunque se ha postulado que los miembros del género *Osedax* habitan en todos los mares (Glover *et al*. 2005), hasta la fecha no se había certificado su existencia en aguas antárticas. En el **Artículo VI** describimos el primer *Osedax* antártico que es

además la especie que se ha encontrado a menor profundidad hasta la fecha. Aparte de proporcionar su descripción morfológica se discute también su posición filogenética en el seno de su clado.

Objetivos de esta Tesis

La Tesis Doctoral que aquí se presenta abarca un amplio abanico de temas relacionados con los invertebrados bentónicos de la Antártida. En función de los temas tratados, el trabajo se puede dividir en tres partes principales: Parte I, que trata sobre ecología química, en la que se incluyen dos artículos. El **Artículo I** recoge una exhaustiva revisión de los productos naturales descritos en aguas antárticas, mientras que el **Artículo II** es una contribución original en la que se investigan las interacciones depredador-presa en diferentes invertebrados marinos del bentos antártico y sub-antártico; Parte II, que trata sobre actividad antitumoral, en la que se incluye el **Artículo III**, donde se discuten los resultados obtenidos tras el mayor estudio farmacológico que se ha hecho hasta la fecha en aguas antárticas y sub-antárticas; y Parte III, que trata sobre biodiversidad, en la que se incluyen tres artículos (**Artículos IV-VI**), donde se describen cuatro nuevas especies antárticas de poliquetos asociados a huesos de ballena de poca profundidad.

Los objetivos particulares para cada una de las publicaciones se especifican a continuación.

Parte I. Ecología química de organismos marinos bentónicos antárticos y sub-antárticos

Artículo I. *Ecología química en ambientes marinos de la Antártida: ¿cuál es su futuro?*

El objetivo principal de este artículo es revisar la información existente sobre ecología química de organismos marinos antárticos, dando una idea de cuál es su grado de conocimiento hasta Mayo de 2007. La información compilada está integrada y discutida para cada grupo taxonómico y se aporta una perspectiva general de futuro.

Artículo II. *Repelencia alimentaria de invertebrados bentónicos antárticos y sub-antárticos frente a la estrella de mar omnívora Odontaster validus*

Con la base de conocimiento establecida tras la revisión del **Artículo I**, nuestra intención era la de profundizar en las interacciones químicas depredador-presa de un amplio elenco de invertebrados marinos bentónicos. En el **Artículo II** se describen estas interacciones usando el depredador simpátrico *O. validus* como modelo para llevar a cabo experimentos de repelencia alimentaria. Aparte de este objetivo general también se pretende: (i) analizar y comparar nuestros resultados sobre organismos de profundidad de dos áreas muy poco estudiadas (este del Mar de Weddell e Isla de Bouvet), con anteriores estudios que han utilizado sobretodo especies de poca profundidad; y (ii) testar la Teoría de Defensa Óptima (‘Optimal Defense Theory’, ODT; Rhoades 1979) que, bajo una hipotética presión de depredación de *O. validus*, predice una localización de los metabolitos de defensa en los tejidos más expuestos.

Parte II. Bioactividad: Potencial antitumoral en aguas antárticas y sub-antárticas

Artículo III. *Actividad antitumoral en organismos bentónicos antárticos y sub-antárticos*

La actividad antitumoral ha sido muy poco investigada en aguas antárticas y sub-antárticas (ver **Artículo I**). Nuestro principal objetivo para el **Artículo III** es establecer la actividad antitumoral de 290 especies diferentes (de un total de 770 muestras de invertebrados bentónicos) frente a tres líneas celulares de tumores humanos (adenocarcinoma colorrectal, carcinoma de pulmón y adenocarcinoma de mama). Con este estudio se pretende probar el potencial farmacológico de tres zonas diferentes: el este del Mar de Weddell, las Islas Shetland del Sur y la Isla de Bouvet.

Parte III. Biodiversidad: nuevos poliquetos asociados a huesos de ballena

A pesar de que los restos de ballena son frecuentes en el bentos del OA, su estudio ha sido obviado sistemáticamente. El principal objetivo de este apartado es describir formalmente algunos de los poliquetos más comunes encontrados asociados a huesos de ballena de poca profundidad en Isla Decepción (Islas Shetland del Sur).

Artículo IV. *El primer Cirratulidae (Annelida: Polychaeta) descrito de un hueso de ballena de poca profundidad en la Antártida*

En este artículo se describe formalmente el primer cirratúlido originalmente descrito de un hueso de ballena. Se aporta además la secuencia del COI con el objetivo de facilitar futuros estudios encaminados a clarificar las relaciones filogenéticas en el grupo.

Artículo V. *Dos nuevos poliquetos antárticos del género Ophryotrocha (Annelida: Dorvilleidae) descritos de huesos de ballena de poca profundidad*

Los miembros del género *Ophryotrocha* han sido poco estudiados en aguas antárticas. Los objetivos de este artículo son describir formalmente dos nuevas especies encontradas en restos de ballena y colocar a ambas especies en su contexto filogenético.

Artículo VI. *Primer Osedax descrito en aguas antárticas*

Los poliquetos del género *Osedax* no han sido nunca investigados en las aguas del OA. En este artículo se describe formalmente la primera especie de *Osedax* de la Antártida y se discute su posición filogenética en el contexto de su grupo.

Resultados

A continuación se resumen, de manera clara y concisa, los principales resultados obtenidos para cada uno de los artículos que conforman esta Tesis.

Capítulo I. Ecología química en ambientes marinos de la Antártida: ¿cuál es su futuro?

Como resultado de las condiciones medioambientales únicas a las que los ecosistemas antárticos están expuestos, sus comunidades están estructuradas tanto por interacciones bióticas como la depredación y la competencia, como por factores abióticos como la estacionalidad y la abrasión causada por el hielo. Resulta importante entender cómo los factores ecológicos pueden desencadenar mecanismos químicos en organismos marinos antárticos como una respuesta para asegurar su supervivencia. No obstante, poco se conoce aún sobre la evolución de los compuestos químicos en organismos antárticos. En los últimos años, la investigación en el campo de la ecología química ha demostrado que los metabolitos defensivos han evolucionado en numerosas especies antárticas. Este hecho contradice anteriores teorías pronosticando variaciones biogeográficas en cuanto a depredación y a defensas químicas se refiere. Como queda demostrado en esta revisión, se han aislado hasta la fecha numerosos e interesantes productos naturales de organismos antárticos, y creemos que quedan aún muchos otros por descubrir. Actualmente, poco o nada se conoce en cuanto a los productos naturales de diversos grupos como los microorganismos, los organismos planctónicos o en general la fauna de profundidad. Además, para muchos de los compuestos descritos, se desconoce cuál es su función ecológica. De hecho, gran parte de las investigaciones llevadas a cabo hasta la fecha se han realizado en condiciones de laboratorio y tan solo en unos pocos casos en un contexto relevante en términos ecológicos. En consecuencia, existe una necesidad de extender estos experimentos en su entorno real, como se ha hecho en ecosistemas marinos tropicales y templados, o como mínimo, probar la actividad de los productos químicos en condiciones naturales y con interacciones ecológicas relevantes. La defensa contra predadores ha sido siempre uno de los principales objetivos en cuanto al estudio de los roles que los productos naturales desempeñan en las interacciones interespecíficas. No obstante, muchos otros aspectos interesantes como la competencia, la quimioatracción, la actividad anti-recubrimiento y la protección contra la radiación ultravioleta, también merecen especial atención. En nuestra opinión, los próximos años van a traer avances muy significativos en el campo de la ecología química marina en el contexto de la Antártida.

Capítulo II. Repelencia alimentaria de invertebrados bentónicos antárticos y sub-antárticos frente a la estrella de mar omnívora *Odontaster validus*

Los invertebrados bentónicos antárticos y sub-antárticos están sometidos a una intensa depredación por parte de macroinvertebrados móviles. En consecuencia, la protección química así como otros mecanismos de defensa, se espera que sea común en los organismos que habitan estos ecosistemas. Con la intención de evaluar la actividad de anti-depredación y la localización de las defensas químicas en la anatomía de invertebrados marinos del bentos antártico y sub-antártico, se probaron un total de 55 especies en experimentos de repelencia alimentaria contra la estrella de mar *Odontaster validus*, un depredador simpátrico y común con una distribución euribática. Los invertebrados probados fueron recogidos de aguas profundas de dos áreas muy poco estudiadas en cuanto a ecología química se refiere: el este del Mar de Weddell (Antártida) y los alrededores de la Isla de Bouvet (sub-Antártida). Los experimentos, que se llevaron a cabo en la Base Antártica Española de Isla Decepción, consistían en trozos de gamba tratados con fracciones lipofílicas crudas obtenidas de cada especie a testar, que eran presentados a las estrellas de mar. Un total de 29 especies (53%) de 7 phyla diferentes (Porifera, Cnidaria, Chordata, Bryozoa, Echinodermata, Mollusca y Annelida) demostraron repelencia alimentaria frente a *O. validus* y en consecuencia están protegidos frente a este depredador clave. Por otro lado, 25 especies fueron diseccionadas para investigar la posible localización de los compuestos defensivos. Algunos de los resultados obtenidos apoyan la predicción de que los tejidos más expuestos/vulnerables concentran las defensas químicas para evitar así ser depredados por las estrellas de mar. En resumen, los resultados obtenidos respaldan la hipótesis de que los invertebrados bentónicos de profundidad de la Antártida y sub-Antártida están bien protegidos químicamente frente a depredadores simpátricos, tal y como ya se había observado en anteriores estudios llevados a cabo con especies antárticas someras.

Capítulo III. Actividad antitumoral en organismos bentónicos antárticos y sub-antárticos

En este artículo se presentan los resultados de una prospección de actividad antitumoral en invertebrados marinos antárticos y sub-antárticos recogidos de tres áreas diferentes: Isla de Bouvet (sub-Antártida), este del Mar de Weddell (Antártida) e Islas Shetland del Sur (Antártida). Un total de 770 muestras de invertebrados bentónicos (pertenecientes a al menos 290 especies diferentes) de 12 phyla diferentes fueron utilizadas en ensayos para establecer su potencial farmacológico frente a tres líneas tumorales (adenocarcinoma colorrectal, carcinoma de pulmón y adenocarcinoma de mama). Los ensayos resultaron en 15 especies de cinco phyla diferentes con actividad anticancerígena: Chordata (5), Porifera (4), Cnidaria (3), Echinodermata (2) y Annelida (1). Nuestro estudio es el mayor estudio farmacológico que se haya llevado a cabo nunca en la Antártida y demuestra resultados muy prometedores para el bentos antártico y sub-antártico.

Capítulo IV. Una nueva especie del género *Cirratulus* (Annelida: Polychaeta) descrita de un hueso de ballena de poca profundidad en la Antártida

Se describe una nueva especie del género *Cirratulus* Lamarck, 1801 de las aguas someras Antárticas de Isla Decepción (Islas Shetland del Sur). *Cirratulus balaenophilus* **sp. nov.** es el primer cirratúlido descrito originalmente de un hueso fresco de ballena colocado experimentalmente durante un año en el fondo marino antártico. Esta especie se caracteriza por la ausencia de espinas (sedas aciculares) y de ojos, por el número de tentáculos dorsales dispuestos en arco, así como por su color amarillo-anaranjado en vida. Se aporta la secuencia de la subunidad I de la citocromo *c* oxidasa (COI), así como algunos comentarios sobre las preferencias alimentarias y ecología de la especie. También se hace una comparación con especies de su mismo género que se encuentran en la Antártida y aguas adyacentes.

Capítulo V. Dos nuevas especies antárticas de *Ophryotrocha* (Annelida: Dorvilleidae) descritas de huesos de ballena de poca profundidad

En este artículo se describen dos nuevas especies del género *Ophryotrocha* de las aguas someras de Isla Decepción (Islas Shetland del Sur, Antártida). *Ophryotrocha* **sp. nov.** 1 y *O.* **sp. nov.** 2 han sido originalmente descritas de una vértebra fresca de rorcual aliblanco (*Balaenoptera acutorostrata*) depositada experimentalmente durante un año en el lecho marino, así como de una vértebra de origen desconocido que presumiblemente data de principios del siglo XX. Se sugiere que *Ophryotrocha* **sp. nov.** 2, relativamente abundante en el hueso fresco, es una especie oportunista en el contexto de los ambientes someros antárticos ricos en materia orgánica. Por otro lado, *Ophryotrocha* **sp. nov.** 1 parece ser la misma especie que *Palpiphitime* sp., near *lobifera* encontrada con anterioridad en un área cercana. Los análisis filogenéticos basados en el gen nuclear H3 y los genes mitocondriales COI y 16S, usando análisis de MrBayes y Máxima Verosimilitud, confirman que *Ophryotrocha* **sp. nov.** 2 es una especie cercana a *Iphitime hartmanae* y que está incluida en el clado 'hartmanni', mientras que *Ophryotrocha* **sp. nov.** 1 se sitúa en el clado 'lobifera'. Aparte de tratar la posición filogenética de ambas especies, se aporta también información sobre sus preferencias alimentarias y ecología. Nuestros hallazgos parecen sugerir el importante papel que los miembros del género *Ophryotrocha* pueden jugar en ambientes eutrofizados del Océano Antártico, como ha sido comprobado para este clado en otras áreas geográficas.

Capítulo VI. El primer *Osedax* (Annelida: Siboglinidae) descrito del Océano Antártico

Hasta la fecha, los miembros del género *Osedax*, comúnmente conocidos como ‘gusanos come-huesos’, han sido descritos únicamente en el hemisferio norte. Aunque solo se conocen del Océano Pacífico y el Mar del Norte, se ha postulado que se podrían encontrar en todo el mundo. En este artículo se describe formalmente al primer *Osedax* del hemisferio sur, encontrado asociado a un hueso de ballena implantado experimentalmente en las aguas someras de Isla Decepción (Islas Shetland del Sur, Antártida). Esta nueva especie se caracteriza por sus palpos pálidos sin pínnulas, su tubo hemisférico gelatinoso y su pequeña talla en comparación con las anteriores unidades taxonómicas operacionales (OTUs) que se conocen. Además, su presencia en aguas someras (21 m) conduce a pensar que estos organismos pueden jugar un papel importante en las costas de la Antártida en cuanto a la degradación de huesos se refiere, ya que en estas zonas habitan un gran número de vertebrados. Finalmente, se discute la posición filogenética del nuevo *Osedax* en el contexto de su clado a partir de análisis basados en un marcador nuclear (18S) y dos marcadores mitocondriales (16S y COI).

Discusión General

Los resultados obtenidos en esta Tesis Doctoral se centran en el estudio de invertebrados marinos del bentos antártico. Las tres aproximaciones: ecología química, bioactividad y biodiversidad, se van a tratar de manera independiente y siguiendo el orden de la lista de capítulos. En esta discusión general comentaré algunos de los principales logros para cada uno de los capítulos sin profundizar demasiado en los aspectos particulares, aspectos que están tratados a fondo en los artículos correspondientes.

Ecología química de organismos marinos bentónicos antárticos y sub-antárticos (Artículos I-II)

En comparación con los ecosistemas templados y tropicales, los productos naturales marinos de organismos del OA han sido muy poco estudiados, debido en parte a lo remoto de estas aguas y a las dificultades climatológicas de muestrear en ellas (Lebar *et al*. 2007, **Artículo I**). Además, anteriores argumentos que consideraban al OA un área empobrecida en términos de biodiversidad y quimiodiversidad (cuestionado por Amsler *et al*. 2000a) tampoco facilitaron el desarrollo de los estudios de ecología química. A pesar de estas y otras dificultades, durante los últimos años, los estudios sobre ecología química en invertebrados marinos del bentos antártico (mayoritariamente de poca profundidad) se han centrado sobretodo en zonas del Estrecho de McMurdo ('McMurdo Sound'; Mar de Ross) y la Península Antártica Oeste, y en menor medida en las aguas profundas del Mar de Weddell (ver McClintock *et al*. 2010, **Artículo I**).

La información que se aporta en el **Artículo I** proporciona una visión general de lo que se conoce (hasta Mayo de 2007) acerca de la ecología química de organismos marinos del OA. Se incluye la información de la estructura, localización en el organismo, origen y papel ecológico de los *ca.* 300 productos naturales descritos en estas aguas. A pesar de haber sido estudiados de manera insuficiente, diferentes experimentos de laboratorio utilizando especies simpátricas han demostrado que los productos naturales están implicados en las relaciones ecológicas de muchos grupos de organismos antárticos. Los experimentos con aproximaciones ecológicamente relevantes contribuyen notablemente a incrementar el conocimiento del funcionamiento de las relaciones químicas en el ecosistema, cosa que es

especialmente importante en el OA, donde muchas de las comunidades parecen estar gobernadas por factores biológicos (Dayton *et al*. 1974, Arntz *et al*. 1994). A continuación destacaré las principales conclusiones alcanzadas en esta revisión. En primer lugar comentaré, brevemente y de manera separada, algunos aspectos acerca de los roles ecológicos que tienen los productos naturales dentro de cada grupo taxonómico. Las contribuciones más destacables publicadas con posterioridad a Mayo de 2007 también se comentan en la discusión, aunque no se hace referencia a la información del **Artículo II**, que se discute en un apartado separado.

- Las macroalgas dominan las comunidades marinas poco profundas de fondos duros a lo largo del continente antártico. Este grupo de organismos representa la fuente más importante de productos naturales con más de 90 especies investigadas. Aunque se disponga de información ecológica de alguno de los productos naturales investigados, con especial énfasis en tests de repelencia alimentaria usando herbívoros simpátricos (*e.g.* Amsler *et al*. 2002, Huang *et al*. 2006), el papel ecológico que desempeñan muchos de los compuestos descritos sigue sin conocerse.

- El grupo de las esponjas es un grupo muy diverso e importante en las aguas antárticas. De hecho, las esponjas, conjuntamente con los cnidarios y los briozoos, juegan una función muy importante estructurando las comunidades bentónicas (Dayton *et al*. 1974, Clarke & Johnston 2003, Brandt *et al*. 2007a). A pesar de ser uno de los objetivos prioritarios en lo que a investigaciones químicas se refiere y de ser el grupo con mayor número de ejemplos donde la ecología química de sus compuestos ha sido investigada (ver **Artículo I** y sus referencias), queda aún mucho trabajo por hacer. Recientemente, tres estudios usando aproximaciones ecológicamente relevantes han aumentado considerablemente la información disponible en el grupo de las esponjas antárticas: Amsler *et al*. (2009) evaluaron los efectos de varios extractos de esponjas sobre un anfípodo simpátrico; Peters *et al.* (2009) investigaron la palatabilidad de varias especies de esponjas de aguas someras frente a la estrella de mar *Odontaster validus*; y Peters *et al*. (2010) analizaron la bioactividad demostrada por los extractos de una selección similar de esponjas frente a microorganismos simpátricos.

- Como se ha mencionado, cnidarios y briozoos son grupos muy importantes en las comunidades bentónicas del OA. No obstante, ambos grupos han sido poco investigados en estudios de ecología química, lo que ha llevado a que solo 10 briozoos y 8 cnidarios hayan sido estudiados químicamente. De estos últimos, tan solo 3 corales blandos de aguas someras y una gorgonia de aguas profundas han sido investigados en tests antidepredación usando *O. validus* (Slattery & McClintock 1995, Iken & Baker 2003).

- Los moluscos son también un grupo muy diverso en las aguas del OA (Clarke & Johnston 2003, De Broyer *et al*. 2011). No obstante, aunque algunas especies han sido estudiadas en detalle (*e.g. Austrodoris kerguelenensis, Bathydoris hodgsoni*; ver discusión del **Artículo I**), muchas especies todavía siguen sin ser investigadas. Además, deberían llevarse a cabo estudios más

precisos en lo que a localización histológica de los compuestos se refiere, tal y como se ha hecho ya con moluscos de otras latitudes (Wägele *et al*. 2006).

- Las investigaciones realizadas con equinodermos antárticos sugieren que los metabolitos bioactivos son comunes en muchas especies, investigaciones que sobretodo se han centrado en compuestos del grupo de las saponinas [ver discusión del **Artículo I**; recientemente varias publicaciones de Antonov *et al*. (2008, 2009, 2011) han incrementado el número de nuevos compuestos de este tipo]. Los diferentes estudios químicos han investigado 36 especies de equinodermos (incluyendo aquí un holoturoideo no mencionado en el **Artículo I**; Antonov *et al*. 2009) siendo las estrellas de mar el grupo más estudiado, con varios ejemplos de especies repelentes frente a *O. validus* (McClintock *et al*. 2003, 2006). Aunque los equinodermos parecen ser un grupo más estudiado que otros, siguen faltando muchos estudios ecológicamente relevantes.

- Hasta el 2007, únicamente 7 tunicados antárticos habían sido investigados químicamente, de los que tan solo 2 se habían utilizado en experimentos ecológicamente relevantes (*e.g.* McClintock & Baker 1997b, McClintock *et al*. 2004). No obstante, dos estudios recientes sobre ascidias solitarias y coloniales de poca profundidad (Koplovitz *et al*. 2009, 2011), y otro estudio sobre dos especies de profundidad del género *Aplidium* (Núñez-Pons *et al*. 2010), han incrementado considerablemente la información para este grupo. Asimismo, algunos estudios han confirmado el papel complementario que puede desempeñar la acidez de las túnicas de algunas especies como mecanismo defensivo frente a potenciales depredadores (McClintock *et al*. 2004, Koplovitz *et al*. 2009).

- En lo que respecta al resto de grupos estudiados en aguas antárticas, tan solo el nemertino *Parborlasia corrugatus*, el braquiópodo *Liothyrella uva* y el crustáceo *Glyptonotus antarcticus* se han utilizado en experimentos ecológicamente relevantes (Heine *et al*. 1991, McClintock *et al*. 1993, 2003).

La revisión del **Artículo I** demuestra que los organismos del bentos antártico son una fuente rica y diversa de productos naturales, con un gran interés tanto desde el punto ecológico como desde el farmacológico. No obstante, el conocimiento sobre los productos naturales del OA dista mucho de ser completo y, en consecuencia, está lejos de poderse comparar en igualdad de condiciones con otras áreas geográficas. Basta con decir que de los más de 22,000 productos naturales de origen marino descritos hasta el 2011 (MarinLit database) tan solo *ca.* 300 han sido descritos en aguas antárticas.

De manera similar a lo que sucede en ambientes templados y tropicales, la depredación ha sido el mecanismo ecológico más explorado. Aún así, estos resultados se antojan insuficientes. Es pues necesario incrementar el número de experimentos con significación ecológica y desarrollar nuevos tests incluyendo experimentos de campo. Aparte de las interacciones depredador-presa, otros mecanismos como la competencia o la actividad antirecubrimiento, entre otros, deberían ser también investigados puesto que los metabolitos secundarios pueden desempeñar diferentes

funciones dentro del ecosistema (Paul 1992). Asimismo, nuevos estudios se deberían centrar en identificar y localizar las moléculas responsables de las actividades ecológicas (*e.g.* Núñez-Pons *et al*. 2010) o en investigar su origen (König *et al*. 2006).

El vacío de información que existe en el OA en el campo de la ecología química únicamente puede llenarse incrementando el número de especies estudiadas en diferentes phyla e investigando nuevas áreas aún inexploradas. No obstante, toda esta información se debería integrar en un marco mucho más amplio y complejo, incluyendo, a través de aproximaciones interdisciplinares, las características físicas y biológicas de los ambientes donde se desarrollan los organismos (Hay 1996, Paul *et al*. 2011). Solo cuando se obtengan y se integren todas estas fuentes de información, seremos capaces de entender como funcionan las comunidades en el OA. Cuando esto se consiga, será posible, por ejemplo, predecir cómo estas comunidades podrían verse afectadas por el cambio climático (Pörtner *et al*. 2007).

El **Artículo II** es una contribución original en el campo de la ecología química marina. En él se profundiza en el estudio de las interacciones depredador-presa de un amplio número de invertebrados bentónicos (55) de 9 phyla diferentes contra un depredador simpátrico muy común y de distribución circumpolar, la estrella de mar *O. validus*. Dos son los aspectos que convierten el **Artículo II** en una contribución destacable cuando la comparamos con anteriores trabajos: (i) se estudian especies de profundidad (muchas de ellas además por primera vez); y (ii) las áreas donde los organismos objeto de estudio fueron recolectados (este del Mar de Weddell e Isla de Bouvet) son áreas muy poco estudiadas en cuanto a estudios de ecología química.

Tal y como se menciona en el **Artículo II**, las comparaciones con contribuciones anteriores en el ámbito del OA presentan dificultades. A pesar de ello, nuestros resultados contribuyen considerablemente a incrementar el conocimiento en los estudios de antidepredación en grupos como Porifera, Cnidaria, Bryozoa, Mollusca, Chordata, Echinodermata, y en menor medida en Annelida (ver discusión del **Artículo II**). También son destacables los resultados obtenidos tras probar la Teoría de Defensa Óptima ('Optimal Defense Theory', ODT; Rhoades 1979). Según esta teoría, presas potenciales sometidas a la presión de depredación de una estrella de mar deberían localizar sus metabolitos defensivos en los tejidos más expuestos, debido al tipo de alimentación extraoral de las estrellas. En nuestro trabajo se diseccionaron en partes un total de 25 especies para testar la ODT. De las 7 esponjas diseccionadas, *Cinachyra barbata* y *Tedania oxeata* acumularon defensas químicas en sus partes más externas. De las 4 holoturias diseccionadas, tan solo los tentáculos de *Ekmocucumis steineri* resultaron ser repelentes frente a *O. validus*, cosa que parece tener relación con el hábito de alimentación de la holoturia (Gutt 1991). En cuanto a los moluscos, algunos de los resultados observados parecen confirmar el papel disuasorio que las secreciones ácidas del manto pueden jugar frente a potenciales depredadores, un mecanismo defensivo que se ha sugerido para algunas ascidias con túnica ácida (McClintock *et al*. 2004, Koplovitz *et al*. 2009). Aparte de los comentarios relacionados con la ODT, una última consideración se debería hacer para el poliqueto *Polyeunoa laevis*, especie que generalmente se encuentra en asociación simbiótica con gorgonias del género *Thouarella* (Pettibone 1969; observaciones no publicadas por los autores).

Nuestros resultados parecen indicar que podría existir una relación de comensalismo basado en la química entre el poliqueto y las dos especies de gorgonias que lo albergaban, algo similar a lo que se ha descrito recientemente en la costa de Japón para un octocoral y su anfípodo huésped (Kumagai 2008).

A modo de resumen, los resultados del **Artículo II** indican que más de la mitad (53%) de los invertebrados marinos del bentos antártico y sub-antártico que fueron testados están químicamente protegidos frente a la depredación de la estrella de mar *O. validus*. Esto confirma que las defensas químicas en invertebrados sésiles y de movimiento lento juegan un importante papel en las relaciones depredador-presa en estos ecosistemas. No obstante, como ya se menciona en el **Artículo I**, aparte de en las interacciones antidepredación, los metabolitos secundarios podrían desempeñar en el ecosistema otros papeles (Paul 1992). En este sentido es importante destacar que nuestro grupo de investigación está trabajando intensivamente en desarrollar esta aproximación holística. En el marco de los proyectos ECOQUIM y ACTIQUIM, nuestros esfuerzos se están centrando en establecer, mediante experimentos que usan macro- y microdepredadores, toxicidad frente a organismos de pequeño tamaño y larvas, citotoxicidad y actividad antirecubrimiento, cuáles son los mecanismos de actividad ecológica que controlan el ecosistema. Los resultados obtenidos hasta la fecha nos han permitido elaborar un modelo preliminar de interacciones químicas que integra la información que hemos obtenido del bentos antártico (Figuerola *et al*. 2012).

Bioactividad: Potencial antitumoral en aguas antárticas y sub-antárticas (Artículo III)

En los últimos años, la farmacología marina ha experimentado un renacimiento tras el reciente lanzamiento al mercado de varios compuestos de origen marino (Molinski *et al.* 2009), y también debido a que varios de los futuros medicamentos anticancerígenos que están actualmente en fase clínica y preclínica derivan de compuestos marinos (Newman & Cragg 2004, Simmons *et al*. 2005, Mayer & Gustafson 2008). La mayoría de estos productos naturales se han descrito de ambientes tropicales y templados, áreas que han centrado hasta la fecha los mayores esfuerzos de prospección (ver Blunt *et al*. 2011 y anteriores revisiones). No obstante, tal y como queda probado en el **Artículo III**, la actividad antitumoral de los organismos bentónicos parece ser un campo muy prometedor especialmente cuando se exploran áreas desconocidas y remotas como las aguas antárticas y sub-antárticas. Esto es particularmente importante en el OA, dado que ha permanecido prácticamente aislado

durante varios millones de años, lo que ha desembocado en altos niveles de endemicidad en algunos grupos (Brandt & Gutt 2011).

El **Artículo III** representa el estudio farmacológico más amplio que se haya llevado a cabo jamás en aguas antárticas y sub-antárticas. A pesar del sesgo en los resultados tras un muestreo cualitativo, la mayoría de los resultados antitumorales activos corresponden a invertebrados sésiles estrictos (esponjas, cnidarios y tunicados) que por otro lado fueron también los grupos mejor representados en el cómputo final de especies analizadas. Nuestros resultados concuerdan con lo que ha sido descrito en otras áreas geográficas, donde los organismos sésiles y de movimiento lento arrojan los mayores porcentajes de compuestos citotóxicos (Schmitz *et al*. 1993, Munro *et al*.1999). Tan solo el grupo de los briozoos, el segundo grupo en número de especies testadas, parece no seguir esta tendencia. A pesar de su relativamente alta diversidad tanto en las aguas del OA como en el resto de océanos, este grupo ha sido muy poco investigado en cuanto a sus productos naturales (Sharp *et al*. 2007, **Artículo I**). No obstante, en otras áreas existen ejemplos realmente destacables para estos organismos. Tal es el caso de la bryostatina 1, aislada de *Bugula neritina*, uno de los compuestos de origen natural con mayor efecto antitumoral que se conocen (Pettit *et al*. 1982).

Sin ningún género de dudas, nuestros resultados más destacables fueron los obtenidos para *Aplidium cyaneum*. Algunos de los alcaloides aislados de esta especie (aplycianinas A-F) demostraron una excelente actividad antitumoral y antimitótica (Reyes *et al*. 2008) y fueron patentados por la empresa PharmaMar SA. Otro de los ejemplos antitumorales encontrados en nuestro estudio pertenece también al género *Aplidium* (*A. falklandicum*), lo que confirma a este género como una fuente potencial de compuestos antitumorales en las aguas antárticas, tal y como ya ha sido reconocido en otras áreas (McKee *et al.* 1998, Tourneau *et al*. 2007). Aparte de estos dos notorios ejemplos, vale la pena mencionar que el phylum Chordata es el que mayor actividad antitumoral demostró en nuestros experimentos. Otras especies de otros phyla (Porifera, Cnidaria, Echinodermata y Annelida) también demostraron efectos antitumorales relevantes y una completa discusión acerca de ellos se puede encontrar en el **Artículo III**.

En nuestro estudio, dos especímenes de *Latrunculia brevis* recolectados de dos estaciones de muestreo diferentes demostraron una actividad antitumoral parecida. Es común que individuos de la misma especie demuestren una actividad similar aunque procedan de áreas geográficas diferentes, tal y como ha sido ya probado, por ejemplo, para la ascidia *Ecteinascidia turbinata* (Munro *et al*. 1987). No obstante, también encontramos especies con actividad antitumoral en una estación de muestreo y que por el contrario no tenían ninguna actividad en el resto de estaciones de muestreo donde se recogieron (ver **Artículo III**). Si esta situación es común o rara en la naturaleza es algo que aún se tiene que establecer y podría guardar relación, entre otras razones, a la presencia de simbiontes (König *et al*. 2006). En consecuencia, sugerimos que es importante prospectar diferentes áreas, aún cuando sea para analizar las mismas especies, ya que se podrían obtener resultados inesperados.

Uno de los mayores logros del **Artículo III** es su contribución incrementado considerablemente la información farmacológica para el área del OA (este del Mar de Weddell e Islas Shetland del Sur) y otra área muy poco estudiada como es la Isla de Bouvet (sub-Antártida). Hasta donde conocemos, el único estudio previo comparable fue llevado a cabo por Blunt *et al*. (1990) en aguas de poca profundidad del Mar de Ross. Aunque utilizando un número de especies considerablemente menor, los principales phyla con actividad en su estudio coinciden con los de nuestro trabajo. Otro interesante logro de nuestro artículo es el hecho de haber estudiado especies de profundidad, a diferencia de los pocos estudios que se han realizado hasta la fecha. Las muestras con actividad antitumoral fueron principalmente encontradas a profundidades comprendidas entre 250–500 m en el este del Mar Weddell y la Isla de Bouvet, mientras que las muestras activas de las Islas Shetland del Sur se encontraron por debajo de los 100 m. No obstante, dado que durante nuestras campañas no se realizó un esfuerzo de muestreo homogéneo a nivel batimétrico, no se puede sacar ninguna conclusión al respecto. De modo similar, la actividad antitumoral observada en las tres zonas de muestreo está proporcionalmente correlacionada con el esfuerzo de muestreo realizado en cada una de las áreas (este del Mar Weddell Sea> Islas Shetland del Sur > Isla de Bouvet).

Los resultados que se discuten en el **Artículo III** revelan el gran potencial farmacológico antitumoral que tienen las aguas antárticas y sub-antárticas. Estos resultados están concordancia con la elevada diversidad de productos naturales descritos hasta la fecha en la región del OA (Lebar *et al.* 2007, **Artículo I**), lo cuál está a su vez relacionado con la alta biodiversidad de organismos suspensívoros sésiles y de movimiento lento que habitan en el bentos de estas aguas (Dayton *et al*. 1974, Clarke & Johnston 2003, Brandt *et al*. 2007a). Nuestros resultados deberían animar a que se continuaran investigando zonas poco conocidas como las que aquí se estudian, y centrarse además en organismos de profundidad ya que, debido a las condiciones ambientales extremas en las que éstos viven, tienen elevadas probabilidades de haber desarrollado metabolitos con estructuras únicas (Skropeta 2008).

Biodiversidad: nuevos poliquetos asociados a huesos de ballena (Artículos IV-VI)

A pesar de los considerables esfuerzos que se han hecho durante las últimas décadas para conocer la fauna del grupo de los poliquetos que habita el bentos de la Península Antártica Oeste (ver Barnes *et al*. 2008, Sicinski *et al*. 2011), se siguen encontrando aún nuevos e interesantes organismos en áreas muy bien estudiadas (**Artículos IV-VI**). En nuestro caso, estos nuevos hallazgos están íntimamente ligados al estudio de substratos como los huesos de ballena, a los que se ha prestado poca atención hasta

la fecha y que han despertado un gran interés en otras áreas geográficas (*e.g.* Rouse *et al*. 2004). El estudio de las comunidades de invertebrados marinos que viven asociadas a carcasas de ballena en el OA puede ser realmente interesante, no solo por el hecho de que los restos de ballena juegan un papel muy importante en este contexto (áreas como la Península Antártica Oeste son muy frecuentadas por diferentes especies de cetáceos; Friedlander *et al*. 2006), sino también por las condiciones de aislamiento en las que ha permanecido este área (Scher & Martin 2006, Lagabrielle *et al*. 2009). Así, la investigación de estas particulares comunidades de invertebrados ofrece una excelente oportunidad para establecer interesantes comparaciones con comunidades de otras áreas.

Los resultados presentados en los **Artículos IV-VI** son los primeros que se obtienen en la Antártida a partir de un experimento con un hueso de ballena. A modo de recordatorio breve, los organismos que se describen en estos artículos fueron recolectados de una vértebra fresca de ballena colocada experimentalmente en Caleta Balleneros (Isla Decepción) y también de un hueso viejo recogido de una área cercana.

Aunque las tres nuevas especies de poliquetos de los **Artículos IV-V** (*Cirratulus balaenophilus*, *Ophryotrocha* **sp. nov.** 1 y *O.* **sp. nov.** 2) se han descrito originalmente en restos de ballena, es poco probable que se trate de especies endémicas de estos substratos. Atendiendo a la abundancia relativamente alta observada para *O.* **sp. nov.** 2 y *C. balaenophilus* en el hueso fresco de Caleta Balleneros, se cree que ambas podrían ser especies oportunistas de ambientes de poca profundidad. Así, aparte de asociadas a huesos frescos de ballena, estos organismos se podrían encontrar también en otros ambientes someros ricos en materia orgánica de la zona de las Islas Shetland del Sur, algo similar a lo que ya ha sido observado para otras especies en el área del Estrecho de McMurdo (Mar de Ross). En muestras bentónicas estudiadas en una zona extremadamente perturbada frente a la Estación de McMurdo, se han encontrado altas densidades de especies oportunistas de poliquetos (Lenihan & Oliver 1995, Lenihan *et al*. 2003, Conlan *et al*. 2004). Aparte de en estos ambientes eutrofizados de origen antropogénico, otros ambientes someros podrían también hospedar estos poliquetos oportunistas. Uno de estos ambientes son las calvas (“patches”) naturales creadas en el bentos tras el efecto combinado de la abrasión del fondo por los icebergs y la acumulación y posterior descomposición de materia orgánica. Estos “patches”, recientemente descritos por Powell *et al*. (2012) aunque previamente observados por Richardson & Hedgpeth (1977), albergan tapetes de bacterias que oxidan el azufre y por consiguiente podrían promover la aparición de *O.* **sp. nov.** 2 y/o *C. balaenophilus* (ver debajo). En este sentido, es importante mencionar que la presencia de tapetes bacterianos se suele correlacionar con la presencia de miembros oportunistas del género *Ophryotrocha* (*e.g.* Wiklund *et al*. 2009a,b).

Respecto a los requerimientos tróficos de las especies descritas en los **Artículos IV-V**, aunque no se pudo hacer observación alguna sobre su alimentación ni tampoco se analizaron sus pellets fecales, se cree que estas especies podrían basar al menos parte de su dieta alimentándose de las bacterias filamentosas que se observaron en el hueso fresco. Esta estrategia de alimentación ha sido ya observada

en diversos poliquetos encontrados en elevadas abundancias en otros restos de ballenas (Glover *et al.* 2005, Wiklund *et al*. 2009b,c).

En lo que respecta al nuevo *Osedax* descrito en el **Artículo VI** deberíamos también hacer constar algunas observaciones. Nuestros resultados confirman la presencia en el OA (y en consecuencia en el hemisferio sur) de estos organismos tan particulares que hasta hoy tan solo se habían descrito en el hemisferio norte. También es importante destacar que nuestro nuevo *Osedax* es la especie que se ha encontrado a menor profundidad, batiendo el anterior record de *O. mucofloris*, encontrado a 30 m de profundidad en el Mar del Norte (Dahlgren *et al*. 2006). La mayoría de trabajos anteriores han encontrado estos organismos sobretodo en aguas de profundidad más que en ambientes litorales (ver Vrijenhoek *et al.* 2009 y sus referencias), lo cuál se explica en parte por factores inherentes de los ecosistemas someros que provocan que su éxito de colonización disminuya (Dahlgren *et al.* 2006, Smith 2006). No obstante, la descripción del nuevo *Osedax* de Isla Decepción abre una nueva perspectiva para el estudio de estos organismos en el contexto de las aguas poco profundas del OA.

Nuestros resultados en los **Artículos IV-VI** confirman a las comunidades asociadas a huesos de ballena como un campo de investigación muy prometedor. En los próximos años, nuevos estudios verán la luz ya que existen experimentos similares que están en marcha (A.G. Glover & T.G. Dahlgren pers. comm.; datos de los autores). Más específicamente, en un futuro muy cercano, el género *Ophryotrocha* se confirmará, a través de la descripción de nuevas especies de ambientes profundos (H. Wiklund pers. comm.), como un clado muy importante en el contexto de los restos de ballena en la Antártida. Aparte de los huesos de ballena, hay que recordar que una lista muy amplia de vertebrados vive (y muere) en las costas antárticas (*e.g.* pinnípedos, pingüinos), lo que significa que existe un inmenso número potencial de huesos que se acumulan en el bentos marino. Dado que algunas de las especies originalmente descritas de huesos de ballena se han encontrado también en otro tipo de huesos (Jones *et al.* 2008, Kiel *et al.* 2010, Rouse *et al*. 2011), las comunidades de invertebrados que se desarrollan en los huesos del OA puede que jueguen un papel ecológico mucho más importante de lo que en un principio se creía. Finalmente pronosticamos que, en un futuro no muy lejano, se conocerán muchos de los procesos y patrones que se dan en estas comunidades y esto ayudará a entender, por ejemplo, de qué manera la materia orgánica retenida en los huesos es devuelta a la cadena trófica antártica.

Conclusiones Finales

A continuación se enumeran, de manera breve y concisa, las conclusiones finales a las que se ha llegado tras la finalización de la presente Tesis Doctoral.

- Los organismos antárticos, aunque investigados en mucha menor medida que los de áreas tropicales y templadas, son ricos y diversos en lo que a productos naturales de origen marino se refiere. Se constata además que los roles ecológicos de los diferentes compuestos han sido muy poco estudiados en la mayoría de los grupos.

- Los invertebrados marinos bentónicos antárticos y sub-antárticos de profundidad están químicamente protegidos frente a la estrella de mar *Odontaster validus*, un depredador simpátrico muy común y con distribución circumpolar. Algunos de los organismos bentónicos estudiados localizan sus metabolitos secundarios defensivos en sus partes más expuestas, lo que concuerda con lo postulado por la Teoría de Óptima Defensa ('Optimal Defense Theory').

- Los invertebrados marinos bentónicos de aguas antárticas y sub-antárticas presentan un potencial farmacológico antitumoral muy importante. Los resultados obtenidos para la ascidia colonial *Aplidium cyaneum* destacan entre los más relevantes.

- Las comunidades de invertebrados asociadas a huesos de ballena juegan un papel importante en el Océano Austral. Las nuevas especies encontradas en nuestro experimento indican que estos substratos necesitan de un mayor estudio. El hallazgo de dos nuevas especies del género *Ophryotrocha* sugiere la importancia de este clado en el contexto de los ambientes eutrofizados del Océano Antártico. También se sugiere a *Cirratulus balaenophilus* sp. Nov. como una especie asociada a ambientes ricos en nutrientes. Con la descripción de una nueva especie del género *Osedax* se constata que estos organismos también se encuentran en el hemisferio sur.

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REVIEW ARTICLE

Antarctic marine chemical ecology: what is next?

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Abstract

Antarctic ecosystems are exposed to unique environmental characteristics resulting in communities structured both by biotic interactions such as predation and competition, as well as abiotic factors such as seasonality and ice-scouring. It is important to understand how ecological factors may trigger chemical mechanisms in marine Antarctic organisms as a response for survival. However, very little is known yet about the evolution of chemical compounds in Antarctic organisms. Investigations in chemical ecology have demonstrated over the last several years that defensive metabolites have evolved in numerous representative Antarctic species. This contradicts earlier theories concerning biogeographic variation in predation and chemical defenses. As reviewed here, a number of interesting natural products have been isolated from Antarctic organisms. However, we believe many more are still to be discovered. Currently, many groups such as microorganisms, planktonic organisms and deep-sea fauna remain almost totally unknown regarding their natural products. Furthermore, for many described compounds, ecological roles have yet to be evaluated. In fact, much of the research carried out to date has been conducted in the laboratory, and only in a few cases in an ecologically relevant context. Therefore, there is a need to extend the experiments to the field, as done in tropical and temperate marine ecosystems, or at least, to test the activity of the chemicals in natural conditions and ecologically meaningful interactions. Defense against predators is always one of the main topics when talking about the roles of natural products in species interactions, but many other interesting aspects, such as competition, chemoattraction, fouling avoidance and ultraviolet (UV) protection, also deserve further attention. In our opinion, challenging future developments are to be expected for Antarctic marine chemical ecology in the years to come.

Problem

Chemical ecology is considered a multidisciplinary field including both chemical and biological research (Paul 1992). Natural products (also called secondary metabolites) are chemicals produced by organisms, which regulate the biology, co-existence, and co-evolution of the species without participating directly in their primary metabolism (Torssel 1983). They are characterized by a restricted distribution, occurring only in some groups or species, and by their wide heterogeneity (*e.g.* Luckner 1984; Avila 1995; Cimino *et al.* 1999, 2001; Pietra 2002). In contrast to terrestrial studies, much less is known about the biological function of natural products in the marine environment. In fact, terrestrial chemical ecology, which has focused on animal–plant interactions, has served as a model for many of the studies in marine chemical ecology (Paul 1992; Pietra 2002). Historically,

the research on marine toxins began in the 1960s, when also an important development in the taxonomy of marine animals took place. Over the 1970–1980s, the field expanded towards the search for new compounds and new skeletons. Soon after, the activity-driven research of secondary metabolites was a priority, as a great potential biomedical interest of new natural products was expected. It was not until all these aspects were developed that marine chemical ecology appeared as an interesting field to explore by the end of the 1980s and the beginning of the 1990s. Currently, with more than 18,000 compounds described (MarinLit database), the field of marine natural products has grown and developed, and actually many compounds are under clinical trials to be used as drugs (*e.g.* Newman & Cragg 2004; Salomon *et al.* 2004; Chin *et al.* 2006). Still, chemical ecology is developing slowly, with many chemical and ecological key aspects yet to be studied and understood, and especially in geographic areas where the access to the organisms is difficult and/or expensive.

Marine organisms are under intense pressure for space, light and food. Thus, it is not surprising that they developed, during evolution, a range of defense mechanisms including behavioral, physical and chemical strategies to ensure survival. Ecological roles for marine natural products include anti-predation, mediation of spatial competition, prevention of fouling, facilitation of reproduction, protection from ultraviolet radiation and others (Sammarco & Coll 1992; McClintock & Baker 2001; Rittschof 2001). The most studied activity is the ability of some of these metabolites to deter predators (Paul 1992; Pawlik 1993; Avila 1995; Hay 1996; McClintock & Baker 1997a; Amsler *et al.* 2001a). Even if there are thousands of published studies describing the natural products present in marine organisms (see Blunt *et al.* 2007 and previous reviews), much less studies provide ecological information about the functional significance of these compounds (*e.g.* Paul 1992; Avila 1995, 2006; Hay 1996; McClintock & Baker 1997a, 2001). In many cases, biological activity has been evaluated as the ability of a compound to cause cell lysis or inhibit growth of a non-marine microbe in laboratory assays. This is very useful for pharmaceutical considerations and possible practical applications; however, it is not representative of the ecological effects of the natural products. More realistic assays are needed to prove the ecologically relevant activities of marine secondary metabolites on natural predators, competitors and fouling organisms (Munro *et al.* 1987; Scheuer 1990; Hay & Fenical 1996). Also, natural products may have multiple defensive functions, and many marine organisms may produce a variety of these substances which affect different species of predators and/or pathogens (Paul 1992). Field experiments are necessary for examining deterrent activities and other ecological roles of these compounds.

Marine natural products have been isolated primarily from sponges, cnidarians, molluscs and ascidians, and in to a lesser extent from other invertebrate groups and seaweeds (Baker 1996; Faulkner 1996; McClintock & Baker 1997a; Pietra 2002). By 1993, nearly 7,000 different chemical structures for marine natural products had been documented; these included terpenes, alkaloids, polyketides, peptides, and shikimate-derived metabolites, as well as compounds of mixed biogenesis (McClintock & Baker 2001; Pietra 2002). However, most of the research on marine invertebrate chemical ecology was focused on tropical and temperate environments (Bakus 1964; Bakus *et al.* 1986; Paul 1992; Avila 1995; Pietra 2002). Geographical comparisons on early chemical ecology studies led to a latitudinal hypothesis, suggesting an inverse correlation between latitude and chemical defense strategies in marine invertebrates (Bakus 1974; see also McClintock *et al.* 1990 and Amsler *et al.* 2000a). According to this latitudinal gradient, chemical defense is mainly driven by predation pressure, which was thought to be proportionally higher in the tropics than in polar zones. Chemical defensive compounds employed by marine invertebrates were then expected to be more frequent at low latitudes than at the poles. However, the incidence of bioactivity detected in recent feeding deterrence and toxicity bioassays conducted with sessile or sluggish Antarctic marine organisms were shown to be comparable with temperate, and perhaps even tropical, marine environments (McClintock 1989; McClintock *et al.* 1990; Baker *et al.* 1993; Amsler *et al.* 2000a; McClintock & Baker 2001; Avila 2006). Predation intensity, mainly on account of fish, is considered to be greatest in the tropics, particularly in the Indo-Pacific region, and plays an important role structuring tropical and temperate benthic communities (Bakus 1964, 1969; Vermeij 1978, 1987; Bertness *et al.* 1981; Gaines & Lubchenco 1982; Steneck 1986; Paul 1992). The Antarctic benthos is also exposed to a high incidence of predation, although the main difference would then be that fish predators that browse on sessile marine invertebrates are rare in high latitudes (Eastman 1993), being substituted in Antarctica by a very high incidence of predation by mobile macroinvertebrates, particularly echinoderms, such as large sea stars. In this case, physical devices like structural skeletal elements, such as spicules from sponges or sclerites from cnidarians, may not have the same relevance compared with tropical sessile organisms subject to intense fish grazing; sea stars often feed by extruding their cardiac stomachs over their prey (Hyman 1955). Thus, it is reasonable to predict that natural selection would favor the evolution of chemical defenses against sea stars in Antarctic organisms

(Amsler *et al.* 2000a). The latitudinal hypothesis was based only on data from the Northern hemisphere, and the high predation pressure produced by sea stars in Antarctic communities was not widely recognized at that time (Dearborn 1977; McClintock & Baker 1997a; Amsler *et al.* 2000a).

The Antarctic marine benthic fauna evolved during the Cretaceous break up of Gondwana and the relative movement and separation of the forming continents, including the Antarctic continent (Clarke & Crame 1989; Crame 1992; Dayton *et al.* 1994; Gili *et al.* 2006). The climate remained temperate to sub-tropical until 22 million years ago when the establishment of a circumpolar current led to a hydrographical isolation of the continent, which promoted a high proportion of endemism (Dayton *et al.* 1994; Crame 1999; Gili *et al.* 2000). Antarctic biota are therefore derived from a relict autochthonous fauna, plus an eurybathic fauna from deeper waters, and also some cool-temperate species, mostly arrived from South America (Brey *et al.* 1996; McClintock & Baker 1997a; Gili *et al.* 2006; Brandt *et al.* 2007). The Antarctic communities inhabiting the shallow continental shelf waters are very diverse (Burton 1932; Koltun 1970; Dayton *et al.* 1974; Dayton 1979, 1989; Blunt *et al.* 1990; Gambi *et al.* 1994; Arntz *et al.* 1997). In some areas, there is a dominant sponge community accompanied by many other invertebrate groups. Below the zone of ice-scour, the physical environment of Antarctic marine community is very stable. Such stability has, in part, led to the conclusion that the Antarctic benthic community is structured mainly by biological factors (biologically accommodated), such as predation and competition (Dayton *et al.* 1974; McClintock & Baker 2001). Thus, Antarctic benthos, like tropical benthic systems, is dominated by biological interactions, and it is expected that many marine invertebrates use chemicals as means of defense from predators, inhibiting settling and fouling organisms and preventing overgrowth (McClintock & Baker 2001). As we will see in this study, recent laboratory experiments using sympatric bioassay species have demonstrated that natural products are involved in mediating ecological relationships in many different groups of Antarctic organisms, including macroalgae, poriferans, cnidarians, nemerteans, molluscs, echinoderms, brachiopods, and tunicates, and we will review these data here.

Currently, there are around 170,000 natural products known from around the world (Laatsch *et al.* 2007), and from these only about 18,000 are compounds from marine sources (MarinLit database). To date, as we will see here, there are only about 300 natural products (excluding fatty acids and sterols) described from Antarctic marine organisms, many of which are not found in congeners from temperate and tropical regions. These natural compounds from Antarctic marine organisms are reviewed here from the perspective of their ecological functions, emphasizing the ecological studies done up to date, as well as the chemistry of the natural products, considering what a marine chemical ecologist may need to know when starting to work in this field. The vast majority of the studies on chemical ecology in Antarctica have been conducted in McMurdo Sound, although other areas, such as the Weddell Sea, Antarctic Peninsula, and some Subantarctic Islands, are starting to be investigated in recent years (McClintock & Baker 1997a; Avila *et al.* 2000; Iken *et al.* 2002; Davies-Coleman 2006). In fact, some reviews on the chemical ecology of Antarctic marine invertebrates, mainly from McMurdo, were published in the past (McClintock & Baker 1997a, 2001; Amsler *et al.* 2001a). Since then, a lot of work has been done in Antarctica. The aim of this study is to provide an overview of what it is known to date on the chemical ecology of Antarctic marine organisms. Thus, in this review we include information on the chemical structure of the natural products described, location in the body, origin, bioactivity, and, when known, ecological role(s). We evaluate the work done to date for each taxonomic group and we outline further developments of the field in the near future, considering the current status of the information available as well as the challenging opportunities for the years to come.

Methods

An extensive bibliographic research has been carried out to obtain the information needed for this review. The results of the review are displayed in the format of a table, including all the details about the natural products and chemical ecology of Antarctic marine organisms described up to May 2007. MarinLit, as well as other searchable databases, have been a useful tool in preparing the table. The formulae and chemical details of every compound are not included here, as it is outside the scope of this review, although they can easily be found in the references quoted in the table. Only a few chemical structures are shown in Figs 1–3, as examples of interesting compounds described in Antarctic organisms.

The general scheme and nomenclature codes for the table have been chosen in conformity with previous reviews (Avila 1995). World Porifera Database, Algae Base and other databases have been used to check current names for all the species. Species names, which have changed after the referenced study was published, are corrected, with the changed name included in brackets. Long chemical names are numbered and reported at the end of the table.

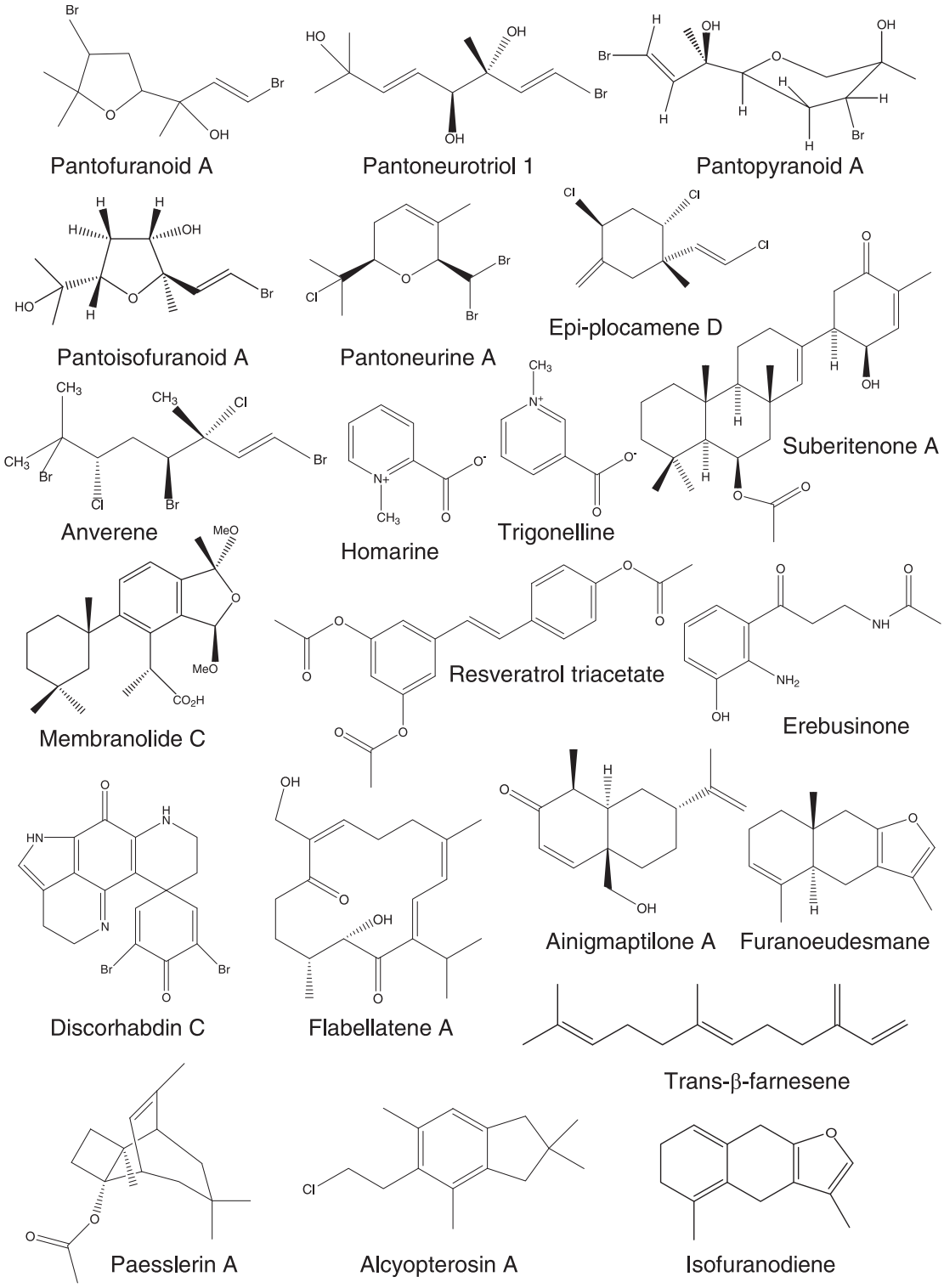

Fig. 1. Chemical structure of some natural products described from Antarctic algae, poriferans and cnidarians.

Unless otherwise specified, the data in the table refer to the whole body extracts of the organisms studied or the compounds when described. Many algal studies have been done in different laboratory conditions of light, and thus may provide different compounds and/or activities in these conditions (*e.g.* Riegger & Robinson 1997; Hannach

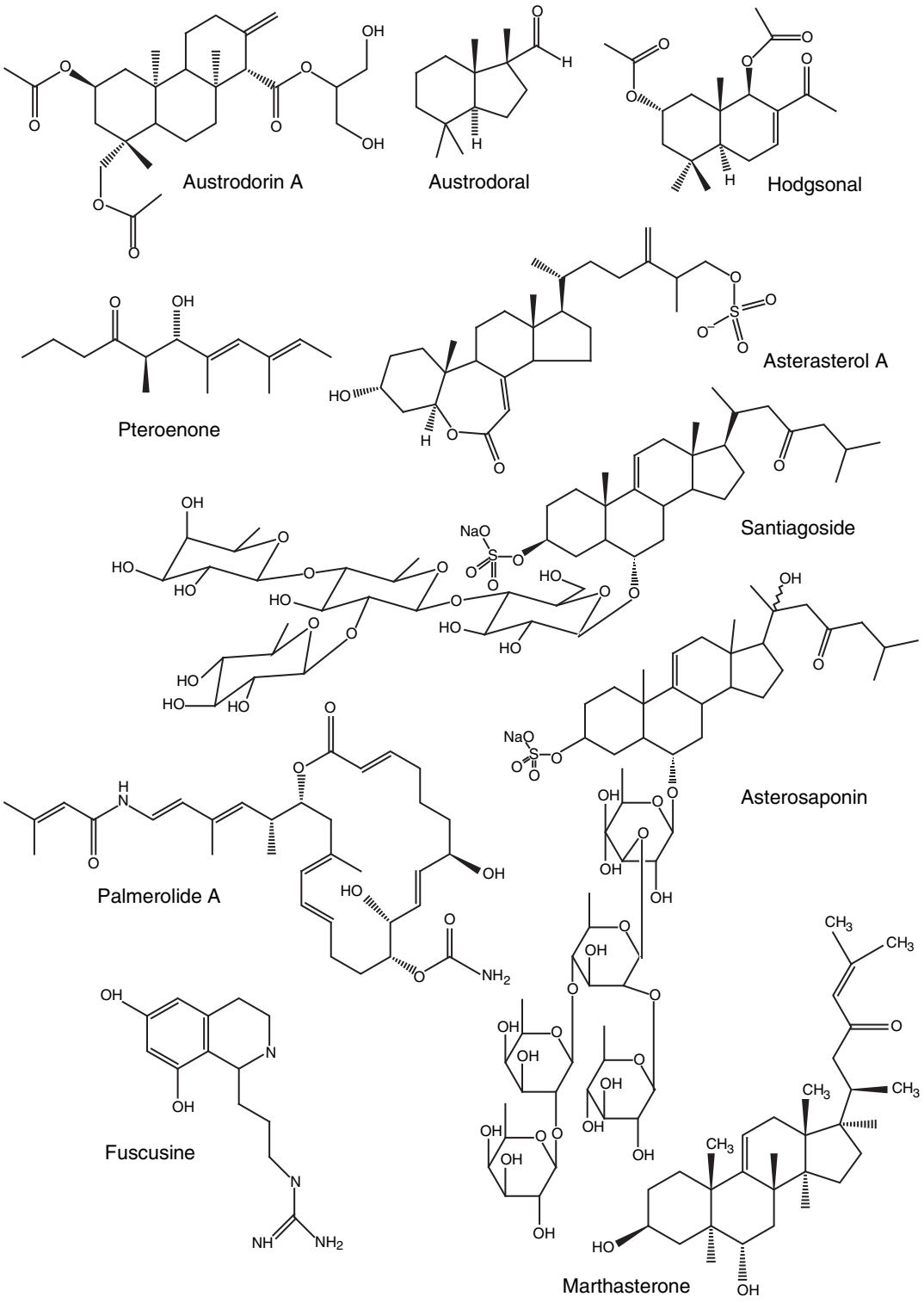

Fig. 2. Chemical structure of some natural products described from Antarctic molluscs, echinoderms and tunicates.

& Sigleo 1998; Laturnus *et al.* 1998b; Hoyer *et al.* 2001); details on these aspects should be confirmed directly in the papers reported.

When activity or origin is suspected but unproven, we include a question mark in the table to indicate it is only a suggestion by the authors of that particular

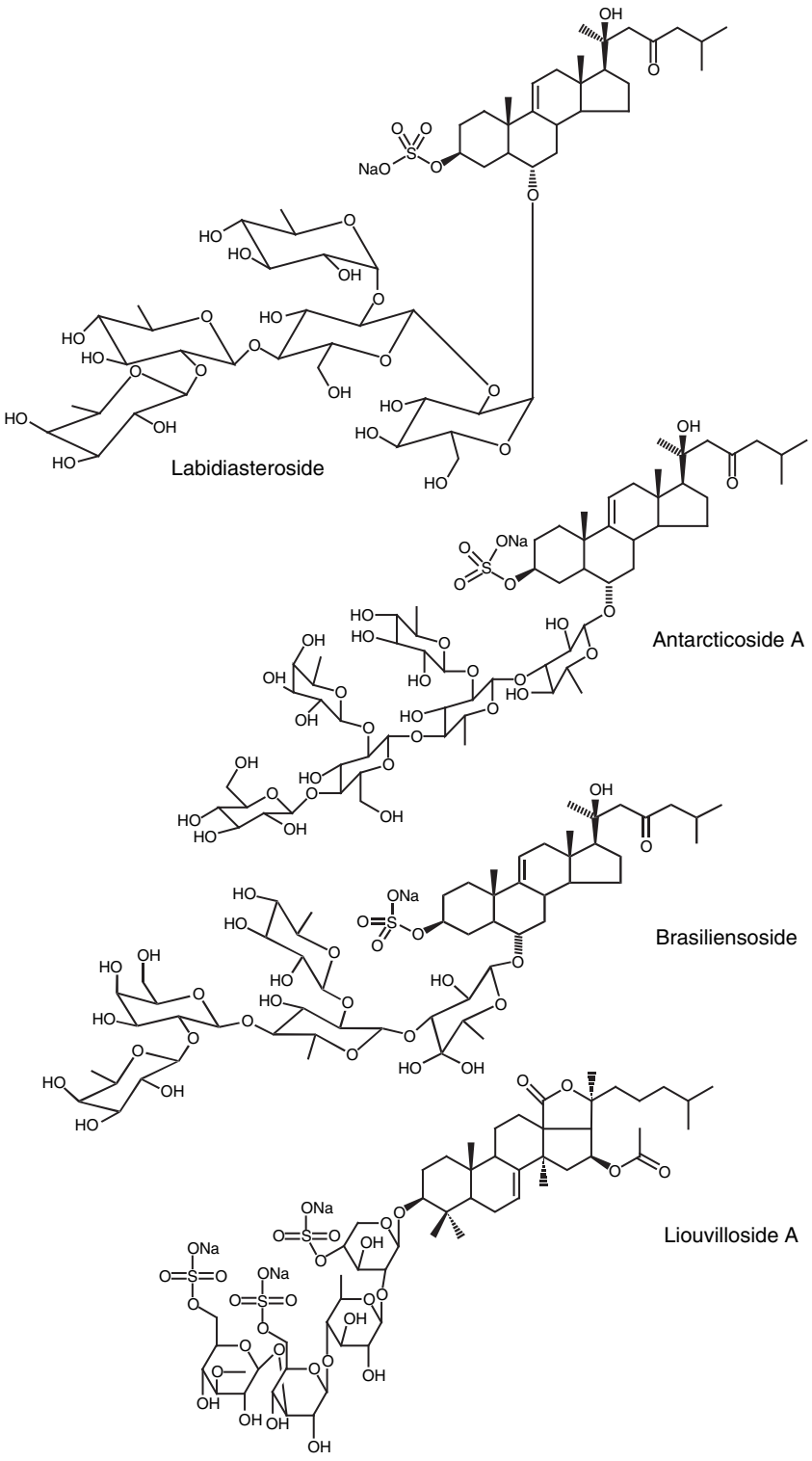

Fig. 3. Chemical structure of some natural products described from Antarctic echinoderms.

study. Activities are usually reported for a single species tested, and thus may or may not be the same if tested for other species. Contradicting results may occasionally be obtained in different studies, which is reflected in the table. As for the origin, most algal compounds are suggested to be biosynthesized, although this has not

been proven and, therefore, it is not included in the table.

For each species, the first study is named first on the reference column; after that they are organized by groups of compounds. Within groups, they are in chronological order. In order to simplify the table, references that are mentioned for one species are not repeated for the different compounds, even if they do contain data for more than one compound, origin or activity.

Results and Discussion

We review here all the natural products described to date (May 2007) from Antarctic marine organisms, their chemical structure, location in the body, origin, as well as bioactivity (if reported), and their ecological role when known (Table 1). There are only about 300 natural products, plus many fatty acids and sterols, described from 263 Antarctic marine organisms (94 algae, 166 invertebrates and 3 fishes). Results are analysed by taxonomic groups, with general remarks and conclusions at the final part. For each taxonomic group, some general comments are provided, and selected examples of chemically mediated ecological interactions are reported.

Algae

Macroalgae dominate shallow marine communities on hard substrates along the Antarctic continent and are the most studied organisms regarding chemical ecology in Antarctica. About 120 species of macroalgae have been described up to now (Clarke & Johnston 2003), and from them, a total of 94 species have been chemically studied so far (Table 1). In general, macroalgae are known to defend against herbivory by both physical and chemical mechanisms. A number of Antarctic marine organisms can be potential consumers of macroalgae, however, there is little evidence of significant macroalgal grazing in the field. With the exception of amphipods, one fish, and two gastropods, macroalgae have been reported only rarely in the guts of potential herbivores (Iken *et al.* 1997, 1999; Iken 1999; McClintock & Baker 2001). Diatoms, other microalgae and green algae possess mainly UV protectants and volatile halogenated compounds. Brown macroalgae (Class Phaeophyceae) elaborate prenylated terpenes, hydrocarbons, and phlorotannins and appear to be the major sources of volatile halogenated organic compounds (VHOC) with ozone-depleting properties. Phlorotannins (polyphenols) are known to have antifeedant effects in temperate and tropical phaeophytes. However, the ecological role of these compounds still remains to be determined in Antarctic brown algae, which have been scarcely studied so far (Iken *et al.* 2001, 2007; McClintock & Baker 2001; Fairhead *et al.* 2005a; Amsler & Fairhead 2006). Antarctic red macroalgae (Class Rhodophyceae), like their temperate and tropical congeners, produce a variety of halogenated terpenes and halogenated alkanes, the latter with ozone-depleting properties. To date, more than 50 compounds have been reported from Antarctic red macroalgae, thus proving them a rich source of natural compounds, although many uncertainities remain about their ecological roles.

Many species of macroalgae possess UV-protectant compounds, such as mycosporine-like amino acids (Table 1). Macroalgal UV-absorbing compounds may vary with development, body part, depth or species (Hoyer *et al.* 2001, 2003) and also with laboratory conditions (Laturnus *et al.* 1998b, 2000; Hoyer *et al.* 2002). They are mainly present in red algae, and only in some green algae, while being scarce in brown algae (Karentz *et al.* 1991; Karentz 1994; Hoyer *et al.* 2001; Rautenberger & Bischof 2006). Also, UVA and UVB-absorbing compounds have been described in Antarctic microalgae, such as *Nitzschia* sp., *Dunaliella* sp., *Geminifera cryophila*, *Pyramimonas gelidicola* and *Phaeocystis pouchetti* (Karentz *et al.* 1991; Marchant *et al.* 1991; Helbling *et al.* 1996; Riegger & Robinson 1997; Jeffrey *et al.* 1999). Some Antarctic diatoms such as *Nitzschia stellata* and *Porosira pseudodenticulata*, contain bromoalkanes, which produce the photolysis of bromoform, which is suggested to be the cause of surface ozone losses (Sturges *et al.* 1993).

Interestingly, crude extracts of two Antarctic red macroalgae, *Iridaea cordata* and *Phyllophora antarctica,* have been found to display antiherbivore effects against the sea urchin *Sterechinus neumayeri* in a phagostimulation assay (Amsler *et al.* 1998). Also, Amsler *et al.* (1999) discovered a unique trophic interaction involving defensive interactions of these two species of macroalgae, the sea urchin *Sterechinus neumayeri*, and the voracious opportunistic sea anemone, *Isotealia antarctica*. *Iridaea cordata* and *Phyllophora antarctica* are chemically defended against herbivory by *Sterechinus neumayeri*, and the sea urchin covers itself with these macroalgae. This algal cover significantly increases the likelihood of escape from *Isotealia antarctica*, and thus protects the sea urchin from predation by the sea anemone. It is a mutualistic relationship in which the macroalgae also benefit from this behavior because fertile drift plants are retained in the photic zone, where they continue to contribute to the gene pool (Amsler *et al.* 1999).

Other interesting studies reported bioassays with different species of Antarctic macroalgae. Grazing experiments using the littorinid gastropod *Laevilacunaria antarctica*

were conducted using intact algae, homogenates and solidified algae in agar, but no chemical defense was detected against this gastropod. The results showed that the five studied macroalgae (*Ascoseira mirabilis*, *Phaeurus antarcticus*, *Himantothallus grandifolius*, *Palmaria decipiens* and *Curdiea racovitzae*) presented physical defenses against mollusc grazing, as all the algae homogenates were eaten by the gastropod. However, none of the intact algae were consumed, showing no chemical implication in this feeding deterrence (Iken 1999). Another study evaluated the palatability and chemical defenses of 35 species of subtidal macroalgae from the Antarctic Peninsula and found out that most species had feeding-deterrent activity against the sea star *Odontaster validus*, the rockfish *Notothenia coriiceps* and the amphipod *Gondogeneia antarctica*, and from these data concluded that Antarctic macroalgae are commonly unpalatable to sympatric herbivores on account of their chemical composition (Amsler *et al.* 2005a). Bioassays to test potential defenses against diatom fouling also showed that antifouling properties are prominent among Antarctic macroalgae (Amsler *et al.* 2005b).

Pantoneura plocamioides has been found to contain a wide variety of terpenoid derivate compounds (Fig. 1), such as several pantofuranoids (Cueto & Darias 1996), pantoneurotriols (which are proposed as biogenic precursors of pantofuranoids; Cueto *et al.* 1998c), pantoneurines (Cueto *et al.* 1998b; Argandoña *et al.* 2002), pantopyranoids and pantoisofuranoids (Cueto *et al.* 1998a). Pantoneurines A and B showed antifeedant properties against *Leptinotarsa decemlineata*, an allopatric chrysomelid insect (Argandoña *et al.* 2002).

Halogenated lactones (fimbrolides, acetoxyfimbrolides and hydroxyfimbrolides) with antimicrobial activity against allopatric bacteria and fungi were described from *Delisea fimbriata* (also called *Delisea pulchra*) (Pettus *et al.* 1977; Cueto *et al.* 1991, 1997; Ankisetty *et al.* 2004b). *Plocamium cartilagineum* is known to contain monoterpenes with antibacterial activity (Rovirosa *et al.* 1990; Cueto *et al.* 1991), as well as two terpenoid compounds, *epi*-plocamene D and anverene (Fig. 1), the latter presenting modest antimicrobial activity, and both of them showing feeding-deterrence against the herbivorous amphipod *Gondogeneia antarctica* (Ankisetty *et al.* 2004b). Also, halogenated monoterpenes from this red alga (plocamene D and *epi*-plocamene D) possess antifungal activity (Cueto *et al.* 1991).

The brown macroalga *Desmarestia menziesii* produces plastoquinones, which have been suggested to present cytotoxic activity against leukemia cells, toxicity to fish, and are thought to inhibit mitosis of fertilized sea urchin eggs (Rivera 1996). *Desmarestia menziesii* and *Desmarestia anceps* are amongst the few species that have been studied in terms of the variation in the chemical and physical defenses in different parts of the algal thallus (Fairhead *et al.* 2005a,b, 2006). UV-induction experiments showing an increase in phlorotannin concentrations and feeding-preference experiments against the amphipod *Gondogeneia antarctica* have also been conducted with these two Antarctic brown macroalgae (Fairhead *et al.* 2005a, 2006). Huang *et al.* (2006) studied three species of macroalgae of the genus *Desmarestia* (*D. anceps*, *D. antarctica* and *D. menziesii*) and found that all of them had feedant-deterrent properties against Antarctic sympatric gammarid amphipods.

Halogenated compounds have been found to be very common in Antarctic macroalgae. Laturnus *et al.* (1997, 2000) conducted some experiments measuring the release of volatile halogenated organic compounds (organobromine, organoiodine and organochlorine derivatives), and their halogenating activity. Giese *et al.* (1999) measured the release of volatile iodinated C-1-C-4 hydrocarbons in 16 algal species. Twenty-eight species of Antarctic macroalgae were found to be the source of halogenated volatiles and these compounds were suggested to act as chemical defenses against microorganisms or herbivores (Laturnus *et al.* 1996). Later, methyl halides were found in 22 species of Antarctic macroalgae, including methyl bromide, methyl iodide, methyl chloride, and bromoform (Laturnus *et al.* 1998a,b).

Novel Antarctic algal compounds, not previously described from any other organism, include several monoterpenes from *Pantoneura plocamioides* (Cueto & Darias 1996; Cueto *et al.* 1998c), *Plocamium* sp. and *Plocamium cartilagineum* (Stierle & Sims 1979; Stierle *et al.* 1979; Darias *et al.* 1987; Rovirosa *et al.* 1990; Cueto *et al.* 1991; Ankisetty *et al.* 2004b), as well as several halogenated compounds and quinones from other species (Laturnus *et al.* 1996; Cueto *et al.* 1997; Ankisetty *et al.* 2004a). Matsuhiro & Urzua (1996a,b) reported some interesting polysaccharides from *Palmaria decipiens*.

UV-protecting molecules, mainly mycosporine-like amino acids, are very common in Antarctic marine algae. They have been detected in a large number of species and are thought to be synthesized by the algae and then transferred through the trophic chain by their consumption. This has been proposed to be an adaptation to ozone depletion (Karentz *et al.* 1991; Kattner *et al.* 1994; McClintock & Karentz 1997; Hoyer *et al.* 2001, 2002, 2003). Some other chemical compounds found to act as natural radiation protectants include some UV-absorbing pigments from *Palmaria decipiens* and *Enteromorpha bulbosa* (Post & Larkum 1993) and some carotenoid pigments from *Leptosomia simplex* which may have a role in protecting from UV and X radiations (Karentz & Bosch 2001).

Although ecological information on some macroalgal natural products is already available (Amsler *et al.* 2001b, 2005a,b; Iken *et al.* 2001), many other natural compounds have been described from different species (Table 1) for which their ecological role remains unknown. As macroalgae are an important component of shallow-water communities, a lot of questions about chemically-mediated interactions with other organisms remain unanswered, thus providing areas to be investigated in the future. Furthermore, regarding their chemical ecology, microalgae remain mostly unknown in Antarctic waters, thus providing a potential source of interesting bioactive natural products.

Porifera

Sponges are the dominant macroinvertebrate organisms in many Antarctic benthic communities and play a central position in the ecology of these ecosystems (Burton 1932; Koltun 1970; Dayton *et al.* 1974). They are one of the major targets of chemical investigations in Antarctica and elsewhere because of their high biomass and the well documented ability to possess interesting natural products. Dayton *et al.* (1974) were among the first to suggest that Antarctic sponges could harbor chemical defenses in their bodies, having observed no predation on the sponges *Leucetta leptoraphis*, *Dendrilla membranosa* and *Isodictya erinacea*. Today, from the ca. 280 species described in Antarctica (Clarke & Johnston 2003), only 55 Antarctic sponge species have been chemically studied, producing terpenes, halogenated compounds, alkaloids and mycosporine-like amino acids (Table 1). The first studies evaluating chemical bioactivity used crude extracts of different sponges to test ichthyotoxicity against the goldfish *Carassius auratus* (McClintock 1987) and inhibition of growth in allopatric microorganisms (McClintock & Gauthier 1992). Also, some antiviral activity was reported by Blunt *et al.* (1990) in several Antarctic and Subantarctic sponges. In addition, the ability of some sponges from McMurdo Sound (*Cynachyra antarctica*, *Latrunculia* sp., *Polymastia* sp.) to reject tissues from congeners producing defensive chemicals was discovered by Battershill (1990) in immunological assays. These data supported the occurrence of a variety of active natural compounds in Antarctic sponges and provided information, which could be useful for pharmacological and agrochemical applications. Nonetheless, these results gave little information on the ecological significance of these natural products.

McClintock *et al.* (1990) used 18 species of Antarctic sponges to carry out three types of ecologically relevant bioassays: cytotoxicity to *Sterechinus neumayeri* gametes, rightening response in *Odontaster validus*, and tube-foot retraction in *Odontaster validus*, *Odontaster meridionalis*, *Diplasterias brucei*, *Acodontaster conspicuus* and *Perknaster fuscus*. Out of the 18 species, nine (50%) showed positive activities to all three tests, six (33%) were negative to all the tests, and three species (17%) showed positive response only to the seastar tube-foot retraction test. Subsequent investigations conducted by McClintock's group (McClintock *et al.* 1993a, 1994b, 2000) focused on the feeding-deterrence activity of hexane, chloroform and methanol (non-polar to polar) extracts of some Antarctic sponges. They designed a tube-foot assay employing an ecologically relevant predator, the common Antarctic spongivorous sea star *Perknaster fuscus*. When the chemosensory tube-feet were presented with sponge extracts applied to a glass rod, responses were either non-deterrent (when tube-feet attached to the glass rod), or deterrent when there was a retraction of the tube-feet for up to 60 s. Significant tube-foot retraction activity was detected in the chloroform and methanol extracts of 75% of the 35 species tested. These results were comparable to those obtained in anti-predation experiments conducted with reef fish and feeding pellets containing extracts of Caribbean sponges (Pawlik *et al.* 1995). Other defensive activities of sponge extracts have been assessed recently. Amsler *et al.* (2000b) detected chemical defenses against diatom fouling in seven out of the eight Antarctic sponges tested. Furthermore, protection against UV radiation was found in methanol extracts of 14 species of Antarctic sponges, likely on account of the presence of a variety of mycosporine-like amino acids, most of them derived from algae (McClintock & Karentz 1997). Among these compounds it is remarkable the presence of mycosporine-glycine:valine, found in some Antarctic sponges and also present in many other invertebrate groups. This compound is absent in algae and it has been suggested to be either *de novo* biosynthesized by the organisms or being chemically modified from another mycosporine-like amino acid.

Over the years, a wide range of secondary metabolites has been isolated from Antarctic sponges, most of them with some bioactive characteristics, but, as already said, not always ecologically significant (Baker *et al.* 1993; Baker & Yoshida 1994; McClintock & Baker 1997a; Amsler *et al.* 2001a). *Suberites* sp. has been found to produce suberitenones and suberiphenol (Shin *et al.* 1995; Lee *et al.* 2004). From these, suberitenones A (Fig. 1) and B produced tube-foot retraction in *Perknaster fuscus*, and they also showed a modest antibacterial activity against sympatric microbes isolated from the hydroid *Halecium arboreum* and the sea star *Acodontaster conspicuous* (Baker *et al.* 1997). Related new compounds were recently described from *Suberites caminatus* (Díaz-Marrero *et al.* 2003, 2004a) although their activity

has not yet been tested. From *Dendrilla membranosa*, 7-methyladenine and picolinic acid produced sea star tube-foot retraction, while the yellow pigment 4,5,8-trihydroxyquinoline-2-carboxylic acid showed antibacterial activity, and membranolides C (Fig. 1) and D displayed antibacterial and antifungal activity (Molinski & Faulkner 1987, 1988; Ankisetty *et al.* 2004a). *Kirkpatrickia variolosa* produces the bioactive stilbene derivative, resveratrol triacetate (Fig. 1), as well as several variolins, a group of alkaloids, some of which have antitumor and antiviral activity (Perry *et al.* 1994; Trimurtulu *et al.* 1994; Jayatilake *et al.* 1995). Moreover, an uncharacterized pigment of *Kirkpatrickia variolosa* caused tube-foot retraction in *Perknaster fuscus* (Baker & Yoshida 1994).

Latrunculia apicalis and other species of the genus *Latrunculia* contain a variety of discorhabdin pigments (Fig. 1) which are cytotoxic (Perry *et al.* 1988a,b; Blunt *et al.* 1990; Baker & Yoshida 1994; Yang *et al.* 1995; Ford & Capon 2000) and cause sea star tube-foot retraction (Furrow *et al.* 2003). Several compounds were isolated from *Isodictya erinacea* (Table 1) but only *p*-hydroxybenzaldehyde produced tube-foot retraction in *Perknaster fuscus* (Baker & Yoshida 1994; Moon *et al.* 1998). Body extracts from *Leucetta leptoraphis* showed antibacterial activity to allopatric microorganisms and antifouling properties against sympatric species. However, the methanolic extract was the only one that caused strong sea star foot tube retraction and ichthyotoxicity against allopatric fish (McClintock 1987; McClintock *et al.* 1993a, 1994b; Amsler *et al.* 2000b). Taurine and rhapsamine have also been isolated from the methanolic extract of this sponge. Rhapsamine promotes cytotoxicity in fertilized sea urchin assay and cytotoxicity against different cell lines (Jayatilake *et al.* 1997). *Lissodendoryx flabellata* possesses two new cembranes, flabellatene A (Fig. 1) and B, the first one with antitumoral properties (Fontana *et al.* 1999).

Cadmium and zinc are present in *Tedania charcoti* and they are included here, although inorganic elements, because they seem to inhibit the growth of some species of allopatric bacteria (*Staphylococcus aureus*, *Micrococcus* sp., *Serratia* sp. and *Escherichia coli*) as well as to modulate protein phosphorylation in chicken forebrain (Capon *et al.* 1993). Guella *et al.* (1988) found sterones (*e.g.* ergosta-4,24(28)dien-3-one) in a group of unidentified Subantarctic shallow-water sponges. In fact, several Antarctic sponges possess steroidal derivates as secondary metabolites, as in the case of *Artemisina apollinis* (Seldes *et al.* 1990b), *Homaxinella balfourensis* (Seldes *et al.* 1986), *Xestospongia* sp. and *Cinachyra barbata* (Seldes *et al.* 1990a; Cueto *et al.* 1991).

Vetter & Janussen (2005) studied five species of Antarctic sponges: *Kirkpatrickia variolosa*, *Halichondria* sp., *Artemisina apollinis*, *Phorbas glaberrima* and *Leucetta antarctica* and obtained halogenated natural products from their tissues. Finally, bioactive metabolites have also been isolated from bacteria associated with the studied sponges. Diketopiperazines (DKP) and phenazine alkaloids are synthesized by *Pseudomonas aeruginosa*, which is associated with *Isodictya setifera* (Jayatilake *et al.* 1996). Symbiotic microorganisms seem to be involved in the production of natural products of many marine invertebrates from tropical and temperate waters (König *et al.* 2006). The relationship between natural products from Antarctic sponges and their symbiotic microorganisms is an important open question which has not yet been studied in depth and therefore is expected to provide interesting results in the future (Webster *et al.* 2004).

Novel natural products described in Antarctic Porifera include many interesting compounds such as alkaloids (Butler *et al.* 1992; Baker *et al.* 1997; Moon *et al.* 1998; Ford & Capon 2000), sterols (Seldes *et al.* 1990a; Díaz-Marrero *et al.* 2004a), and diterpenes (Molinski & Faulkner 1987; Baker *et al.* 1993; Fontana *et al.* 1999; Díaz-Marrero *et al.* 2004b).

The spongivorous sea star *Perknaster fuscus* is a specialist feeder whose diet is almost exclusively based on the fast-growing and potentially space-dominating sponge *Mycale acerata* (Amsler *et al.* 2000a). This predation prevents competitive exclusion of slow-growing sponge species. This brings up the hypothesis that there might be a correlation between growth rate and production of chemical defenses in Antarctic sponges suggesting that slow-growing species are more likely to possess chemical defenses, although this has yet to be tested (Amsler *et al.* 2000a). In fact, very few data exist on this topic even in other areas of the world.

The primary predators of Antarctic sponges are described to be sea stars (McClintock 1994), which are able to chemically orientate towards their prey (Sloan 1980), but are not visually oriented. Thus, it is unlikely that Antarctic sponges use warning colorations or aposematism to avoid being predated by them, while instead a wide range of chemical and physical strategies may increase their survival. Nevertheless some pigments have demonstrated to play a role as defensive metabolites, such as erebusinone (Fig. 1) from *Isodictya erinacea* which causes molt inhibition (Moon *et al.* 2000) and a purple uncharacterized pigment from *Kirkpatrickia variolosa* producing foot tube retraction on sympatric sea stars (Jayatilake *et al.* 1995). As mentioned above, however, only a few studies really demonstrate the activity of their described natural compounds against sympatric species. Therefore, a lot of work still needs to be done regarding field or ecologically meaningful testing.

Cnidarians

Cnidarians also are an ecologically important group in Antarctic benthic communities and they possess a variety of natural products with interesting bioactivities. There are 272 species of Antarctic cnidaria described (Clarke & Johnston 2003); however, only eight species have been chemically studied so far (Table 1). The most studied Antarctic cnidarians belong to the group of the soft corals (O. Alcyonacea) and include *Clavularia frankliniana*, *Alcyonium paessleri* and *Gersemia antarctica*. These three species are chemically defended (McClintock & Baker 1997a). Experiments showed that extracted tissues are not ichthyodeterrent compared to non-extracted tissues, suggesting that sclerites have no apparent effect in deterring potential predatory fish. This indicates that chemical compounds, removed during the organic extraction process, are responsible for predator deterrence. Organic extracts of *Alcyonium paessleri* and *Gersemia antarctica* have also been found to possess antifouling and antimicrobial activities and both are toxic to larvae of the Antarctic sea urchin *Sterechinus neumayeri*. Moreover, *Perknaster fuscus* and *Odontaster validus*, two potential soft coral predators, showed tube-foot retraction to organic and aqueous extracts of all three soft coral species (Slattery & McClintock 1995, 1997; Slattery *et al.* 1995).

Clavularia frankliniana has been shown to produce chimyl alcohol, which was suggested to deter predation by the omnivorous sea star *Odontaster validus* (McClintock & Baker 2001). Homarine and trigonelline (Fig. 1), two water-borne metabolites which cause growth inhibition in Antarctic microbes such as *Alteromonas* sp., *Moraxella* sp. and *Psychrobacter* sp. have been extracted from *Gersemia antarctica* (Slattery *et al.* 1997a). Other water-borne sterol compounds (like cholesterol, 22-dehydrocholesterol, 24-methylenecholesterol and 22-dehydro-7β-hydroxy-cholesterol) have been isolated from *Alcyonium paessleri* and all of them except 24-methylenecholesterol promote sea star tube-foot retraction. A strong chemo-avoidance in the Y-maze experiments of water-borne cholesterol from *Alcyonium paessleri* was also observed for three Antarctic echinoderms and the nemertean *Parborlasia corrugatus* (Slattery *et al.* 1997a). Some other metabolites have been identified in *Alcyonium paessleri*, such as paesslerins (Rodríguez-Brasco *et al.* 2001) and alcyopterosins (Palermo *et al.* 2000) (Fig. 1), but no ecological activity has been reported so far. Slattery *et al.* (1997b) studied the steroid metabolism in the two soft corals *Clavularia frankliniana* and *Alcyonium paessleri* reporting the presence of steroid metabolic enzymes with the capacity to metabolize precursors like progesterone and androstenedione into other steroid products; this ability has no ecological role described at the moment.

Novel compounds described in Antarctic alcyonarians are mainly terpenes and steroids from *Alcyonium paessleri* (Palermo *et al.* 2000; Rodríguez-Brasco *et al.* 2001) and *Dasystenella acanthina* (Gavagnin *et al.* 2003c; Mellado *et al.* 2004). Crude extracts from *Ainigmaptilon antarcticus* possess feeding-deterrent activity against *Odontaster validus*, and two sesquiterpenes, ainigmaptilones A and B (Fig. 1), have been isolated from this species. Ainigmaptilone A shows sympatric antimicrobial activity, antifouling activity against sympatric diatoms, and feeding-deterrence against *Odontaster validus* (Iken & Baker 2003). The Antarctic gorgonian *Dasystenella acanthina*, has also been found to contain sesquiterpenes: *trans*-β-farnesene, furanoeudesmane and isofuranodiene (Fig. 1), the two latter being ichthyotoxic against allopatric fish (Gavagnin *et al.* 2003c). At least eight other polyoxygenated steroids with cytotoxic activities against human tumor cell lines have been obtained from this octocoral (Mellado *et al.* 2004). *Anthomastus bathyproctus*, another Antarctic octocoral, is responsible for the production of a variety of steroids, some of them with a slight cytotoxicity against human tumor cell lines (Mellado *et al.* 2005).

Furthermore, mycosporine-like amino acids providing UV radiation protection were found in the soft coral *Alcyonium paessleri*, in the sea anemone *Isotealia antarctica*, and in another unidentified Antarctic sea anemone (Karentz *et al.* 1991; McClintock & Karentz 1997).

Further studies on the chemical ecology of cnidarian natural products are strongly needed. Other cnidarian groups in Antarctica remain totally unexplored in chemical ecology studies.

Molluscs

The diversity of Antarctic molluscs has triggered a lot of interest in studying their biology and ecology, even if only 17 species, out of ca. 700 (Clarke & Johnston 2003) have been chemically analysed to date (Table 1). Most of them have only been tested for the presence of UV-protectant compounds, mycosporine-like amino acids (Table 1). Chemical defense has been studied in several circumpolar molluscan species. For some species, it has been observed that their chemical defensive systems are similar across a wide geographic range, while for others, geographical variations seem to exist. McClintock's group, studying the nudibranchs *Austrodoris kerguelenensis* and *Tritoniella belli*, and the prosobranch *Marseniopsis mollis*, found that their mantle tissues were rejected by two species of sympatric fish, and their aqueous extracts caused sea star tube-foot retraction, arm retraction, and

had cytotoxic activity against *Sterechinus neumayeri* sperm cells (McClintock *et al.* 1992a). The sea slug *Austrodoris kerguelenensis* produces a series of bioactive acid glycerides, terpenoid acylglycerols such as austrodorins (Fig. 2), and two nor-sesquiterpene compounds called austrodoral (Fig. 2) and austrodoric acid (Davies-Coleman & Faulkner 1991; Gavagnin *et al.* 1995, 1999a,b, 2003a,b). Diterpene acylglycerols from *Austrodoris kerguelenensis* have been found to deter potential predators such as the sea star *Odontaster validus* in ecologically significant experiments. This species has been suggested to biosynthesize their own defensive compounds (Iken *et al.* 2002), and we recently tried to prove this by doing biosynthetic experiments with labeled precursors (*e.g.* Cimino *et al.* 2004; Fontana 2006). In fact, *de novo* biosynthesis does occur in *A. kerguelenensis*, although the produced compounds show a large variability between individuals, even from the same population (Avila *et al.* 2007). To our knowledge, this is the first demonstration of *de novo* biosynthesis in an Antarctic organism.

Tritoniella belli contains chimyl alcohol which apparently is derived from its main diet the soft coral *Clavularia frankliniana*, and was shown to be a feeding-deterrent against *Odontaster validus* (McClintock *et al.* 1994c,d). Also, the mantle mucus of *Tritoniella belli* generates tube-foot retraction in *Odontaster validus* and *Perknaster fuscus* and feeding-deterrence in the sympatric fish *Pseudotrematomus bernacchii* (Bryan *et al.* 1998). Moreover, egg masses of this nudibranch seem to be chemically defended and deter the sympatric predator *Odontaster validus* but neither the amphipod *Paramoera walkeri* or the sea anemone *Isotealia antarctica* (McClintock & Baker 1997b).

Mantle tissues and aqueous extracts of the prosobranch *Marseniopsis mollis* are rejected by Antarctic fish and omnivorous sea stars, and homarine (Fig. 1) has been isolated from its mantle, foot and viscera (McClintock *et al.* 1992a, 1994a,d). Homarine has also been isolated from the dense assemblage of epizooites fouling the tunic of the ascidian *Cnemidocarpa verrucosa*, the presumed primary prey of this gastropod. A dietary origin from fouling organisms (basically bryozoans and hydroids) could explain the presence of homarine in the viscera of *Marseniopsis mollis* (McClintock *et al.* 1992a, 1994a). Homarine is a very common chemical substance in marine invertebrates and it is a feeding-deterrent against *Odontaster validus* (McClintock *et al.* 1994a,d).

Bathydoris hodgsoni is another dorid nudibranch, which has been found to possess a sesquiterpene, hodgsonal (Fig. 2), which is accumulated in the mantle and papillae and causes feeding-deterrence to the sea star *Odontaster validus* (Iken *et al.* 1998; Avila *et al.* 2000; Gavagnin *et al.* 2000). *De novo* biosynthesis has also been suggested for this species (Iken *et al.* 1998; Avila *et al.* 2000), although our experiments to prove this have been not successful so far (C. Avila & A. Fontana, unpublished observations).

The common pelagic pteropod *Clione antarctica* is a very exciting example in marine chemical defensive strategies. Living individuals of these sea butterflies and whole body homogenates are consistently rejected by the Antarctic zooplanktivorous fish *Pagothenia borchgrevinki* (Foster *et al.* 1987) indicating the presence of chemical defenses (McClintock & Janssen 1990). The nature of the compound responsible for the chemical deterrence is a linear hydroxyketone, named pteroenone (Fig. 2) (Bryan *et al.* 1995; Yoshida *et al.* 1995). This is one of the first defensive compounds isolated from a planktonic macroinvertebrate. Interestingly, the hyperiid amphipod, *Hyperiella dilatata*, abducts and carries a single individual of *Clione antarctica* on its back thus providing itself with chemical defenses against fish predators (McClintock & Janssen 1990). *Clione antarctica* seems to feed mainly on *Limacina helicina*, another pteropod. Both have been chemically studied and found to possess exceptional lipophilic secondary metabolites and fatty acids (Phleger *et al.* 1997; Kattner *et al.* 1998). Among the compounds isolated from *Clione antarctica* are triacylglycerols and 1-O-alkyldiacylglycerol ethers (not reported in Table 1). These compounds seem to be derived from its main diet, *Limacina helicina*. All these fatty acids and lipophilic compounds are thought to have a buoyancy function in these pelagic pteropods. *Limacina helicina* also contains triacylglycerols, phospholipids, sterols, fatty acids and wax esters, and the triacylglycerols are apparently obtained from its phytoplankton diet. The same kind of chemical products were found in the pteropod *Spongiobranchaea australis* (Phleger *et al.* 1997) (not reported in Table 1).

Novel natural products in Antarctic molluscs include those mentioned for the nudibranchs *Austrodoris kerguelenensis* (Davies-Coleman & Faulkner 1991; Gavagnin *et al.* 1995, 1999a,b, 2003b) and *Bathydoris hodgsoni* (Iken *et al.* 1998) as well as the pteroenone from *Clione antarctica* (Yoshida *et al.* 1995). Although both dietary and *de novo* biosynthesized compounds have been found in Antarctic molluscs, it is remarkable that chemically-established prey-predator relationships as those reported for molluscs from other latitudes (Cimino & Sodano 1994; Avila 1995) have not been reported in Antarctica yet, for example dietary compounds from predation upon Porifera and tunicates.

Several studies have identified mycosporine-like amino acids in Polyplacophora, Prosobranchia, Opistobranchia and Bivalvia (Karentz *et al.* 1991, 1992; McClintock & Karentz 1997; Whitehead *et al.* 2001).

Although some Antarctic molluscs have been studied in greater detail, many species still remain to be further investigated. In addition, more accurate investigations should be conducted in terms of histological localization of these chemical defensive compounds as it has been done in Mollusca from other latitudes (Wägele *et al.* 2006).

Bryozoans

Antarctic bryozoans are very abundant and diverse, and they are amongst the dominant members of some benthic communities. As an example, in the Ross Sea the described bryofauna alone comprises around 250 species, and the total Antarctic fauna consists of at least 322 species (Clarke & Johnston 2003). However, there are very few studies that investigate their chemical ecology and only 10 species have been chemically studied (Table 1). Colon-Urban *et al.* (1985) tested the antibiotic activity of crude extracts of six species, finding a strong inhibition of growth for *Staphylococcus aureus* when exposed to extracts of *Himantozoum antarcticum* and *Cyclicopora polaris* and a moderate inhibition with extracts from *Caberea darwini*, *Nematoflustra flagellata* and *Flustra thysanica*. Another bioassay examining the hemolytic activity against various mammalian erythrocytes was carried out using extracts of five species of Antarctic bryozoans collected from the Antarctic Peninsula. These studies showed that the extracts of *Carbasea curva* caused significant lysis of mammalian cells, showing a trace presence of bioactive natural products (Winston & Bernheimer 1986). However, the nature of these secondary metabolites and their ecological significance are still unknown to date. The signs of toxic substances being used for chemical defense by *Carbasea curva* would explain the success of its weakly calcified body, considering that this is one of the most abundant bryozoans in benthic samples from the Antarctic Peninsula and the Ross Sea (Winston & Bernheimer 1986). Furthermore, McClintock & Karentz (1997) found mycosporine-like amino acids providing UV-radiation protection in an unidentified Antarctic bryozoan and other species which are similarly protected (Table 1).

This group remains largely ignored and the recent advances in their taxonomy (Gordon 2000; Taylor 2000; Todd 2000) should provide a good basis for further development of their promising chemical ecology.

Echinoderms

The research conducted with echinoderms suggests that bioactive metabolites are very common in a large number of species, particularly saponin-related compounds. Saponins are a group of water-soluble isoprenoid glycosides and sulphated glycosides generally regarded as toxins, and are isolated especially from sea cucumbers and sea stars. In asteroids, these saponins are primarily steroidal glycosides, whereas in ophiuroids they are basically polyhydroxysteroids and their sulphates (Paul 1992; McClintock & Baker 2001). Chemical studies have been done for 35 species of Antarctic echinoderms [out of more than 400 existing species (Clarke & Johnston 2003)]: one crinoid, 19 sea stars, five ophiuroids, four sea urchins and six sea cucumbers (Table 1).

McClintock (1989) examined the toxicity of the body wall of 23 species of shallow-water Antarctic echinoderms to the allopatric mosquito fish *Gambusia affinis*, finding that 39% of the total species were toxic. The highest levels of toxicity causing fish mortality occurred in the body tissues of holothurians and asteroids. The first saponin isolated from an Antarctic sea star was santiagoside (Fig. 2), extracted from *Neosmilaster georgianus* (Vázquez *et al.* 1992). Crude extracts from this species induced avoidance behavior to the limpet *Nacella concinna* (Mahon *et al.* 2000). Feeding deterrence against *Odontaster validus* was observed when presented to intact animals, extracts, mucus or intact embryos or juveniles of *Neosmilaster georgianus* (McClintock *et al.* 2003, 2006). Intact animals and body wall crude extracts of the sea star *Granaster nutrix* showed feeding-deterrence activity against *Odontaster validus* as well (McClintock *et al.* 2006). Crude homogenates extracted from the body wall of *Perknaster fuscus* caused significant tube-foot retractions in sympatric sea stars, inhibition in the rightening response of *Odontaster validus*, and have toxic properties against the sperm of the sea urchin *Sterechinus neumayeri* (McClintock *et al.* 1992b). The bioactive tetrahydroisoquinoline alkaloid fuscusine (Fig. 2) has been isolated from the body wall tissues of *Perknaster fuscus* (Kong *et al.* 1992) and is thought to be responsible for these diverse reactions (McClintock *et al.* 1992b). Fuscusine has not been detected in the sea star's main diet, the sponge *Mycale acerata*, therefore, this compound is supposed to be *de novo* synthesized by *Perknaster fuscus*. It is remarkable that *Perknaster fuscus* has never been observed as a prey item while a number of other Antarctic sea stars are commonly included in the diets of many other echinoderms and anemones (Dearborn 1977). This might be attributable to its previously mentioned chemical activities.

The saponins marthasterone (Fig. 2) and dihydromarthasterone were isolated from *Diplasterias brucei* and shown to possess hemolytic activity against sheep blood cells when assayed as a mixture (Mackie *et al.* 1977). Their ecological significance has not been studied yet. De Marino *et al.* (1997b) found sulphated polyhydroxy-

lated sterols, asterasterols A-C (Fig. 2), in an unidentified echinoderm pertaining to the Asteriidae family. Similarly, the sea star *Acodontaster conspicuus* and the ophiuroids *Ophionotus victoriae* and *Ophiosparte gigas* were found to possess steroidal glycosides and/or polyhydroxylated steroids (D'Auria *et al.* 1993, 1995; De Marino *et al.* 1997a; Duque *et al.* 1997) while asterosaponins (Fig. 2), halityloside 1 and acodontasterosides were isolated from *Acodontaster conspicuus*. Most of these compounds promote growth inhibition in three species of Antarctic bacteria isolated from the surfaces of Antarctic sponges and echinoderms (De Marino *et al.* 1997a). Moreover, *Acodontaster conspicuus* contains polyhydroxylated steroids and some acodontasterosides, the majority of which have antimicrobial activity (De Marino *et al.* 1997a). These results suggest a possible ecological role for these compounds related to the prevention of microbial fouling. The sea star *Labidiaster annulatus* has been found to possess two novel sulphated pentaglycosides (saponins), labidiasteroside A (Fig. 3) and ovarian asterosaponin 1, with still unknown chemical activities (Díaz de Vivar *et al.* 2000).

The ophiuroids *Astrotoma agassizii* and *Gorgonocephalus chilensis* also possess sulphated polyhydroxysteroids in their tissues. Some of the compounds found in *Astrotoma agassizii* have also been described in *Ophiosparte gigas* (Roccatagliata *et al.* 1998; Comin *et al.* 1999; Maier *et al.* 2000). More polyhydroxylated steroids, antarcticosides, and other asterosaponins such as brasiliensoside, 24S-methylbrasiliensoside, pectinoside A and 24S-methylpectinoside (Fig. 3) were found in a sea star of the family Echinasteridae, probably of the genus *Henricia* (De Marino *et al.* 1996; Iorizzi *et al.* 1996). Steroidal diglycosides, asteriidosides, have been obtained from an unknown sea star (Fam. Asteriidae). Bioassays indicate that most of these compounds have cytotoxic activity against human carcinoma cells (De Marino *et al.* 1998) but no ecological activity is known so far. Similarly, the sea cucumber *Staurocucumis liouvillei* contains trisulphated triterpene glycosides, liouvillosides A (Fig. 3) and B, which have been shown to possess antiviral activity against *Herpes simplex* virus type 1 (HSV-1) (Maier *et al.* 2001), but no ecological information is available.

Some studies focused on chemical defenses in early life stages. McClintock & Vernon (1990) examined the ichthyotoxic characteristics of the eggs and embryos of 15 species of Antarctic echinoderms, using the allopatric killifish *Fundulus grandis*. Feeding-deterrent chemical compounds were detected in eggs and embryos of the sea stars *Diplasterias brucei*, *Perknaster fuscus*, *Notasterias armata* and *Porania antarctica*, all of which produce large yolky lecithotrophic eggs. Other authors found that whole embryos, juveniles and their extracts from *Lysasterias perrieri* showed feeding deterrence to *Odontaster validus* (McClintock *et al.* 2003). Also, lecithotrophic eggs, embryos and larvae of three species of Antarctic echinoderms were found unpalatable or chemically defended against ecologically relevant predators such as the sea star *Odontaster validus*, the sea anemone *Isotealia antarctica* and the amphipod *Paramoera walkeri* in further studies; however, the sea urchin *Sterechinus neumayeri* and the sea star *Odontaster validus*, both possessing planktotrophic development, lacked chemical defenses in their eggs or larvae (McClintock & Baker 1997b). This may indicate that lecitotrophic embryos and larvae are more likely to be defended, similarly to what is reported for tropical marine invertebrates (Lindquist & Hay 1996), and it is consistent with the 'Optimal Defense Theory' (Rhoades 1979). In early life stages of Antarctic organisms, this fact may be especially relevant as developmental times are usually much longer (Pearse *et al.* 1991).

Many Antarctic echinoderms have been found to contain mycosporine-like amino acids, which have protectant activity against UV radiation. Some examples include *Promachocrinus kerguelensis*, *Sterechinus neumayeri*, *Diplasterias brucei*, *Odontaster validus*, *Cucumaria ferrari*, *Granaster nutrix*, *Amphioplus affinis* and *Ekmocucumis steineni* (Karentz *et al.* 1991, 1997; McClintock & Karentz 1997). Eggs and embryos of the sea star *Psilaster charcoti* contain carotenoids, which also have been suggested to protect them against UV radiation in their early life stages (Karentz & Bosch 2001).

Novel natural products in Antarctic echinoderms include saponins and steroids in several sea star species such as *Acodontaster conspicuus* (De Marino *et al.* 1997a), *Labidiaster annulatus* (Díaz de Vivar *et al.* 2000), *Neosmilaster georgianus* (Vázquez *et al.* 1992), *Perknaster fuscus* (Kong *et al.* 1992) and two unidentified species (De Marino *et al.* 1996, 1997b) as well as from the ophiuroid *Astrotoma agassizii* (Roccatagliata *et al.* 1998) and the sea cucumber *Staurocucumis liouvillei* (Maier *et al.* 2001).

Although echinoderms seem to be more studied than other groups, relevant ecological experiments are lacking in most cases and the taxonomic difficulties for some of them are an important handicap in the development of further studies.

Tunicates

Many ascidians have been identified in the Antarctic benthos and they are both abundant and diverse. Clarke & Johnston (2003) mentioned a total of 118 species; however, only seven species have been chemically investigated to date (Table 1). The common solitary ascidian

Cnemidocarpa verrucosa, which has a circumpolar distribution, was studied by McClintock's group. They conducted an analysis of the palatability and chemical defense of the tunic, ovitestes, branchial basket, body wall, endocarps and intestines. The results showed that the tunic was deterrent to sympatric pelagic and benthic fishes in addition to an allopatric fish (McClintock *et al.* 1991a,b). Their tunic surface is heavily fouled by hydroids and bryozoans, which indicates that there are no effective antifouling chemicals. Mature ovitestes are rejected by the Antarctic fish *Pagothenia borchgrevinki*, and alginate krill pellets containing lipophilic extracts of ovitestes deter predation by the sea star *Odontaster validus*, indicating that eggs and larvae may possess chemical defenses (McClintock & Baker 1997a).

Feeding deterrence against *Odontaster validus* was also detected in the whole tissue extract and the lipophilic extract of *Distaplia cylindrica*, and antifouling activity against chain-forming pennate diatoms was detected in both its lipophilic and hydrophilic extracts (McClintock *et al.* 2004).

Synoicum adareanum produces palmerolide A (Fig. 2), which has been found to be cytotoxic against melanoma cells (Diyabalanage *et al.* 2006; Jiang *et al.* 2007). Furthermore, *Cnemidocarpa verrucosa*, *Molgula enodis*, and another unidentified Antarctic ascidian contain mycosporine-like amino acids which provide protection against UV radiation. Among these compounds the presence of mycosporine-glycine:valine in *Molgula enodis* is noteworthy; this compound is also present in other invertebrate groups (as mentioned for Porifera) and has been suggested to be either *de novo* biosynthesized or chemically modified from related compounds (Karentz *et al.* 1991; McClintock & Karentz 1997).

Salps are an important component of the Southern Ocean food webs. Several polyunsaturated acids with hemolytic activity have been isolated from individuals of *Salpa thompsoni* (Mimura *et al.* 1986). Also, a complex sterol mixture containing brassicasterol has been obtained from another tunicate salp, *Ihlea racovitzai* (Schor & Seldes 1989). The ecological roles of these compounds are still unknown.

Many abundant, large synascidians are observed when sampling the Antarctic benthos (personal observations from the authors), which are not obviously overgrown by any other organisms or predated upon by any omnivorous species; however they remain largely unexplored regarding their chemical ecology. This, therefore, is a very interesting unexplored group, expected to provide not only ecologically active compounds but perhaps potentially useful pharmacological products too, as found in their tropical and temperate congeners.

Other groups

Nichols *et al.* (1993, 1997) isolated polyunsaturated fatty acids (PUFA), eicosapentaenoic acid and arachinoic acid from different strains of the Antarctic bacteria *Pseudoalteromonas* sp. Although outside the scope of this review, it has to be mentioned that many other Antarctic bacteria have been studied for their fatty acid composition (Nichols 1999). Some exopolysaccharides have been suggested to play a role as cryoprotectants and to participate in iron sequestration (Nichols *et al.* 2005), while some fatty acids seem to modulate fluidity in response to temperature within cellular membranes (Nichols *et al.* 1997).

The following remaining groups have been only occasionally studied to date: protozoans (three spp), ctenophores (two spp), platyhelminthes (two spp), nemerteans (three spp), annelids (eight spp), crustaceans (12 spp), pycnogonids (two spp), brachiopods (one sp), chaetognaths (one sp) and fishes (three spp) (Table 1). Hemichordates and other minor groups have not been studied at all.

The diterpenes epoxyfocardin and focardin, both with cytotoxic activity, have been isolated from the ciliate *Euplotes focardii* (Guella *et al.* 1996). Focardin is suggested to be the precursor of epoxyfocardin. Another ciliate *Euplotes nobilii* (Strain AC-1) produces nitrogenated compounds that act as pheromones, named pheromone En-1 and pheromone En-2, which cause mating induction between cells of complementary strains (Felici *et al.* 1999).

Two species of ctenophores have been analysed for UV-protectants but none have been found so far (Karentz *et al.* 1991). In the same study, two platyhelminthes and three nemerteans were found to possess mycosporine-glycine:valine for UV protection (Table 1). The nemertean worm *Parborlasia corrugatus* is a very abundant invertebrate in the Antarctic benthos. It has been observed that this organism is rarely preyed upon, despite their lack of skeletal protection and rich energy content (Dayton *et al.* 1974; Heine *et al.* 1991), which suggests the presence of chemical defenses. Bioassays indicate that homogenates of whole body tissues of this nemertean cause mortality in gametes of the Antarctic sea urchin *Sterechinus neumayeri*, feeding deterrence in two species of Antarctic fish, *Dissostichus mawsoni* and *Trematomus bernacchii* (Heine *et al.* 1991; McClintock *et al.* 1991b), and hemolytic activity against bovine erythrocytes (Berne *et al.* 2003). These defensive properties, the cytotoxicity and the feeding-deterrence may be on account of the production of a copious acidic mucus (pH = 3.5). Furthermore, *Parborlasia corrugatus* possesses in its mucus a potent toxic neuropeptide, parbolysin, with hemolytic activity

against mammalian erythrocytes (Berne *et al.* 2003). This compound could also be involved in ecologically relevant interactions.

A novel bromophenolic compound (Table 1) was described in two Antarctic polychaete species of the genus *Thelepus* (Terebellidae). Both terebellid species have been found to contain some of their bromophenols in the distal regions of the worm, suggesting a role as antibiotics in fouling and infection control (Goerke *et al.* 1991). The rest of annelid species studied has only been analysed for the presence of UV-protectants, with the presence of mycosporine-glycine:valine in *Neanthes kerguelensis*, *Trachelobdella australis* and an unidentified polychaete species (Table 1). Considering that there are more than 600 species of Antarctic polychaetes (Clarke & Johnston 2003) it is obvious that very little is known so far about this group.

Four species of copepods have been chemically studied: *Calanoides acutus*, *Calanus propinquus* (Hagen *et al.* 1993), *Rhincalanus gigas* and *Metridia gerlachei* (Graeve *et al.* 1994), and all of them have been found to contain wax esters and/or triacylglycerols stored in their tissues, sometimes in lipidic oil sacs. Their ecological role is still unknown, although a buoyancy function similar to that described for pteropods and krill may be suggested. In fact, lipids and wax esters have been proposed to have a role in buoyancy in polar zooplankton, especially in cold deep waters (Lee *et al.* 2006). These data are not reflected on Table 1 as they are outside the scope of this review.

Antarctic krill contains high levels of prostaglandins, even higher than in mammalian tissues (Mezykowski & Ignatowska-Switalska 1981; Pawlowicz 1989). High levels of prostanoids in the tropical soft coral *Plexaura homomalla* are known to deter fish predation (Weinheimer & Spraggins 1969; Gerhart 1984), which rises the question whether they play a similar role in Antarctic krill (McClintock & Baker 2001). Three species of Antarctic krill, *Euphasia superba*, *Euphasia crystallorophias* and *Thysanoessa macrura*, have been found to accumulate phospholipids and phosphotidylcholine, which they use to achieve neutral buoyancy in the water column (Hagen *et al.* 1996). Data on these cumulative lipid compounds are not shown on Table 1.

Intact juvenile individuals of the isopod *Glyptonotus antarcticus* and body extracts cause feeding deterrence of the sea star *Odontaster validus* (McClintock *et al.* 2003). Other isopods and amphipods have only been tested for the presence of mycosporine-like amino acids (Table 1).

Liothyrella uva is an Antarctic brachiopod and a common component of the benthic system in the Southern Ocean. Crude extracts of whole brachiopod soft tissues caused significant retraction of sensory tube-feet in six species of sympatric sea stars, and also significant feeding deterrence in the allopatric fish *Cyprinidon variegatus* (McClintock *et al.* 1993b). More detailed investigations with different anatomic parts of the brachiopod reported that the peduncle was rejected by the sympatric fish *Notothenia coriiceps* and the sea star *Odontaster validus*. This is consistent with the 'Optimal Defense Theory' (Rhoades 1979) as the peduncle is the most exposed and unprotected part of the animal. Antimicrobial activity against psycotrophic marine bacteria was detected in the lophophore, stomach-intestine, and female reproductive tissues (Mahon *et al.* 2003).

Mycosporine-like amino acids with UV radiation-protectant activity have been isolated from all the studied species of crustaceans and pycnogonids. Also other organisms such as the nemertine *Parborlasia corrugatus* and some fish have been found to possess UV-protectants (Table 1) (Nakamura & Kobayashi 1982; Karentz *et al.* 1991; McClintock & Karentz 1997; Newman *et al.* 2000). All the UV protecting compounds mentioned in the different groups may play an important role in Antarctica (Bandaranayake 1998; Karentz & Bosch 2001) on account of the high levels of radiation in the area, and in fact they seem to be quite widespread among different groups of Antarctic organisms.

General remarks

The Antarctic marine ecosystems have classically been categorized as old and stable, and for this reason, the interactions between organisms play an essential role in the communities structure (Dayton *et al.* 1974). However, there also are some variability and perturbations on account of the marked seasonality in light regime, variations in ice cover, erosion caused by icebergs and seasonal and interannual variations in currents pattern (Arntz & Gallardo 1994; Gili *et al.* 2000, 2006; Gutt 2000; Orejas *et al.* 2000). The erosive action of the icebergs produces devastating effects on the platform sea floor that are followed by a long and slow process of recolonization. The available substrate after a perturbation will be initially colonized by mobile, invasive species, and pioneer sessile species (Gutt 2000). Both in their adult and their larval phases and in the settlement after a perturbation produced by an iceberg, the community interactions may be regulated by chemical products. The study of these interactions between the organisms and the environment, and between organisms at intra- and inter-specific level mediated by natural products, gives us information about the ecology and biology of the involved species, the functioning and the structure of the community, and, simultaneously, new compounds

that may be useful to humans from a pharmacological point of view (*e.g.* Avila 1995, 2006; Bhakuni 1998; Munro *et al.* 1999; Faulkner 2000; Cimino & Gavagnin 2006).

Marine chemical ecology is several decades behind terrestrial chemical ecology, although in the last two decades great advances have been made thanks to the new technologies for collecting and studying marine samples and in the identification of small amounts of molecules (Faulkner 2000; Paul *et al.* 2006). Marine organisms are currently providing larger percentages of bioactive natural products than terrestrial organisms (Munro *et al.* 1999). Temperate and tropical organisms have been the most studied so far, while polar organisms have received relatively less attention (Paul 1992; Blunt 2003; Blunt *et al.* 2007 and previous reviews). The review provided here, however, shows that Antarctic benthic organisms are a rich and diverse source of natural products, with great interest from both ecological and pharmacological viewpoints. From the 263 studied organisms from the Southern Oceans, ca. 300 compounds have been described; in some cases, a defensive role has been demonstrated. This contradicts early theories concerning biogeographic variation in predation and in chemical defenses (see also Amsler *et al.* 2000a). A number of interesting natural products have been isolated from Antarctic invertebrates and macroalgae; however, we believe many more are still to be discovered. Also, further evaluations of the ecological functional roles of known compounds need to be undertaken. Much of the research done to date on chemical ecology has been conducted only in the laboratory, occasionally using ecologically relevant predators. There is a need to extend experiments to the field, as has been done in tropical marine environments (Paul 1992; Pawlik 1993; Hay 1996). More realistic assays need to be developed to test the real effects of marine secondary metabolites on sympatric predators, competitors and fouling organisms (Munro *et al.* 1987; Scheuer 1990; Hay & Fenical 1996) and complemented with field experiments, even if difficult, as they are most useful for examining ecological activities. Defense from predation has been the most studied ecological role for Antarctic secondary metabolites, however, other functional roles including fouling control and alellochemical interactions are also important and need to be understood.

Another interesting feature about the Antarctic chemical investigations is how secondary metabolic pathways of Antarctic organisms compare with those in organisms from Northern latitudes in terms of evolution. For example, few investigations have evaluated the defensive metabolites in Antarctic macroalgae, although it is of particular interest to understand biogeographic patterns of herbivory. Brown algae are known to produce polyphenolic compounds, which could be responsible for the apparently low levels of herbivory, as it happens to their temperate and tropical congeners; nonetheless, these experiments are still to be conducted. On the other hand, the fact that many Antarctic organisms (which are generally considered to be old) do possess chemical defenses may actually be an indication that chemical mechanisms evolved very early in the evolution of different taxa, but more data are needed in the different groups to support this hypothesis.

Several groups, as already mentioned, remain almost ignored. Little is known about defensive chemistry employed by Antarctic microorganisms and if some of the metabolites observed in macroinvertebrates may actually have their source in microorganisms. This has been hypothesized to occur in other geographic areas (*e.g.* König *et al.* 2006), but only recently Antarctic organisms, in this case sponges, have been studied for microbial symbionts. These studies provide very interesting results, which include the presence of diatoms, archaea, bacteria and dinoflagellates (Bavestrello *et al.* 2000; Cerrano *et al.* 2000; Webster *et al.* 2004). In planktonic systems, more information is needed on how secondary metabolites mediate patterns of predation on the pelagic embryos and larvae of macroinvertebrates, as well as on cyanobacteria, dinoflagellates, diatoms, protozoans, and other organisms. The Antarctic deep sea, which is proving to be very interesting (Brandt *et al.* 2007) remains unknown from the chemical ecology side. In general, we believe it is important to understand how ecological factors may trigger chemical mechanisms in marine Antarctic organisms as a response for survival.

As many important aspects of the reproduction of Antarctic organisms remain poorly understood, it seems that the significance of chemical ecology along the reproductive cycle and in the different developmental phases is difficult to evaluate. The few known studies have been mentioned throughout the previous sections (*e.g.* echinoderms) but further data are needed to correlate both fields. Recently, Palma *et al.* (2007) showed that Antarctic broadcaster echinoderms are predominant in ice-disturbed areas, while brooders only occurred in less ice-disturbed areas. Whether reproduction and development patterns correlate with natural products and chemical ecology largely remains to be evaluated.

An important topic in chemical ecology is the possible antifouling activity displayed by some organisms. This may act at different levels: initial stages (primary colonizers such as bacteria and diatoms), secondary stages (such as macroalgal spores or protozoans), and later stages, when larvae of macrofouling organisms arrive and settle. At these different levels, natural products may have different effects, but very few data are available for

recruitment and colonization in Antarctic organisms so far (Webster *et al.* 2006). Effects may include inhibition of settlement, attachment and/or germination of spores and zygotes, growth inhibition for bacteria, fungi, protozoa and/or larvae. Further research is needed to understand these mechanisms in the benthic communities of Antarctica.

MAAs (mycosporine-like aminoacid compounds) seem to be an important, common trend in many Antarctic organisms, related to the acquisition of UV-protection, which is considered a more primitive way than that of terrestrial organisms (Karentz *et al.* 1991). Changes in global climate and the ozone layer may have, therefore, important effects in Antarctic marine communities (Karentz & Bosch 2001; Poppe *et al.* 2002; Rautenberger & Bischof 2006). Furthermore, ice melting on account of climate change is showing new unexplored communities (*e.g.* Larssen Ice Shelf areas) and how these new areas could be colonized by the surrounding organisms, although the same climate change may block the further development of these Antarctic communities (Odling-Smee 2007). These changes may have a terrible effect on Antarctic organisms, their biology and their chemical ecology, with enormous potential losses both in biological and chemical diversity.

Faulkner (2000) stated that chemical defense mechanisms cannot be directly equated with potential biomedical activity, but that it was remarkable how well the two correlate in reality. Possible applications of marine natural products, including those from the Antarctic, are enormous for obtaining pharmaceutical drugs, such as antitumor, antiviral (including HIV), antibacterial, antifungal, antituberculosis, antiparasites (against malaria, leishmaniasis, trypanosomiasis, *etc.*), antiinflammation, antiobesity, for use against Alzheimer, Parkinson and other neural diseases, against cystic fibrosis or against osteoporosis, as inhibitors of insuline-like growth factors, for producing or regulating apoptosis, *etc*. But they may also be useful for UV protection, antiaging and skin protecting, as well as for agrochemistry and other industrial applications (*e.g.* Blunt *et al.* 2007 and previous reviews). The search for active compounds is currently ongoing in areas considered the last frontiers of marine natural products chemistry, such as unexplored polar areas, the deep sea and the microbial communities (natural or cultured). Therefore, this is a field presently under strong developmental pressure, and chemical ecology should greatly benefit from this interest in natural products. Once the field expands to cover all the possibilities reviewed here, it will be very interesting to see how Antarctic organisms compare to similar species from other latitudes and whether any biogeographical patterns can be observed.

Fenical (2007) mentioned six areas with most potential future interest in marine chemical ecology to be undertaken from a multidisciplinary perspective. These areas included (i) studying small marine organisms (such as fungi, bacteria, radiolarians, ciliates, foraminifera, and others, including their culturing conditions); (ii) studying 'difficult' organisms (difficult on account of collection, taxonomy, culture, chemistry, *etc.*); (iii) focusing on symbiotic relationships between microbes and invertebrates (exo- and endosymbionts); (iv) investigating unexplained chemical phenomena (*e.g.* translocation of metabolites); (v) answering 'old' problems that have not yet been solved (origins of many toxins, *etc.*); and (vi) integrating molecular approaches and marine genomics. Although in respect of Antarctic chemical ecology we are still far from the basic knowledge which would allow us to pursue these objectives, we agree these could be very interesting future research lines. However, to achieve good results in these areas, we still need much basic information on Antarctic species, their natural products and their biology and ecology. Natural history and even taxonomy in some Antarctic groups is still poorly known and therefore, future research should provide useful information to develop all these challenging research lines. We should not forget our main aim: to know how, what for and why the species possess these natural compounds, before they (both species and natural products) disappear.

Conclusions

In the future development of marine chemical ecology, effort has to be dedicated to underexplored areas such as Antarctica. Randomly collecting material is not a satisfying methodology anymore, but focusing on biologically interesting species or groups and collecting these selectively should improve our chances to understand their ecology and evolution. The recent developments in natural products chemistry and associated technologies do provide good chances of detecting compounds in small amounts, thus making the ecological work easier. Also, collaboration with marine natural products chemists is a must for all marine chemical ecology studies to be done well. And finally, we should not forget the new developments in the fields of molecular genetics and genomics, which are opening new areas connected to chemical ecology, which will surely lead to challenging new approaches. In any of the related fields (collection, location, growth, activity, culture, chemistry, synthesis, *etc.*), technical advances are improving, and will continue to improve, our chances to get chemical ecology questions answered, even in the cold, remote, serendipitous waters of Antarctica.

Table 1. Antarctic natural products described up to May 2007: taxonomic group, species, location in the body (if provided), natural products, chemical structure, origin, activity and references.

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
'**ALGAE**'				
Unidentified sea ice algae				
?porphyra-334	MA	–	UV?	Ryan *et al.* (2002)
CL. CRYPTOPHYCEAE				
Geminigera cryophila				
UVA and UVB absorbing compounds	–	–	UV	Jeffrey *et al.* (1999)
CL. DINOPHYCEAE				
Amphidinium carterae				
mycosporine-like amino acid	MA	–	–	Hannach & Sigleo (1998)
CL. PRASYNOPHYCEAE (PHYTOFLAGELLATE)				
Pyramimonas gelidicola				
UVA and UVB absorbing compounds	–	–	UV	Jeffrey *et al.* (1999)
Pyramimonas parkeae				
mycosporine-like amino acid	MA	–	–	Hannach & Sigleo (1998)
CL. PRYMNESIOPHYCEAE				
Isochrysis sp.				
mycosporine-like amino acid	MA	–	–	Hannach & Sigleo (1998)
Pavlova gyrans				
3 mycosporine-like amino acids	MA	–	–	Hannach & Sigleo (1998)
Phaeocystis antarctica				
mycosporine-like amino acid	MA	–	UV	Riegger & Robinson (1997)
Phaeocystis pouchetii				
UVA and UVB absorbing compounds	–	–	UV	Marchant *et al.* (1991); Jeffrey *et al.* (1999)
CL. CHRYSOPHYCEAE				
Antarctosaccion applanatum				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
CL. BACILLARIOPHYCEAE (DIATOMS)				
Chaetoceros sp. 1 and *Chaetoceros* sp. 2				
porphyra-334	MA	–	UV	Riegger & Robinson (1997)
shinorine	MA	–	UV	
Coretron cryophilum				
porphyra-334	MA	–	UV	Helbling *et al.* (1996)
shinorine	MA	–	UV	
Coscinodiscus centralis				
porphyra-334	MA	–	UV	Riegger & Robinson (1997)
shinorine	MA	–	UV	
Fragilariopsis cylindrus				
porphyra-334	MA	–	UV	Helbling *et al.* (1996);
shinorine	MA	–	UV	Riegger & Robinson (1997)
mycosporine-glycine:valine	MA	–	UV	
Fragilariopsis linearis				
porphyra-334	MA	–	UV	Riegger & Robinson (1997)
shinorine	MA	–	UV	
Navicula sp.				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
Nitzschia stellata				
bromoform	VH	–	–	Sturges *et al.* (1993)
dibromomethane	VH	–	–	
bromomethane	VH	–	–	
mixed bromochloromethanes	VH	–	–	
Nitzschia sp.				
UVA and UVB absorbing compounds	–	–	UV	Jeffrey *et al.* (1999)
Porosira glacialis				
porphyra-334	MA	–	UV	Riegger & Robinson (1997)
shinorine	MA	–	UV	
Porosira pseudodenticulata				
bromoform	VH	–	–	Sturges *et al.* (1993)
dibromomethane	VH	–	–	
bromomethane	VH	–	–	
mixed bromochloromethanes	VH	–	–	
porphyra-334	MA	–	UV	Riegger & Robinson (1997)
mycosporine-glycine	MA	–	UV	
shinorine	MA	–	UV	
Proboscia inermis				
porphyra-334	MA	–	UV	Riegger & Robinson (1997)
shinorine	MA	–	UV	
Pseudonitzschia sp.				
porphyra-334	MA	–	UV	Helbling *et al.* (1996)
Stellarima microtrias				
porphyra-334	MA	–	UV	Riegger & Robinson (1997)
shinorine	MA	–	UV	
Thalassiosira antarctica				
porphyra-334	MA	–	UV	Riegger & Robinson (1997)
shinorine	MA	–	UV	
Thalassiosira tumida				
porphyra-334	MA	–	UV	Riegger & Robinson (1997)
shinorine	MA	–	UV	
Thalassiosira weissflogii				
mycosporine-like amino acid	MA	–	–	Hannach & Sigleo (1998)
Thalassiosira sp.				
porphyra-334	MA	–	UV	Helbling *et al.* (1996)
shinorine	MA	–	UV	
Diatom mat (mixture of *Achnantes* sp., *Licmophora* sp., *Navicula* sp.)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
CL. CHLOROPHYCEAE (GREEN ALGAE)				
Dunaliella tertiolecta				
mycosporine-like amino acid	MA	–	–	Hannach & Sigleo (1998)
Dunaliella sp. (Ace Lake) and *Dunaliella* sp. (Burton Lake)				
UVA and UVB absorbing compounds	–	–	UV	Jeffrey *et al.* (1999)
Enteromorpha bulbosa				
UV-absorbing pigments	–	–	UV	Post & Larkum (1993)
porphyra-334	MA	–	UV	Hoyer *et al.* (2001)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
Enteromorpha compressa				
bromomethane	VH	–	–, UV	Laturnus *et al.* (1998a,b)
bromoform	VH	–	–, UV	
dibromomethane	VH	–	UV	
bromochloromethane	VH	–	UV	
bromodichloromethane	VH	–	UV	
bromoethane	VH	–	UV	
dibromoethane	VH	–	UV	
chloromethane	VH	–	UV	
iodomethane	VH	–	–, UV	Giese *et al.* (1999)
iodoethane	VH	–	UV, –	
chloroiodomethane	VH	–	UV, –	
diiodomethane	VH	–	UV, –	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
Lambia antarctica				
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified iodating activity	–	–	–	
bromomethane	VH	–	–	Laturnus *et al.* (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	
iodoethane	VH	–	–	Giese *et al.* (1999)
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
thallus	–	–	D_{SS}, no D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SC}	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SC}	
Monostroma hariotii				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
shinorine	MA	–	UV	Hoyer *et al.* (2001)
lipophilic extract (CH_2Cl_2:methanol)	–	–	FO_S	Amsler *et al.* (2005b)
Prasiola crispa ssp. *antarctica*				
mycosporine-glycine	MA	–	UV	Hoyer *et al.* (2001, 2003)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	–	UV	
mycosporine-like amino acid	–	–	UV	
Green algal mat (mixture of *Ulothrix* cf. *australis, Urospora* cf. *penicilliformis*)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
asterina-330	MA	–	UV	
CL. PHAEOPHYCEAE (BROWN ALGAE)				
Adenocystis utricularis				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001)
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, no D_{SF}, no D_{SC}, FO_S	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SF}, D_{SC}, FO_S	
phlorotannin	PT	–	–	Iken *et al.* (2007)
Ascoseira mirabilis				
bromomethane	VH	–	–	Laturnus (1995); Laturnus *et al.* (1998a)
dibromomethane	VH	–	–, B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	–, B_S? or D_S?	
bromoethane	VH	–	–	
1,2-dibromoethane	VH	–	–, B_S? or D_S?	
bromochloromethane	VH	–	–	
bromodichloromethane	VH	–	–, B_S? or D_S?	
dibromochloromethane	VH	–	–, B_S? or D_S?	
diiodomethane	VH	–	–, B_S? or D_S?	
iodoethane	VH	–	–	
chloroiodomethane	VH	–	–, B_S? or D_S?	
chloromethane	VH	–	–	
iodomethane	VH	–	–	
unspecified no brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified no iodating activity	–	–	–	
homogenated algae	–	–	no G_{SM}	Iken (1999)
intact tissue	–	–	G_{SM}	
no mycosporine-like amino acid	–	–	–	Hoyer *et al.* (2001)
thallus	–	–	no D_{SS}, D_{SF}	Amsler *et al.* (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, noD_{SF}, no D_{SC}, FO_S	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no $D_{SC,}$ FO_S	
phlorotannin	PT	–	–	Iken *et al.* (2007)
Chordaria linearis				
thallus	–	–	D_{SS}	Amsler *et al.* (2005a)
phlorotannin	PT	–	–	Iken *et al.* (2007)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
Cystosphaera jacquinotii				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
cystosphaerol	TS	–	–	Ankisetty *et al.* (2004b)
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, noD_{SC}	
hydrophilic extract (methanol:water)	–	–	D_{SS}, D_{SC}	
phlorotannin	PT	–	G_S?	Iken *et al.* (2007)
Desmarestia anceps				
bromomethane	VH	–	–	Laturnus (1995)
dibromomethane	VH	–	–, B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	–, B_S? or D_S?	
bromoethane	VH	–	–	
1,2-dibromoethane	VH	–	–, B_S? or D_S?	
bromodichloromethane	VH	–	–, B_S? or D_S?	
dibromochloromethane	VH	–	–, B_S? or D_S?	
diiodomethane	VH	–	–. B_S? or D_S?	
iodoethane	VH	–	–	
chloroiodomethane	VH	–	–, B_S? or D_S?	
thallus	–	–	D_{SS}, $D_{SF,}$ D_{SC}	Amsler *et al.* (2005a,b);
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SF}, no D_{SC}, FO_S	Huang *et al.* (2006)
hydrophilic extract (methanol:water)	–	–	D_{SS}, D_{SF}, D_{SC}, FO_S	
extracts of different parts of thallus	–	–	D_{SC}	Fairhead *et al.* (2005a)
phlorotannin	PT	–	–	Fairhead *et al.* (2005b, 2006); Iken *et al.* (2007)
Desmarestia antarctica				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
thallus	–	–	D_{SC}	Huang *et al.* (2006)
Desmarestia antarctica (1st year)				
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, no D_{SF}, no D_{SC}, FO_S	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SC}, FO_S	
Desmarestia antarctica (2nd year)				
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SC}, FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	D_{SS}, D_{SC}	
phlorotannin	PT	–	–	Iken *et al.* (2007)
Desmarestia menziesii				
bromoform	VH	–	B_S? or D_S?, –	Laturnus *et al.* (1996, 1998a)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
bromomethane	VH	–	–	
dibromomethane	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
iodomethane	VH	–	–	
plastoquinones	QN	–	S?, I?, L?	Rivera *et al.* (1990)
benzoquinones[1,2]	QN	–	S?, I?, L?	Rivera (1996)
hydroquinone	QN	–	–	
menzoquinone	QN	–	–	Ankisetty *et al.* (2004b)
sargadiol-l	CR	–	–	
sargadiol	CR	–	–	
palythene	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
mycosporine-glycine	MA	–	UV	
unspecified no brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified iodating activity	–	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001)
thallus	–	–	D_{SS}, D_{SF}, D_{SC}	Amsler *et al.* (2005a,b);
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, D_{SF}, D_{SC}, FO_S	Huang *et al.* (2006)
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SF}, no D_{SC} , FO_S	
extracts of different parts of thallus	–	–	D_{SC}	Fairhead *et al.* (2005a)
phlorotannin	PT	–	–, no D_{SC}	Fairhead *et al.* (2005b, 2006); Iken *et al.* (2007)
Geminocarpus geminatus				
thallus	–	–	no D_{SS}	Amsler *et al.* (2005a)
Halopteris obovata				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
thallus	–	–	no D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SC}	
hydrophilic extract (methanol:water)	–	–	no D_{SC}	
Himantothallus grandifolius				
bromomethane	VH	–	–	Laturnus (1995)
dibromomethane	VH	–	–, B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	–, B_S? or D_S?	
bromoethane	VH	–	–	
1,2-dibromoethane	VH	–	–, B_S? or D_S?	
bromochloromethane	VH	–	–	
bromodichloromethane	VH	–	–, B_S? or D_S?	
dibromochloromethane	VH	–	–, B_S? or D_S?	
diiodomethane	VH	–	–, B_S? or D_S?	
iodoethane	VH	–	–	
chloroiodomethane	VH	–	–, B_S? or D_S?	
homogenated algae	–	–	no G_{SM}	Iken (1999)
intact tissue	–	–	G_{SM}	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
porphyra-334	MA	–	UV	Hoyer *et al.* (2001)
palythine	MA	–	UV	
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, no D_{SF}, D_{SC}, no FO_S	
hydrophilic extract (methanol:water)	–	–	D_{SS}, D_{SF}, D_{SC}, FO_S	
phlorotannin	PT	–	G_S?	Iken *et al.* (2007)
Phaeurus antarcticus				
dibromomethane	VH	–	–, B_S? or D_S?	Laturnus (1995);
bromoform	VH	–	–, B_S? or D_S?	Laturnus *et al.* (1996)
bromoethane	VH	–	–	
1,2-dibromoethane	VH	–	–, B_S? or D_S?	
bromochloromethane	VH	–	–	
bromomethane	VH	–	–	
bromodichloromethane	VH	–	–, B_S? or D_S?	
dibromochloromethane	VH	–	–, B_S? or D_S?	
diiodomethane	VH	–	–, B_S? or D_S?	
iodoethane	VH	–	–	
chloroiodomethane	VH	–	–, B_S? or D_S?	
homogenated algae	–	–	no G_{SM}	Iken (1999)
intact tissue	–	–	G_{SM}	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001)
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SC}	
hydrophilic extract (methanol:water)	–	–	D_{SC}	
phlorotannin	PT	–	G_S?	Iken *et al.* (2007)
CL. RODOPHYCEAE (RED ALGAE)				
Antarcticothamnion polysporum				
bromomethane	VH	–	–	Laturnus *et al.* (1998a)
iodomethane	VH	–	–	
bromoform	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002)
Audouinella purpurea				
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002)
Ballia callitricha				
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)
bromomethane	VH	–	–	Laturnus *et al.* (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	
iodoethane	VH	–	–	Giese *et al.* (1999)
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002)
Bangia atropurpurea				
porphyra-334	MA	–	UV	Hoyer *et al.* (2001)
palythinol	MA	–	UV	
Callophyllis atrosanguinea				
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SC}	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
hydrophilic extract (methanol:water)	–	–	D_{SS}, no D_{SF}, no D_{SC}	
Curdiea racovitzae				
palythine	MA	–	UV	Karentz *et al.* (1991);
shinorine	MA	–	UV	Hoyer *et al.* (2001)
mycosporine-glycine	MA	–	UV	
palythene	MA	–	UV	
palythinol	MA	–	UV	
porphyra-334	MA	–	UV	
asterina-330	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 324nm)	MA	–	UV	Hoyer *et al.* (2003)
unknown mycosporine-like amino acid (max. absorb. 357nm)	MA	–	UV	
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
homogenated algae	–	–	no G_{SM}	Iken (1999)
intact tissue	–	–	G_{SM}	
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, no D_{SC}, FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	D_{SS}, no D_{SC}, FO_S	
Delesseria lancifolia				
bromoform	VH	–	B_S? or D_S?	Laturnus *et al.* (1996, 1998a)
bromomethane	VH	–	–	
1,2-dibromoethane	VH	–	B_S? or D_S?	
dibromomethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S? , –	Giese *et al.* (1999)
chloroiodomethane	VH	–	B_S? or D_S? , –	
iodomethane	VH	–	–	
iodoethane	VH	–	–	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
unspecified no brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified no iodating activity	–	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002)
thallus	–	–	no D_{SS}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SC}	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, D_{SC}	
Delesseria salicifolia				
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, D_{SF}, D_{SC}	
hydrophilic extract (methanol:water)	–	–	D_{SS}, no D_{SF}, D_{SC}, no FO_S	
Delisea fimbriata (= *Delisea pulchra)*				
acetoxyfimbrolides A, B, C, D, E, and F	HP	–	B_A	Pettus *et al.* (1977)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
2 acetoxyfimbrolides	HP	–	–	Cueto *et al.* (1991)
2 acetyl derivatives	HP	–	–	Cueto *et al.* (1997)
4 fimbrolides	HP	–	–	
fimbrolide	HP	–	B_A, F	Ankisetty *et al.* (2004b)
acetoxyfimbrolide	HP	–	B_A, F	
hydroxyfimbrolide	HP	–	B_A, F	
pulchralides A, B and C	HP	–	–	
2 polyhalogenated unsaturated ketones	HP	–	–	
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, D_{SC}	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SC}	
Georgiella confluens				
dibromomethane	VH	–	B_S? or D_S?, UV	Laturnus *et al.* (1996, 1998b)
bromoform	VH	–	B_S? or D_S? , UV, –	Laturnus *et al.* (1998a)
bromomethane	VH	–	–, UV	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S? , UV	
dibromochloromethane	VH	–	B_S? or D_S?	
bromoethane	VH	–	UV	
bromochloromethane	VH	–	UV	
dibromoethane	VH	–	UV	
chloroiodomethane	VH	–	B_S? or D_S?, UV, –	Giese *et al.* (1999)
chloromethane	VH	–	–, UV	
diiodomethane	VH	–	B_S? or D_S? , UV, –	
iodomethane	VH	–	–, UV	
iodoethane	VH	–	UV, –	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
unspecified no brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified no iodating activity	–	–	–	
shinorine	MA	–	UV	Hoyer *et al.* (2001)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al.* (2003)
thallus	–	–	no D_{SS}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	FO_S	
Gigartina papillosa				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
Gigartina skottsbergii				
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)
chloromethane	VH	–	–	Laturnus *et al.* (1998a)
bromomethane	VH	–	–	
iodomethane	VH	–	–	
bromoform	VH	–	–	
iodoethane	VH	–	–	Giese *et al.* (1999)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
shinorine	MA	–	UV	Hoyer *et al.* (2001)
palythine	MA	–	UV	
asterina-330	MA	–	UV	
porphyra-334	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al.*(2003)
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	no FO_S	
Gymnogongrus antarcticus				
dibromomethane	VH	–	B_S? or D_S?, UV	Laturnus *et al.* (1996, 1998b)
bromoform	VH	–	B_S? or D_S?, –, UV	Laturnus *et al.* (1998a, 2000)
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromomethane	VH	–	–, UV	
bromochloromethane	VH	–	UV	
bromoethane	VH	–	UV	
dibromoethane	VH	–	UV	
bromodichloromethane	VH	–	B_S? or D_S?, UV	
dibromochloromethane	VH	–	B_S? or D_S? , UV, –	Giese *et al.* (1999)
chloroiodomethane	VH	–	B_S? or D_S? , UV, –	
chloromethane	VH	–	–, UV	
iodomethane	VH	–	–, UV	
iodoethane	VH	–	UV, –	
1-iodopropane	VH	–	–, UV	
2-iodopropane	VH	–	–, UV	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–, UV	
2-iodobutane	VH	–	–, UV	
iodoethane	VH	–	UV	
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified iodating activity	–	–	–	
shinorine	MA	–	UV	Hoyer *et al.* (2001, 2002)
palythine	MA	–	UV	
asterina-330	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al.* (2003)
thallus	–	–	no D_{SS}, D_{SF}	Amsler *et al.* (2005a)
hydrophilic extract (methanol:water)	–	–	no D_{SC}	
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SC}, FO_S	Amsler *et al.* (2005b)
Gymnogongrus turquetii				
mycosporine-glycine	MA	–	UV	Hoyer *et al.* (2001)
shinorine	MA	–	UV	Hoyer *et al.* (2002, 2003)
porphyra-334	MA	–	UV	
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, D_{SF}, D_{SC}, FO_S	Amsler *et al.* (2005b)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
hydrophilic extract (methanol:water)	–	–	D_{SS}, no D_{SF}, D_{SC}, FO_S	
Hymenocladiopsis crustigena				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002, 2003)
Iridaea cordata				
palythine	MA	–	UV	Karentz *et al.* (1991); McClintock & Karentz (1997);
shinorine	MA	–	UV	Hoyer *et al.* (2001)
mycosporine-glycine	MA	–	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al.* (2003)
bromomethane	VH	–	–	Laturnus (1995); Laturnus *et al.* (1998a)
dibromomethane	VH	–	–, B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	–, B_S? or D_S?, –	
bromoethane	VH	–	–	
1,2-dibromoethane	VH	–	–, B_S? or D_S?	
bromochloromethane	VH	–	–	
bromodichloromethane	VH	–	–, B_S? or D_S?	
dibromochloromethane	VH	–	–, B_S? or D_S?	
iodomethane	VH	–	–	
diiodomethane	VH	–	–, B_S? or D_S?	Giese *et al.* (1999)
iodoethane	VH	–	–	
chloroiodomethane	VH	–	–, B_S? or D_S?	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
unspecified no brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified no iodating activity	–	–	–	
thallus	–	–	P_{SU}, D_{SS}, no D_{SF}	McClintock & Baker (1995)
thallus on *S. neumayeri*	–	–	PP_S	Amsler *et al.* (1998, 2005a)
thallus without chemicals on *S. neumayeri*	–	–	PP_S	Amsler *et al.* (1999)
lipophilic extract (CH_2Cl_2:methanol)	–	–	P_{SU}, no D_{SS}, no D_{SC}, FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	P_{SU}, D_{SS}, D_{SC}, FO_S	
Kallymenia antarctica				
bromoform	VH	–	B_S? or D_S? , –	Laturnus *et al.* (1996, 1998a)
bromomethane	VH	–	–	
dibromomethane	VH	–	B_S? or D_S?	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
iodomethane	VH	–	–	
unspecified no brominating activity	–	–	–	Laturnus *et al.* (1997)
mycosporine-glycine	MA	–	UV	Hoyer *et al.* (2001)
shinorine	MA	–	UV	Hoyer *et al.* (2002, 2003)
palythine	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	–	UV	
mycosporine-glycine	MA	–	UV	
porphyra-334	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	
Leptosomia simplex				
carotenoids	CA	–	UV?, X?	Karentz & Bosch (2001)
Lithothamnion cf. *antarcticum*				
porphyra-334	MA	–	UV	Karentz *et al.* (1991)
shinorine	MA	–	UV	
Myriogramme manginii				
bromoform	VH	–	B_S? or D_S? , –	Laturnus *et al.* (1996, 1998a)
bromomethane	VH	–	–	
dibromomethane	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
iodomethane	VH	–	–	
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified iodating activity	–	–	–	
shinorine	MA	–	UV	Hoyer *et al.* (2001)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
asterina-330	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al.*(2003)
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, no D_{SC}, FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SC}, FO_S	
Myriogramme smithii				
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002, 2003)
p-hydroxybenzaldehyde	AA	–	–	Ankisetty *et al.* (2004b)
p-methoxyphenol	QN	–	–	
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, D_{SF}, no D_{SC}, FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	D_{SS}, no D_{SF}, no D_{SC}, no FO_S	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
Nereoginkgo adiantifolia				
thallus	–	–	no D_{SS}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	FO_S	Amsler *et al.* (2005b)
Neuroglossum ligulatum				
iodoethane	VH	–	–	Giese *et al.* (1999)
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
shinorine	MA	–	UV	Hoyer *et al.* (2001, 2002, 2003)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	
Notophycus fimbriatus				
mycosporine-glycine	MA	–	UV	Hoyer *et al.* (2001)
shinorine	MA	–	UV	
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
asterina-330	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al.* (2003)
Pachymenia orbicularis				
mycosporine-glycine	MA	–	UV	Hoyer *et al.* (2001)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al.* (2003)
thallus	–	–	D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SC}, FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SC}	
Palmaria decipiens				
palythine	MA	–	UV	Karentz *et al.* (1991);
shinorine	MA	–	UV	Hoyer *et al.* (2001, 2002)
porphyra-334	MA	–	UV	Hoyer *et al.* (2003)
mycosporine-glycine	MA	–	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
usujirene	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	
UV-absorbing pigments	–	–	UV	Post & Larkum (1993)
bromomethane	VH	–	–	Laturnus (1995)
bromomethane	VH	–	–	Laturnus *et al.* (1998a)
dibromomethane	VH	–	–, B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	–, B_S? or D_S?	
bromoethane	VH	–	–	
1,2-dibromoethane	VH	–	–, B_S? or D_S?	
bromochloromethane	VH	–	–	
bromodichloromethane	VH	–	–, B_S? or D_S?	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
dibromochloromethane	VH	–	–, B_S? or D_S?	
diiodomethane	VH	–	–, B_S? or D_S?	
iodoethane	VH	–	–	
chloroiodomethane	VH	–	–, B_S? or D_S?	
chloromethane	VH	–	–	
iodomethane	VH	–	–	
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified no iodating activity	–	–	–	
homogenated algae	–	–	no G_{SM}	Iken (1999)
intact tissue	–	–	G_{SM}	
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al.* (2005a)
Pantoneura plocamioides				
bromoform	VH	–	B_S? or D_S? , –	Laturnus *et al.* (1996, 1998a)
bromomethane	VH	–	–	
dibromomethane	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
iodomethane	VH	–	–	
diiodomethane	VH	–	B_S? or D_S?, –	Giese *et al.* (1999)
chloroiodomethane	VH	–	B_S? or D_S? , –	
iodoethane	VH	–	–	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified no iodating activity	–	–	–	
pantofuranoids A, B, C, D, E and F	MT	–	–	Cueto & Darias (1996)
pantoneurotriol 1a and 2a	MT	–	–	Cueto *et al.* (1998c)
2 epimeric alcohols	–	–	–	
pantoneurines A and B	MT	–	–, D_{AI}	Cueto *et al.* (1998b); Argandoña *et al.* (2002)
pantopyranoids A, B and C	MT	–	–	Cueto *et al.* (1998a)
pantoisofuranoids A, B and C	MT	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002)
thallus	–	–	no D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SF}, no D_{SC}, FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	no D_{SF}, no D_{SC}, no FO_S	
Picconiella plumosa				
bromoform	VH	–	B_S? or D_S? , –	Laturnus *et al.* (1996, 1998a)
bromomethane	VH	–	–	
dibromomethane	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
iodomethane	VH	–	–	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
chloromethane	VH	–	–	
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
unspecified no iodating activity	–	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2003)
thallus	–	–	no D_{SS}, D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SC}	
hydrophilic extract (methanol:water)	–	–	D_{SC}, FO_S	Amsler *et al.* (2005b)
Phycodrys austrogeorgica				
unspecified no brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified no iodating activity	–	–	–	
bromomethane	VH	–	–	Laturnus *et al.* (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002, 2003)
thallus	–	–	no D_{SS}	Amsler *et al.* (2005a)
Phycodrys quercifolia				
bromomethane	VH	–	–, UV	Laturnus *et al.* (1998a,b)
bromoform	VH	–	–, UV	
dibromomethane	VH	–	UV	
bromochloromethane	VH	–	UV	
bromodichloromethane	VH	–	UV	
bromoethane	VH	–	UV, –	Giese *et al.* (1999)
chloromethane	VH	–	–, UV	
chloroiodomethane	VH	–	UV, –	
iodomethane	VH	–	–, UV	
iodoethane	VH	–	UV	
diiodomethane	VH	–	UV, –	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002)
Phyllophora ahnfeltioides				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?, –	Giese *et al.* (1999)
chloroiodomethane	VH	–	B_S? or D_S?, –	
iodoethane	VH	–	–	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
no mycosporine-like amino acids	–	–	–	Hoyer *et al.* (2001, 2002)
Phyllophora antarctica				
shinorine	MA	–	UV	McClintock & Baker (1995)
palythine	MA	–	UV	McClintock & Karentz (1997)
bromomethane	VH	–	–	Laturnus *et al.* (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	
thallus	–	–	P_{SU}	Amsler *et al.* (1998)
polar extract	–	–	P_{SU}	
non polar extract	–	–	P_{SU}	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
thallus on *S. neumayeri*	–	–	PP_S	Amsler *et al.* (1999)
thallus without chemicals on *S. neumayeri*	–	–	PP_S	
lipophilic extract (CH_2Cl_2:methanol)	–	–	FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	FO_S	
Phyllophora appendiculata				
palythine	MA	–	UV	Karentz *et al.* (1991)
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
iodoethane	VH	–	–	Giese *et al.* (1999)
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
Plocamium cartilagineum				
mixture of compounds (TLC)	–	–	F_T	Stierle & Sims (1979)
cyclohexanes[3,4,5,6]	MT	–	F_T	
plocamene D	MT	–	–, B_A, Y	Darias *et al.* (1987); Cueto *et al.* (1991)
epi-plocamene D	MT	–	–, B_A, no Y, Y, D_{SC}, no D_{SS}	Rovirosa *et al.* (1990); Ankisetty *et al.* (2004b)
acyclic halogenated monoterpene	MT	–	–	
monoterpene 7	MT	–	B_A, Y	
monoterpene 8	MT	–	–	
monoterpene 9 and 11	MT	–	B_A, no Y	
monoterpene 10	MT	–	B_A, no Y, Y, IN,	
anverene	MT	–	B_A, no Y, $D_{SC,}$ no D_{SS}	
pyranoid	MT	–	no B_A, Y, no D_{SC}, no D_{SS}	
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified iodating activity	–	–	–	
bromomethane	VH	–	–	Laturnus *et al.* (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	
iodoethane	VH	–	–	Giese *et al.* (1999)
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
shinorine	MA	–	UV	Hoyer *et al.* (2001, 2002)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al.* (2003)
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al.* (2005a)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, D_{SF}, D_{SC}, FO_S	Amsler *et al.* (2005b)
hydrophilic extract (methanol:water)	–	–	D_{SS}, no D_{SF}, D_{SC}, FO_S	
Plocamium coccineum				
dibromomethane	VH	–	B_S? or D_S?	Laturnus *et al.* (1996)
bromoform	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?	
chloroiodomethane	VH	–	B_S? or D_S?	
Plocamium sp.				
mixture compounds in TLC	–	–	F_T	Stierle *et al.* (1979)
4 monoterpenes	MT	–	F_T	
Plumariopsis peninsularis				
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	D_{SS}, no D_{SF}, no D_{SC}	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, D_{SC}	
Porphyra endiviifolium				
unspecified brominating activity	–	–	–	Laturnus *et al.* (1997)
unspecified no iodating activity	–	–	–	
bromoform	VH	–	B_S? or D_S?, –	Laturnus *et al.* (1996, 1998a)
bromomethane	VH	–	–	
dibromomethane	VH	–	B_S? or D_S?	
1,2-dibromoethane	VH	–	B_S? or D_S?	
bromodichloromethane	VH	–	B_S? or D_S?	
dibromochloromethane	VH	–	B_S? or D_S?	
diiodomethane	VH	–	B_S? or D_S?, –	Giese *et al.* (1999)
chloromethane	VH	–	–	
chloroiodomethane	VH	–	B_S? or D_S? , –	
iodomethane	VH	–	–	
iodoethane	VH	–	–	
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
mycosporine-glycine	MA	–	UV	Hoyer *et al.* (2001)
shinorine	MA	–	UV	Hoyer *et al.* (2002)
porphyra-334	MA	–	UV	Hoyer *et al.* (2003)
palythine	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 332-334nm)	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	
Porphyra plocamiestris				
shinorine	MA	–	UV	Hoyer *et al.* (2002)
porphyra-334	MA	–	UV	
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al.* (2005a)
Rhodymenia subantarctica				
bromomethane	VH	–	–	Laturnus *et al.* (1998a)
bromoform	VH	–	–	
iodomethane	VH	–	–	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
iodoethane	VH	–	–	Giese *et al.* (1999)
1-iodopropane	VH	–	–	
2-iodopropane	VH	–	–	
1-iodo-2-methylpropane	VH	–	–	
1-iodobutane	VH	–	–	
2-iodobutane	VH	–	–	
diiodomethane	VH	–	–	
chloroiodomethane	VH	–	–	
porphyra-334	MA	–	UV	Hoyer *et al.* (2001)
Sarcothalia papillosa				
shinorine	MA	–	UV	Hoyer *et al.* (2001)
palythine	MA	–	UV	
unknown mycosporine-like amino acid (max. absorb. 321-337nm)	MA	–	UV	
mycosporine-like amino acid	MA	–	UV	Hoyer *et al.* (2003)
Trematocarpus antarcticus				
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al.* (2005a,b)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, no D_{SF}, no D_{SC}, FO_S	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SF}, no D_{SC}	
Undescribed species, probably *Pugetia* sp. (Kallymeniaceae)				
thallus	–	–	no D_{SS}, no D_{SF}	Amsler *et al.* (2005a)
lipophilic extract (CH_2Cl_2:methanol)	–	–	no D_{SS}, D_{SF}, no D_{SC}	
hydrophilic extract (methanol:water)	–	–	no D_{SS}, no D_{SF}, D_{SC}	
PH. CILIATA				
Euplotes focardii				
epoxyfocardin	DT	–	C_S, C_A	Guella *et al.* (1996)
focardin	DT	–	C_S, C_A	
Euplotes nobilii (strain AC-1)				
pheromone En-1	NC	–	MI	Felici *et al.* (1999)
pheromone En-2	NC	–	MI	
PH. SARCOMASTIGOPHORA				
Gromia oviformis				
no mycosporine-like amino acids	–	–	–	Karentz *et al.* (1991)
PH. PORIFERA				
Unidentified species (#1)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
palythinol	MA	–	UV	
Unidentified species (#3)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
Unidentified species (#5)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Unidentified species (#6)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Unidentified species				
sesquiterpene alcohol	SQ	–	B_A	Urban *et al.* (1995)
Unidentified species (#6)				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
Unidentified species (#20)				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
Unidentified species (#21)				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	no T_S	
Unidentified species (#23)				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
Unidentified species (#29)				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
CL. CALCAREA, O. CALCINEA				
Leucetta antarctica				
bromochlorophenol	HP	–	–	Vetter & Janussen (2005)
2,4-dibromophenol	HP	–	–	
2,6-dibromophenol	HP	–	–	
bromochloroanisole	HP	–	–	
bromodichlorophenol	HP	–	–	
dibromoanisole	HP	–	–	
dibromochlorophenol	HP	–	–	
2,4,6-tribromoanisole	HP	–	–	
tribromooctenone	HP	–	–	
2,4,6-tribromophenol	HP	–	–	
mixed halogenated compounds (MHC-1)	HP	–	–	
Leucetta leptoraphis				
methanolic extract	–	–	I_A, B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
methanolic extract fraction 1 (taurine)	–	–	–	Baker *et al.* (1993)
methanolic extract fraction 2	–	–	C	
methanolic extract fraction 3	–	–	C	
methanolic/dichloromethanolic extract	–	–	L_A	Jayatilake *et al.* (1997)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al.* (1990)
hexane extract	–	–	B_A, no T_S, no Y	
chloroform extract	–	–	B_A, no T_S, no Y	
rhapsamine	NC	–	L_A, S	
non polar extract	–	–	FO_S	Amsler *et al.* (2000b)
polar extract	–	–	FO_S	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
CL. HEXACTINELLIDA, O. LYSSACINOSA				
Unidentified species				
ergosta-4,24(28)-dien-3-one	TS	–	–	Guella *et al.* (1988)
Rossella nuda				
methanolic extract	–	–	no I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, T_S, no Y	
palythine	MA	–	UV	McClintock & Karentz (1997)
Rossella racovitzae				
methanolic extract	–	–	no I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al.* (1990)
hexane extract	–	–	no B_A, T_S, no Y	
chloroform extract	–	–	B_A, no T_S, no Y	
mycosporine-glycine	MA	–	UV	McClintock & Karentz (1997)
palythine	MA	–	UV	
Scolimastra joubini				
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al.* (1990)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
hydrophilic extract	–	–	T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
CL. DEMOSPONGIAE, O. POECILOSCLERIDA				
Artemisina apollinis				
12 sterols	TS	–	–	Seldes *et al.* (1990b)
mixture steroidal ketones	TS	–	–	
bromochlorophenol	HP	–	–	Vetter & Janussen (2005)
2,4-dibromophenol	HP	–	–	
2,6-dibromophenol	HP	–	–	
dibromoanisole	HP	–	–	
dibromochlorophenol	HP	–	–	
2,4,6-tribromoanisole	HP	–	–	
tribromooctenone	HP	–	–	
2,4,6-tribromophenol	HP	–	–	
mixed halogenated compound (MHC-1)	HP	–	–	
Ectyodoryx ramilobosa (=*Lissodendoryx* (*Ectyodoryx*) *ramilobosa*)				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
Inflatella belli				
methanolic extract	–	–	I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al.* (1990)
hexane extract	–	–	no B_A, T_S, no Y	
chloroform extract	–	–	no B_A, T_S, no Y	
palythine	MA	–	UV	McClintock & Karentz (1997)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
Isodictya erinacea				
methanolic extract	–	–	no I_A, T_S, no B_A, T_S, no Y	McClintock (1987); Moon *et al.* (1998); McClintock *et al.* (1993a, 1994b); Baker & Yoshida (1994)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al.* (1990)
chloroform extract	–	–	T_S, B_A, no Y	Baker *et al.* (1993)
hexane extract	–	–	B_A, no T_S, no Y	
erinacean	NC	–	B_A, S, no T_S	
inosine	NC	–	no T_S	
uridine	NC	–	no T_S	
2′-deoxycytidine	NC	–	no T_S	
1,9-demethylguanine	NC	–	no T_S	
7-methyladenine	NC	–	no T_S	
p-hydroxybenzaldehyde	AA	–	T_S	
erebusinone (erebusphenone)	NC	–	no T_S, M_S	Moon *et al.* (2000)
palythine	MA	–	UV	McClintock & Karentz (1997)
palythinol	MA	–	UV	
Isodictya setifera				
methanolic extract	–	–	no I_A, B_A, no T_S, no Y	McClintock (1987); McClintock *et al.* (1993a)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	B_A, no T_S, no Y	
whole body sponge	(no DK, no PA)	–	–	Jayatilake *et al.* (1996)
eggs	–	–	D_{SS}, D_{SA}, D_{SC}	McClintock & Baker (1997b)
associated bacteria (*Pseudomonas aeruginosa*)				
cyclo-(L-Pro-L-Met)	DK	–	no C_A, no B_A	Jayatilake *et al.* (1996)
cyclo-(L-Pro-L-Val)	DK	–	no C_A, no B_A	
cyclo-(L-Pro-L-Leu)	DK	–	no C_A, no B_A	
cyclo-(L-Pro-L-Ile)	DK	–	no C_A, no B_A	
cyclo-(L-Pro-L-Phe)	DK	–	no C_A, no B_A	
cyclo-(L-Pro-L-Tyr)	DK	–	no C_A, no B_A	
phenazine-1-carboxylic acid	PA	–	B_A	
phenazine-1-carboxamide	PA	–	B_A	
Isodictya spinigera				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
Kirkpatrickia variolosa				
methanolic extract	–	–	I_A, B_A, no T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
			T_S	Baker & Yoshida (1994)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	no C_S, no R_S, T_S	McClintock *et al.* (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, T_S, no Y	
crude extract	–	–	no B_A	Trimurtulu *et al.* (1994)
variolin A	PY	–	S, no T_S	
variolin B	PY	–	A, S	Perry *et al.* (1994)
variolin D	PY	–	no A, no S	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
N(3')-methyl tetrahydrovariolin B	PY	–	F, S	
resveratrol triacetate	SF	–	–	Jayatilake *et al.* (1995)
purple uncharacterized pigment	–	–	T_S	
shinorine	MA	–	UV	McClintock & Karentz (1997)
mycosporine-glycine:valine	MA	–	UV	
palythine	MA	–	UV	
non polar extract	–	–	FO_S	Amsler *et al.* (2000b)
polar extract	–	–	FO_S	
2,4-dibromophenol	HP	–	–	Vetter & Janussen (2005)
2,6-dibromophenol	HP	–	–	
bromochloroanisole	HP	–	–	
bromodichlorophenol	HP	–	–	
dibromoanisole	HP	–	–	
dibromochlorophenol	HP	–	–	
2,4,6-tribromoanisole	HP	–	–	
tribromooctenone	HP	–	–	
2,4,6-tribromophenol	HP	–	–	
mixed halogenated compounds (MHC-1)	HP	–	–	
Latrunculia apicalis (=*Latrunculia* (*Latrunculia*) *apicalis*)				
methanolic extract	–	–	I_A, B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al.* (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	B_A, no Y	
discorhabdin C	DA	–	T_S, B_S, B_A	Baker & Yoshida (1994); Yang *et al.* (1995)
discorhabdin G	DA	–	D_{SS}, B_A, B_S	Furrow *et al.* (2003)
shinorine	MA	–	UV	McClintock & Karentz (1997)
porphyra-334	MA	–	UV	
mycosporine-glycine:valine	MA	–	UV	
palythine	MA	–	UV	
Latrunculia sp.				
discorhabdins B and R	DA	–	B_A	Ford & Capon (2000)
Lissodendoryx flabellata (= *Lissodendoryx (Lissodendoryx) flabellata*)				
flabellatene A	DT	–	S	Fontana *et al.* (1999)
flabellatene B	DT	–	–	
Mycale acerata (= *Mycale (Oxymycale) acerata*)				
methanolic extract	–	–	I_A, no B_A, no T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al.* (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, no T_S, no Y	
non polar extract	–	–	FO_S	Amsler *et al.* (2000b)
polar extract	–	–	no FO_S	
palythine	MA	–	UV	McClintock & Karentz (1997)
Myxodoryx hanitschi				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	no T_S	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
Phorbas areolatus				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
Phorbas glaberrimus				
bromochlorophenol	HP	–	–	Vetter & Janussen (2005)
2,4-dibromophenol	HP	–	–	
2,6-dibromophenol	HP	–	–	
bromochloroanisole	HP	–	–	
bromodichlorophenol	HP	–	–	
dibromoanisole	HP	–	–	
dibromochlorophenol	HP	–	–	
2,4,6-tribromoanisole	HP	–	–	
1,1,2-tribromooct-1-en-3-one	HP	A?	–	
2,4,6-tribromophenol	HP	–	–	
mixed halogenated compound (MHC-1)	HP	–	–	
Psammopemma sp. (= *Psammoclema* sp.)				
psammopemmins A, B and C	BA	–	–	Butler *et al.* (1992)
Tedania charcoti (= *Tedania* (*Tedaniopsis*) *charcoti*)				
Cd	IC	S	B_A	Capon *et al.* (1993)
Zn	IC	S	B_A	
O. HAPLOSCLERIDA				
Calyx arcuaria				
aqueous extract	–	–	no C_S, no R_S, T_S	McClintock *et al.* (1990)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
hexane extract	–	–	no B_A, T_S, no Y	McClintock *et al.* (1993a, 1994b)
chloroform extract	–	–	no B_A, T_S, no Y	
methanolic extract	–	–	no B_A, T_S, no Y	
non polar extract	–	–	no FO_S	Amsler *et al.* (2000b)
polar extract	–	–	no FO_S	
Clathria nidificata (= *Clathria* (*Axosuberites*) *nidificata*)				
hydrophilic extract	–	–	T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	no T_S	
Gellius benedeni (=*Haliclona* (*Gellius*) *benedeni*)				
methanolic extract	–	–	no I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al.* (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, T_S, no Y	
mycosporine-glicine	MA	–	UV	McClintock & Karentz (1997)
shinorine	MA	–	UV	
palythine	MA	–	UV	
Gellius tenella (= *Haliclona* (*Gellius*) *tenella*)				
methanolic extract	–	–	no I_A, B_A, no Y	McClintock (1987); McClintock *et al.* (1993a)
aqueous extract	–	–	no C_S, no R_S, T_S	McClintock *et al.* (1990)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
hexane extract	–	–	no B_A, no Y	
chloroform extract	–	–	B_A, no Y	
Haliclona dancoi (=*Haliclona* (*Rhizoniera*) *dancoi*)				
methanolic extract	–	–	I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al.* (1990)
hexane extract	–	–	B_A, T_S, no Y	
chloroform extract	–	–	B_A, no T_S, no Y	
non polar extract	–	–	FO_S	Amsler *et al.* (2000b)
polar extract	–	–	FO_S	
Haliclona scotti				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	no T_S	
Haliclona sp.				
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
hexane extract	–	–	no B_A, T_S, no Y	McClintock *et al.* (1993a, 1994b)
chloroform extract	–	–	no B_A, T_S, no Y	
methanolic extract	–	–	no B_A, T_S, no Y	
mycosporine-glicine	MA	–	UV	McClintock & Karentz (1997)
palythine	MA	–	UV	
Hemigellius fimbriatus				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	no T_S	
Microxina charcoti				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	no T_S	
Xestospongia sp.				
(22E)-24-norcolesta-5,22-dien-3β-ol	TS	–	–	Seldes *et al.* (1990a)
(22E)-27-nor-24-metilcolesta-5,22-dien-3β-ol	TS	–	–	
(22E)-colesta-5,22-dien-3β-ol	TS	–	–	
colest-5-en-3β-ol	TS	–	–	
5α-colestan-3β-ol	TS	–	–	
(22E,24ϵ)-24-metilcolesta-5,22-dien-3β-ol	TS	–	–	
(24ϵ)-24-metilcolesta-5-en-3β-ol	TS	–	–	
24-metilcolesta-5,24(28)-dien-3β-ol	TS	–	–	
(22E,24E)-24-etilcolesta-5,22-dien-3β-ol	TS	–	–	
24-etilcolesta-5,24(28)-dien-3β-ol	TS	–	–	
24E-etilcolest-5-en-3β-ol	TS	–	–	
24-propilcolesta-5,24(28)-dien-3β-ol	TS	–	–	
Xestospongia sp.				
11 steroids	TS	P?	–	Cueto *et al.* (1991)
Xestospongia sp.				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
O. ASTROPHORIDA				
Cinachyra antarctica				
methanolic extract	–	–	no I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al.* (1990)
hexane extract	–	–	no B_A, T_S, no Y	
chloroform extract	–	–	B_A, T_S, no Y	
polar extract	–	–	FO_S	Amsler *et al.* (2000b)
Cinachyra antarctica (white phenotip)				
hydrophilic extract	–	–	no T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
Cinachyra antarctica (yellow phenotip)				
shinorine	MA	–	UV	McClintock & Karentz (1997)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
hydrophilic extract	–	–	T_S	McClintock *et al.* (2000)
lipophilic extract	–	–	T_S	
Cinachyra barbata				
(22E)-24-norcholesta-5,22-dien-3β-ol	TS	–	–	Seldes *et al.* (1990a)
(22E)-27-nor-24-methylcholesta-5,22-dien-3β-ol	TS	–	–	
(22E)-cholesta-5,22-dien-3β-ol	TS	–	–	
cholest-5-en-3β-ol	TS	–	–	
5α-cholestan-3β-ol	TS	–	–	
(22E,24ϵ)-24-methylcholesta-5,22-dien-3β-ol	TS	–	–	
(24ϵ)-24-methylcholesta-5-en-3β-ol	TS	–	–	
24-methylcholesta-5,24(28)-dien-3β-ol	TS	–	–	
(22E,24E)-24-ethylcholesta-5,22-dien-3β-ol	TS	–	–	
24-ethylcholesta-5,24(28)-dien-3β-ol	TS	–	–	
24E-ethylcholest-5-en-3β-ol	TS	–	–	
24-propylcholesta-5,24(28)-dien-3β-ol	TS	–	–	
11 steroids	TS	P?	–	Cueto *et al.* (1991)
Tetilla leptoderma				
methanolic extract	–	–	I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b)
methanol-toluenic extract	–	–	B_A, Y, no F	McClintock & Gauthier (1992)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al.* (1990)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, Y	
shinorine	MA	–	UV	McClintock & Karentz (1997)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
O. AXINELLIDA				
Homaxinella balfourensis				
cholest-5-en-3β-ol	TS	–	–	Seldes *et al.* (1986)
cholestan-3β-ol	TS	–	–	
22-trans-24ξ-methyl-5α-cholest-22-en-3β-ol	TS	–	–	
24ξ-methyl-5α-cholestan-3β-ol	TS	–	–	
24-methyl-5α-cholest-24(28)-en-3β-ol	TS	–	–	
22-trans-24ξ-ethyl-5α-cholest-22-en-3β-ol	TS	–	–	
24ξ-ethyl-5α-cholestan-3β-ol	TS	–	–	
aqueous extract	–	–	no C_S, no R_S, no T_S	McClintock *et al.* (1990)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
methanolic extract	–	–	no B_A, no T_S, no Y	McClintock *et al.* (1993a, 1994b)
hexane extract	–	–	no B_A, no T_S, no Y	
chloroform extract	–	–	no B_A, T_S, no Y	
non polar extract	–	–	FO_S	Amsler *et al.* (2000b)
polar extract	–	–	FO_S	
shinorine	MA	–	UV	McClintock & Karentz (1997)
porphyra-334	MA	–	UV	
mycosporine-glycine:valine	MA	–	UV	
palythine	MA	–	UV	
Homaxinella sp.				
methanolic extract	–	–	I_A	McClintock (1987)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
O. HADROMERIDA				
Polymastia invaginata				
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al.* (1990)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
methanolic extract	–	–	no B_A, T_S, no Y	McClintock *et al.* (1993a, 1994b)
hexane extract	–	–	B_A, T_S, no Y	
chloroform extract	–	–	B_A, no Y	
Sphaerotylus antarcticus				
hexane extract	–	–	no B_A, no T_S, no Y	McClintock *et al.* (1993a, 1994b)
chloroform extract	–	–	B_A, T_S, no Y	
methanolic extract	–	–	B_A, no T_S, no Y	
shinorine	MA	–	UV	McClintock & Karentz (1997)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
Suberites caminatus				
caminatal	TS	–	–	Díaz-Marrero *et al.* (2003)
oxaspirosuberitenone	ST	–	–	Díaz-Marrero *et al.* (2004a)
19-episuberitenone	ST	–	–	
suberitenone B	ST	–	–	
Suberites sp.				
suberitenone A	ST	–	no C_A, no A, T_S, B_S, no B_A, no F, no Y	Shin *et al.* (1995); Baker *et al.* (1997)
suberitenone B	ST	–	no C_A, no A, CE, T_S, B_S, no B_A, no F, no Y	
suberitenone C and D	ST	–	no S, no B_A, no F	Lee *et al.* (2004)
suberiphenol	ST	–	no S, no B_A, no F	
O. DENDROCERATIDA				
Dendrilla membranosa				
methanolic extract	–	–	I_A, no B_A, T_S, no Y	McClintock (1987); McClintock *et al.* (1993a, 1994b);
			no T_S	Baker & Yoshida (1994)
methanol-toluenic extract	–	–	B_A, Y, F	McClintock & Gauthier (1992)
dichlorometane extract	–	–	B_A	Molinski & Faulkner (1987)
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al.* (1990)
hexane extract (mainly norditerpenes)	–	–	no T_S	Baker *et al.* (1995)
hexane extract	–	–	no B_A, no T_S, T_S, no Y	
chloroform extract	–	–	no B_A, T_S, no Y	
non polar extract	–	–	FO_S	Amsler *et al.* (2000b)
polar extract	–	–	FO_S	
picolinic acid	NA	–	T_S?	
7-methyladenine	NC	–	T_S?	
4,5,8-trihydroxyquinoline-2-carboxylic acid	QA	–	B_A, –	Molinski & Faulkner (1988)
9,11-dihydrogracillin A (DGHA)	DT	–	–, no T_S	Baker *et al.* (1993); Puliti *et al.* (1993)
membranolide	DT	–	–, no T_S	Manríquez *et al.* (1990); Díaz-Marrero *et al.* (2004b)
membranolide B	DT	–	–	Ankisetty *et al.* (2004a)
membranolide C and D	DT	–	B_A, F	
dendrinolide	DT	–	–	Fontana *et al.* (1997)
DGHA epoxy derivative	DT	–	no T_S	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
dendrillin	DT	–	no T_S	
norditerpene gracilane skeleton derivative	DT	–	–	
3 C-20 aplysulphurane type diterpenes	DT	–	–	
polyrhaphin D	DT	–	–	
shinorine	MA	–	UV	McClintock & Karentz (1997)
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
O. HALICHONDRIDA				
Halichondria sp.				
aqueous extract	–	–	C_S, R_S, T_S	McClintock *et al.* (1990)
bromochlorophenol	HP	–	–	Vetter & Janussen (2005)
2,4-dibromophenol	HP	–	–	
2,6-dibromophenol	HP	–	–	
dibromoanisole	HP	–	–	
dibromochlorophenol	HP	–	–	
2,4,6-tribromoanisole	HP	–	–	
tribromooctenone	HP	–	–	
2,4,6-tribromophenol	HP	–	–	
mixed halogenated compound (MHC-1)	HP	B? or MI?	–	
PH. CNIDARIA, CL. ANTHOZOA, SUB CL. ZOANTHARIA (=HEXACORALLIA), O. ACTINIARIA (SEA ANEMONES)				
Unidentified species (#1)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Isotealia antarctica				
mycosporine-glycine	MA	–	UV	McClintock & Karentz (1997)
shinorine	MA	–	UV	
porphyra-334	MA	–	UV	
mycosporine-glycine-valine	MA	–	UV	
palythine	MA	–	UV	
asterina-330	MA	–	UV	
SUB CL. ALCYONARIA (=OCTOCORALLIA), O. ALCYONACEA				
Alcyonium paessleri				
aqueous extract	–	–	C_S	McClintock *et al.* (1991b)
aqueous methanolic extract	–	–	no FO_S, G_S, L_S, T_S	Slattery *et al.* (1995); Slattery & McClintock (1995)
aqueous homogenate	–	–	L_S	
hexane extract	–	–	no FO_S, no G_S, no L_S, T_S	
chloroform extract	–	–	FO_S, G_S, L_S, T_S	
methanolic extract	–	–	no FO_S, no G_S, no L_S, T_S	
tissue	–	–	D_{SF}	
tissue without metabolites	–	–	no D_{SF}	
mycosporine-glycine	MA	–	UV	McClintock & Karentz (1997)
alcyopterosins A, B, C, D, E, F, G, H, I, J, K, L, M, N and O	SQ	–	–	Palermo *et al.* (2000)
paesslerins A and B	SQ	–	–	Rodríguez-Brasco *et al.* (2001)
cholesterol	TS	–	T_S, YM_S	Slattery *et al.* (1997a)
22-dehydrocholesterol / 24-methylene-cholesterol	TS	–	T_S	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
24-methylenecholesterol	TS	–	no T_S	
22-dehydro-7β-hydroxycholesterol	TS	–	T_S	
progesterone	TS	–	–	Slattery *et al.* (1997b)
androstenedione	TS	–	–	
testosterone	TS	–	–	
estradiol	TS	–	–	
Anthomastus bathyproctus				
methyl 3-oxocholesta-1,4-dien-26-oate	TS	–	no S	Mellado *et al.* (2005)
methyl (24E)-3-oxocholesta-1,4,24-trien-26-oate	TS	–	S	
(20S)-20-hydroxyergosta-1,4,24(28)-trien-3-one	TS	–	S	
triterpenes[7,8]	TS	–	S	
triterpenes[9,10]	TS	–	no S	
Clavularia frankliniana				
hexane extract	–	–	no FO_S, no G_S, no L_S, T_S	Slattery *et al.* (1995); Slattery & McClintock (1995)
chloroform extract	–	–	no FO_S, no G_S, no L_S, T_S	
methanolic extract	–	–	no FO_S, no G_S, no L_S, T_S	
aqueous methanolic extract	–	–	no FO_S, no G_S, no L_S, T_S	
aqueous homogenate	–	–	no L_S	
tissue	–	–	D_{SF}	
tissue without metabolites	–	–	no D_{SF}	
chimyl alcohol	FA	–	D_{SS}	McClintock & Baker (2001)
Gersemia antarctica				
hexane extract	–	–	no FO_S, no G_S, no L_S, T_S	Slattery *et al.* (1995); Slattery & McClintock (1995)
chloroform extract	–	–	FO_S, G_S, L_S,T_S	
methanolic extract	–	–	no FO_S, no G_S, no L_S, T_S	
aqueous methanolic extract	–	–	FO_S, G_S, L_S, T_S	
aqueous homogenate	–	–	L_S	
tissue	–	–	D_{SF}	
tissue without metabolites	–	–	no D_{SF}	
organic extract	–	–	G_S	Slattery *et al.* (1997a)
homarine	NA	–	B_S, G_S	
trigonelline	NA	–	B_S, no G_S	
progesterone	TS	–	–	Slattery *et al.* (1997b)
androstenedione	TS	–	–	
testosterone	TS	–	–	
estradiol	TS	–	–	
O. GORGONACEA (GORGONIANS)				
Ainigmaptilon antarcticus				
diethyl ethereal extract	–	–	D_{SS}	Iken & Baker (2003)
ainigmaptilon A	SQ	–	D_{SS}, B_S, FO_S	
ainigmaptilon B	SQ	–	–	
Dasystenella acanthina				
furanoeudesmane	SQ	–	I_A, no D_A	Gavagnin *et al.* (2003c)
isofuranodiene	SQ	–	I_A, no D_A	
trans-β-farnesene (pheromone)	SQ	–	no I_A, no D_A, –	Mellado *et al.* (2004)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
(24R,22E)-24-hydroxycholest-4,22-dien-3-one	TS	–	S	
23-acetoxy-24,25-epoxycholest-4-en-3-one	TS	–	S	
12β-acetoxycholest-4-en-3,24-dione	TS	–	S	
12β-acetoxy-24,25-epoxycholest-4-en-3-one	TS	–	S	
(22E)-25-hydroxy-24-norcholest-4,22-dien-3-one	TS	–	S	
3α-acetoxy-25-hydroxycholest-4-en-6-one	TS	–	S	
3α,11α-diacetoxy-25-hydroxycholest-4-en-6-one	TS	–	S	
steroid	TS	–	S	
PH. CTENOPHORA				
Bolinopsis n. sp.				
no mycosporine-like amino acids	–	–	–	Karentz *et al.* (1991)
Callianira antarctica				
no mycosporine-like amino acids	–	–	–	Karentz *et al.* (1991)
PH. PLATYHELMINTHES, O. TRICLADIDA				
Obrimoposthia wandeli				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
O. EULECITHOPHORA				
Unidentified planarian (#2, tentatively named *Plagiostomum* n. sp)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
PH. NEMERTEANS, CL. ANOPLA, O. HETERONEMERTEA				
Parborlasia corrugatus				
aqueous extract	–	–	C_S, D_{SF}	Heine *et al.* (1991);
tissue	–	–	D_{SF}	McClintock *et al.* (1991b)
intact animal	–	–	D_{SF}	
porphyra-334	MA	–	UV	Karentz *et al.* (1991)
mycosporine-glycine	MA	–	UV	
shinorine	MA	–	UV	McClintock & Karentz (1997)
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythine	MA	–	UV	
parborlysin (from mucus)	NC	–	no CR, H	Berne *et al.* (2003)
liophilized extract of integumentary tissues	–	–	H	
liophilized extract of non integumentary tissues	–	–	no H	
Parborlasia fueguina				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
O. HOPLONEMERTEA				
Amphiporus michaelseni (both in adults and embryos)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
PH. MOLLUSCA, CL. POLYPLACOPHORA				
Tonicina zschaui				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
CL. GASTROPODA, SUB CL. PROSOBRANCHIA				
Margarella antarctica				
porphyra-334	MA	–	UV	Karentz *et al.* (1991)
shinorine	MA	–	UV	
asterina-330	MA	–	UV	
palythine (in body, shell and egg ribbons)	MA	–	UV	
Marseniopsis mollis				
living animal	–	–	D_{SS}	McClintock *et al.* (1994a)
homarine (in mantle, viscera and foot)	NA	E	D_{SS}	McClintock *et al.* (1994d)
mycosporine-glycine	MA	–	UV	McClintock & Karentz (1997)
shinorine	MA	–	UV	
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
aqueous extract of mantle	–	–	C_S, T_S, E_S	McClintock *et al.* (1992a)
mantle tissue	–	–	D_{SF}	
Nacella concinna				
no mycosporine-like amino acids (in shell)	–	–	–	Karentz *et al.* (1992)
shinorine (in body, gut, gonads and eggs)	MA	–	UV	
porphyra-334 (in body, gut, gonads and eggs)	MA	–	UV	
Paludestrina antarctica				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
Trophon cf. *geversianus*				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
asterina-330	MA	–	UV	
no mycosporine-like amino acids in egg masses	–	–	–	
SUB CL. OPISTOBRANCHIA, O. THECOSOMATA				
Limacina helicina				
sterols	TS	–	–	Kattner *et al.* (1998)
shinorine	MA	P	UV	Whitehead *et al.* (2001)
porphyra-334	MA	P	UV	
mycosporine-glycine	MA	MO	UV	
palythine	MA	MO	UV	
palythenic acid	MA	MO	UV	
Limacina helicina ssp. *antarctica*				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
O. GYMNOSOMATA (PTEROPODA)				
Clione antarctica				
hexanic extract	–	–	D_{SF}	McClintock & Janssen (1990)
chloroformic extract	–	–	no D_{SF}	McClintock *et al.* (1994d)
methanolic extract	–	–	no D_{SF}	Bryan *et al.* (1995)
aqueous methanolic extract	–	–	no D_{SF}	
hexanic extract	–	–	D_{SF}	
pteroenone	PK	B?, –	D_{SF}	Yoshida *et al.* (1995)
triglyceride	FA	–	D_{SF}	
2 fatty acids	FA	–	no D_{SF}	
sterol	TS	–	no D_{SF}	
sterols	TS	–	–	Kattner *et al.* (1998)
odd-chain length fatty acids	FA	B?	F?	
shinorine	MA	M	UV	Whitehead *et al.* (2001)
porphyra-334	MA	M	UV	
mycosporine-glycine	MA	M	UV	
palythine	MA	M	UV	
palythenic acid	MA	M	UV	
O. NUDIBRANCHIA				
Unidentified species (#1, tentatively named *Telarma antarctica*)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Austrodoris kerguelenensis				
acetoxyglyceryd[11] from mantle	DT	B?	–	Davies-Coleman & Faulkner (1991)
acetoxyglyceryd[12] from mantle	DT	B?	–	
2 diketones	DT	B?	–	
glyceryl (5R,10R,13R)-7-ketolabda-8-en-15-oate	DT	B?	–	
austrodorin from mantle	DT	–	–	Gavagnin *et al.* (1995)
diterpene diacylglicerides (in mantle, gills, foot and mucus)	DT	–	–	Iken *et al.* (2002)
diterpene diacylglycerol metabolite from mantle	DT	B?	D_{SS}	
diterpene monoacylglycerides from mantle	DT	B?	D_{SS}	
austrodorin A and B (in mantle and mucus)	DT	–	–	Gavagnin *et al.* (1999a)
2 1,3-diacylglyceryl esters (in mantle and mucus)	DT	–	–	Gavagnin *et al.* (1999b)
diterpene diacylglicerides (in gills and foot)	DT	–	–	
no diacylglicerides in viscera	DT	–	–	
diterpene diacylglicerides (from mucus)	DT	–	–	
aqueous extract of mantle	–	–	C_S, T_S, E_S	McClintock *et al.* (1992a)
living animal	–	–	D_{SS}	
mantle tissue	–	–	D_{SF}, D_{SS}	
butanolic extract of mantle	–	–	no D_{SS}	
ethereal extract of mantle	–	–	D_{SS}	
ethereal extract of viscera	–	–	no D_{SS}	
butanolic extract of viscera	–	–	no D_{SS}	
sterols from mantle	TS	–	no D_{SS}	
triglycerids + lipophilic compounds from mantle	FA	–	no D_{SS}	
fatty acids from mantle	FA	–	no D_{SS}	Gavagnin *et al.* (2003b)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
monoacylglycerides of regular fatty acids from mantle	FA	B?	D_{SS}	
2 2-monoacylglycerols from mantle	DT	–	–	
2 1,2-diacylglyceryl esters from mantle	DT	–	–	
austrodoral from mantle	SQ	–	–	Gavagnin *et al.* (2003a)
austrodoric acid from mantle	SQ	B?	–	
Bathydoris hodgsoni				
hodgsonal from mantle	SQ	B?	–, D_{SS}	Iken *et al.* (1998); Avila *et al.* (2000)
tissue (mantle and papillae)	–	–	D_{SS}	
butanolic extract of mantle	–	–	no D_{SS}	
ethereal extract of mantle	–	–	D_{SS}	
high and low Rf compounds from mantle	–	–	no D_{SS}	
fatty acids from mantle	FA	–	no D_{SS}	
sterols from mantle	TS	–	no D_{SS}	
ethereal extract of viscera	–	–	no D_{SS}	
butanolic extract of viscera	–	–	no D_{SS}	
Notaeolidia gigas				
mycosporine-glycine	MA	–	UV	McClintock & Karentz (1997)
Tritoniella belli				
chimyl alcohol	FA	C	D_{SS}	McClintock *et al.* (1994d)
mycosporine-glycine	MA	–	UV	McClintock & Karentz (1997)
shinorine	MA	–	UV	
mantle tissue	–	–	D_{SF}	McClintock *et al.* (1992a)
aqueous extract of mantle	–	–	C_S, T_S, E_S	
ethyl acetate extract of mantle	–	–	T_S	Bryan *et al.* (1998)
mantle mucus	–	–	T_S, D_{SF}	
egg masses	–	–	D_{SS}, no D_{SA}, no D_{SC}	McClintock & Baker (1997b)
CL. BIVALVIA				
Limatula hodgsoni				
shinorine	MA	–	UV	McClintock & Karentz (1997)
palythine	MA	–	UV	
Limatula cf. *ovalis*				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Cyamium cf. *commune*				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
PH. ANNELIDA, CL. POLYCHAETA				
Unidentified species (#2)				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
O. PHYLLODOCIDA				
Aglaophamus trissophyllus (=*Aglaophamus ornatus*)				
palythine	MA	–	UV	Karentz *et al.* (1991)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
palythene	MA	–	UV	
Neanthes kerguelensis				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Tomopteris carpenteri				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
mycosporine-glycine	MA	–	UV	
O. TEREBELLIDA				
Terebella ehlersi				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
Thelepus extensus				
3,5-dibromo-4-hydroxybenzaldehyde	HP	–	–	Goerke *et al.* (1991)
3,5-dibromo-4-hydroxybenzyl alcohol	HP	–	–	
bis(3,5-dibromo-4-hydroxybenzyl)methane	HP	–	–	
bis(3,5-dibromo-4-hydroxybenzyl)ether	HP	–	–	
thelepin	HP	–	B?	
thelephenol	HP	–	–	
Thelepus cincinnatus				
3,5-dibromo-4-hydroxybenzaldehyde	HP	–	–	Goerke *et al.* (1991)
3,5-dibromo-4-hydroxybenzyl alcohol	HP	–	–	
bis(3,5-dibromo-4-hydroxybenzyl)methane	HP	–	–	
bis(3,5-dibromo-4-hydroxybenzyl)ether	HP	–	–	
thelepin	HP	–	B?	
thelephenol	HP	–	–	
CL. CLITELLATA, O. HIRUDINEA				
Trachelobdella australis				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
PH. ARTROPODA, CL. CRUSTACEA, SUB CL. COPEPODA				
Calanus propinquus				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
palythene	MA	–	UV	
SUB CL. MALACOSTRACA, O. EUPHAUSIACEA				
Euphasia superba				
palythenic acid	MA	–	–	Nakamura & Kobayashi (1982)
palythine	MA	–	–, UV	Karentz *et al.* (1991)
porphyra-334	MA	–	–, UV	
shinorine	MA	–	–, UV	
asterina-330	MA	–	–, UV	
palythinol	MA	–	–, UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
mycosporine-like amino acid	MA	A	UV	Newman *et al.* (2000)
O. ISOPODA				
Cymodocella tubicauda				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Notasellus sarsii				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Glyptonotus antarcticus				
palythine	MA	–	UV	McClintock & Karentz (1997)
living juveniles	–	–	D_{SS}	McClintock *et al.* (2003)
lipophilic extract (dichloromethane/methanol) of juveniles	–	–	D_{SS}	
hydrophilic extract (methanol/water) of juveniles	–	–	no D_{SS}	
O. AMPHIPODA				
Bovallia gigantea				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
Halirages sp.				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Jassa sp.				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Orchomene sp.				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Paraceradocus sp.				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
Pariphimedia integricauda				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
Pontogeneia sp.				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
palythinol	MA	–	UV	
CL. PYCNOGONIDA (=PANTOPODA)				
Unidentified species				
shinorine	MA	–	UV	McClintock & Karentz (1997)
palythine	MA	–	UV	
Achelia spicata				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
PH. BRYOZOA				
Unidentified species				
palythine	MA	–	UV	McClintock & Karentz (1997)
Beania livingstonei				
lipid soluble fraction	–	–	no B_A	Colon-Urban *et al.* (1985)
porphyra-334	MA	–	UV	Karentz *et al.* (1991)
shinorine	MA	–	UV	
Carbasea curva				
crude extract	–	–	H	Winston & Bernheimer (1986)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
Caberea darwinii				
lipid soluble fraction	–	–	B_A	Colon-Urban *et al.* (1985)
crude extract	–	–	no H	Winston & Bernheimer (1986)
Cycliopora polaris				
lipid soluble fraction	–	–	B_A	Colon-Urban *et al.* (1985)
Flustra thysanica				
lipid soluble fraction	–	–	B_A	Colon-Urban *et al.* (1985)
crude extract	–	–	no H	Winston & Bernheimer (1986)
Himantozoum antarcticum				
lipid soluble fraction	–	–	B_A	Colon-Urban *et al.* (1985)
crude extract	–	–	no H	Winston & Bernheimer (1986)
Inversiula nutrix				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Klugeflustra vanhoffeni				
crude extract	–	–	no H	Winston & Bernheimer (1986)
Nematoflustra flagellata				
lipid soluble fraction	–	–	B_A	Colon-Urban *et al.* (1985)
PH. BRACHIOPODA				
Liothyrella uva				
homogenated tissue	–	–	T_S	McClintock *et al.* (1993b)
homogenated & freezed	–	–	T_S	
liophilized	–	–	no D_{AF}	
living male	–	–	D_{SS}	Mahon *et al.* (2003)
living female	–	–	D_{SS}	
juvenile	–	–	D_{SS}	
hydrophobic extract	–	–	D_{SS}, no D_{SF}	
liophilized tissue (whole animal)	–	–	D_{SS}	
tissue of the lophophore	–	–	no D_{SS}	
liophilized tissue of the lophophore	–	–	no D_{SS}, no D_{SF}	
hydrophobic extract of the lophophore	–	–	B_S	
hydrophilic extract of the lophophore	–	–	B_S	
male liophilized reproductive tissue	–	–	D_{SS}, no D_{SF}	
female liophilized reproductive tissue	–	–	no D_{SS}, no D_{SF}	
male hydrophobic extract of reproductive tissue	–	–	no B_S	
male hydrophilic extract of reproductive tissue	–	–	no B_S	
female hydrophobic extract of reproductive tissue	–	–	B_S	
female hydrophilic extract of reproductive tissue	–	–	no B_S	
liophilized tissue of pedicle	–	–	D_{SS}, D_{SF}	
hydrophobic extract of pedicle	–	–	no B_S	
hydrophilic extract of pedicle	–	–	no B_S	
liophilized tissue of intestine-stomach	–	–	D_{SS}, no D_{SF}	
hydrophobic extract of intestine-stomach	–	–	B_S	
hydrophilic extract of intestine-stomach	–	–	B_S	
PH. CHAETOGNATA				
Unidentified species				
no mycosporine-like amino acids	–	–	–	Karentz *et al.* (1991)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
PH. ECHINODERMATA, CL. CRINOIDEA				
Promachocrinus kerguelensis				
aqueous extract of arms	–	–	no D_{AF}	McClintock (1989)
mycosporine-glycine	MA	–	UV	McClintock & Karentz (1997)
shinorine	MA	–	UV	
porphyra-334	MA	–	UV	
palythine	MA	–	UV	
CL. ASTEROIDEA				
Unidentified species (family Asteriidae)				
asterasterol A and B	TS	–	no S	De Marino *et al.* (1997b)
asterasterol C	TS	–	S	
asteriidoside A, B, C, D, E, F, I and L	GS	–	S	De Marino *et al.* (1998)
asteriidosides G and H	GS	–	–	
Unidentified species (tentatively named *Henricia* sp., family Echinasteridae)				
brasiliensoside	GS	–	S	De Marino *et al.* (1996); Iorizzi *et al.* (1996)
24S-methylbrasiliensoside	GS	–	S	
pectinoside A	GS	–	S	
24S-methylpectinoside	GS	–	S	
antarcticoside A and B	GS	–	S, –	
antarcticoside C, D, G, H, J, K and L	GS	–	S	
antarcticosides E, F, M, N, O and P	GS	–	–	
antarcticoside I	GS	–	no S	
polyhydroxylated steroids (compound #14, 16, 20, 21, 22, 23, 24 and 25)	TS	–	S	
polyhydroxylated steroid (compound #15)	TS	–	no S	
polyhydroxylated steroids (compounds #17, 18, 19, 26, 27)	TS	–	–	
Acodontaster conspicuus				
aqueous extract of body wall	–	–	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
3 asterosaponins	GS	–	no B_S	De Marino *et al.* (1997a)
halityloside I	GS	–	no B_S	
acodontasteroside A, B and C	GS	–	no B_S	
acodontasteroside D, E, F, G, H and I	GS	–	B_S	
polyhydroxylated steroids (compound #14 and 16)	TS	–	no B_S	
polyhydroxylated steroid (compound #15, 18 and 19)	TS	–	B_S	
polyhydroxylated steroid (compound #17)	TS	–	–	
Acodontaster hodgsoni				
aqueous extract of body wall	–	–	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
Bathybiaster loripes				
aqueous extract of body wall	–	–	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
Cueonotaster involutus				
aqueous extract of body wall	–	–	no D_{AF}	McClintock (1989)
Diplasterias brucei				
mixture of saponins	GS	–	H	Mackie *et al.* (1977)
marthasterone	TS	–	–	
dihydromarthasterone	TS	–	–	
liophilized tissue of egg mass & embryos	–	–	D_{AF}	McClintock & Vernon (1990)
tissue of embryos	–	–	D_{SS}, no D_{SA}, no D_{SC}	McClintock & Baker (1997b)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
lipophilic extract of embryos	–	–	no D_{SS}, D_{SA}	
hydrophilic extract of embryos	–	–	D_{SS}, no D_{SA}	
aqueous extract of body wall	–	–	D_{AF}	McClintock (1989)
palythine	MA	–	UV	McClintock & Karentz (1997)
Granaster nutrix				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
asterina-330	MA	–	UV	
living animal	–	–	D_{SS}	McClintock *et al.* (2006)
methanolic extract of body wall	–	–	D_{SS}	
Labidiaster annulatus				
labidiasteroside A	GS	–	–	Díaz de Vivar *et al.* (2000)
ovarian asterosaponin 1	GS	–	–	
Lophaster gaini				
aqueous extract of body wall	–	–	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
Lysasterias perrieri				
embryos tissue	–	–	D_{SS}	McClintock *et al.* (2003)
methanolic extract of embryos	–	–	D_{SS}	
juveniles tissue	–	–	D_{SS}	
methanolic extract of juveniles	–	–	no D_{SS}	
Macroptychaster accrescens				
aqueous extract of body wall	–	–	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
Neosmilaster georgianus				
santiagoside	GS	–	–	Vázquez *et al.* (1992)
hydrophilic extract	–	–	AV_S	Mahon *et al.* (2000)
living animal	–	–	D_{SS}	McClintock *et al.* (2006)
embryos tissue	–	–	D_{SS}	McClintock *et al.* (2003)
methanolic extract of embryos	–	–	no D_{SS}	
juveniles tissue	–	–	D_{SS}	
body wall tissue	–	–	D_{SS}	
fresh mucus (pH=7.75)	–	–	D_{SS}	
methanolic extract of body wall	–	–	D_{SS}	
Notasterias armata				
aqueous extract of body wall	–	–	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	D_{AF}	McClintock & Vernon (1990)
Odontaster meridionalis				
aqueous extract of body wall	–	–	no D_{AF}	McClintock (1989)
no mycosporine-like amino acids	–	–	–	McClintock & Karentz (1997)
Odontaster validus				
aqueous extract of body wall	–	–	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990);
ovaries tissue	–	–	no D_{SS}, no D_{SC}, no D_{SA}	McClintock & Baker (1997b)
mycosporine-glycine (in body wall)	MA	–	UV	McClintock & Karentz (1997)
palythine (in ovaries)	MA	–	UV	
Perknaster fuscus				
aqueous extract of body wall	–	–	D_{AF}, L_S, R_S, T_S	McClintock (1989); McClintock *et al.* (1992b)
ethanolic extract of body wall	–	–	–	Kong *et al.* (1992)
fuscusine (in body wall)	NC	B?	–, L_S?, R_S?, T_S?	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
liophilized tissue of egg mass & embryos	–	–	D_{AF}	McClintock & Vernon (1990)
embryos tissue	–	–	D_{SS}, D_{SA}, D_{SC}	McClintock & Baker (1997b)
larvae tissue	–	–	D_{SS}, D_{SA}, D_{SC}	
no mycosporine-like amino acids (in ovaries)	–	–	–	McClintock & Karentz (1997)
Porania antarctica				
aqueous extract of body wall	–	–	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	D_{AF}	McClintock & Vernon (1990)
Psilaster charcoti				
aqueous extract of body wall	–	–	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
larvae tissue	–	–	D_{SS}, D_{SA}, D_{SC}	McClintock & Baker (1997b)
embryos tissue	–	–	D_{SS}, D_{SA}, D_{SC}	
carotenoids (in embryos and eggs)	CA	–	UV?	Karentz & Bosch (2001)
no mycosporine-like amino acids	–	–	–	
CL. OPHIUROIDEA				
Amphioplus affinis				
palythine	MA	–	UV	Karentz *et al.* (1991)
Astrotoma agassizii				
aqueous extract of arms	–	–	no D_{AF}	McClintock (1989)
sterols[13,14,15]	TS	–	–, A	Roccatagliata *et al.* (1998); Comin *et al.* (1999)
2 sulphated polyhydroxysteroids	TS	–	–	
Gorgonocephalus chilensis				
5 disulphated polyhydroxysteroids	TS	–	–	Maier *et al.* (2000)
mixture of monosulphated steroids	TS	–	–	
Ophionotus victoriae				
aqueous extract of arms	–	–	no D_{AF}	McClintock (1989)
sterols[16,17,18]	TS	–	–	D'Auria *et al.* (1995)
2 sulphated polyhydroxysteroids	TS	–	–	
(22E)-24-norcholesta-5,22-dien-3β-ol	TS	–	–	Duque *et al.* (1997)
24-methyl-27-norcholesta-5,22-dien-3β-ol	TS	–	–	
22-dehydrocholesterol	TS	–	–	
24-methylcholesta-5,24(28)-dien-3β-ol	TS	–	–	
(22E)-24S-methylcholesta-5,22-dien-3β-ol	TS	–	–	
(22E)-24R-methylcholesta-5,22-dien-3β-ol	TS	–	–	
24ξ-ethylcholesta-5,24(28)-dien-3β-ol	TS	–	–	
24ξ-n-propylcholesta-5,24(28)-dien-3β-ol	TS	–	A	
cholest-5-en-3β-ol	TS	–	–	
24ξ-ethylcholesta-5,22-dien-3β-ol	TS	–	–	
24ξ-ethylcholesta-5-en-3β-ol	TS	–	–	
Ophiosparte gigas				
aqueous extract of arms	–	–	no D_{AF}	McClintock (1989)
cholest-5-ene-2α,3α,4β,21-tetraol 3,21-disulphate	TS	–	C	D'Auria *et al.* (1993)
cholest-5-ene-2β,3α,21-triol 2,21-disulphate	TS	–	A	
steroid	TS	–	A	
CL. ECHINOIDEA (SEA URCHINS)				
Abatus nimrodi				
aqueous extract of testes	–	–	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
Abatus shackletoni				
aqueous extract of testes	–	–	no D_{AF}	McClintock (1989)
liophilized tissue of embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
no mycosporine-like amino acids	–	–	–	McClintock & Karentz (1997)

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
Ctenocidaris perrieri				
aqueous extract of testes	–	–	no D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
Sterechinus neumayeri				
mycosporine-glycine (in digestive tract, eggs and ovaries)	MA	–	UV	McClintock & Karentz (1997); Karentz *et al.* (1997)
mycosporine-glycine:valine (in ovaries and testes)	MA	–	UV	
shinorine (in body wall, digestive tract, eggs, ovaries and testes)	MA	–	UV	
porphyra-334 (in body wall, digestive tract, eggs, ovaries and testes)	MA	–	UV	
palythine (in body wall, digestive tract, eggs, ovaries and testes)	MA	–	UV	
lipophilic extract of eggs	–	–	no D_{SS}, no D_{SA}, no D_{SC}	McClintock & Baker (1997b)
hydrophilic extract of eggs	–	–	no D_{SS}, no D_{SA}, no D_{SC}	
lipophilic extract of larvae	–	–	no D_{SA}	
hydrophilic extract of larvae	–	–	no D_{SA}	
CL. HOLOTHUROIDEA (SEA CUCUMBERS)				
Bathyplotes moseleyi				
aqueous extract of body wall	–	–	D_{AF}	McClintock (1989)
liophilized tissue of egg mass & embryos	–	–	no D_{AF}	McClintock & Vernon (1990)
Cucumaria ferrari				
aqueous extract of body wall	–	–	no D_{AF}	McClintock (1989)
mycosporine-glycine (in ovary and eggs)	MA	–	UV	McClintock & Karentz (1997)
shinorine (in ovary and eggs)	MA	–	UV	
porphyra-334 (in ovary and eggs)	MA	–	UV	
palythine (in ovary)	MA	–	UV	
mycosporine-glycine:valine (in eggs)	MA	–	UV	
Cucumaria cf. *georgiana*				
no mycosporine-like amino acids in body wall	–	–	–	Karentz *et al.* (1991)
Cucumaria steineni				
aqueous extract of body wall	–	–	D_{AF}	McClintock (1989)
Ekmocucumis steineni				
no mycosporine-like amino acids in body wall	–	–	–	Karentz *et al.* (1991)
porphyra-334 (in ovarian tubule)	MA	–	UV	
shinorine (in ovarian tubule)	MA	–	UV	
mycosporine-glycine (in ovarian tubule)	MA	–	UV	
mycosporine-glycine:valine (in ovarian tubule)	MA	B?, MO?	UV	
Staurocucumis liouvillei				
liouvilloside A and B	GS	–	A	Maier *et al.* (2001)
PH. TUNICATA, CL. ASCIDIACEA				
Unidentified benthic species				
mycosporine-glycine	MA	–	–	McClintock & Karentz (1997)
shinorine	MA	–	–	
Cnemidocarpa verrucosa				
tunic tissue	–	–	I_S, D_{SF}	McClintock *et al.* (1991a,b)
liophilized tunic tissue	–	–	I_A	
aqueous extract of tunic	–	–	C_S, no C_S	
body wall tissue	–	–	no I_S, no D_{SF}	
endocarps tissue	–	–	I_S, no D_{SF}	
intestines tissue	–	–	no I_S, no D_{SF}	
ovistestes tissue	–	–	I_S	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
tissue of the branchial basket	–	–	I_S, no D_{SF}	
shinorine	MA	–	–	McClintock & Karentz (1997)
porphyra-334	MA	–	–	
palythine	MA	–	–	
Distaplia cylindrica				
body tissue	–	–	D_{SS}	McClintock *et al.* (2004)
lipophilic extract (CH_2Cl_2:MeOH)	–	–	D_{SS}, FO_S	
lipophilic extract ($CHCl_3$)	–	–	D_{SS}, FO_S	
hydrophilic extract (butanolic extract)	–	–	D_{SS}, FO_S	
hydrophilic extract (MeOH:H_2O)	–	–	no D_{SS}, FO_S	
Molgula enodis				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
asterina-330	MA	–	UV	
Synoicum adareanum				
palmerolide A	PK	–	S	Diyabalanage *et al.* (2006); Jiang *et al.* (2007)
CL. THALIACEA (SALPS)				
Ihlea racovitzai				
24-nor-cholesta-5,22-dien-3β-ol	TS	–	–	Schor & Seldes (1989)
24-nor-5α-cholest-22-en-3β-ol	TS	–	–	
27-nor-24ξ-methyl-cholesta-5,22-dien-3β-ol	TS	–	–	
cholesta-5,22-dien-3β-ol	TS	–	–	
5α-cholest-22-en-3β-ol	TS	–	–	
cholest-5-en-3β-ol	TS	–	–	
5α-cholestan-3β-ol	TS	–	–	
brassicasterol	TS	–	–	
cholesta-5,24-dien-3β-ol	TS	–	–	
24ξ-methyl-5α-cholest-22-en-3β-ol	TS	–	–	
24ξ-methyl-cholest-5-en-3β-ol	TS	–	–	
24ξ-methyl-5α-cholestan-3β-ol	TS	–	–	
24-methyl-cholesta-5,24(28)-dien-3β-ol	TS	–	–	
24ξ-ethyl-cholesta-5,22-dien-3β-ol	TS	–	–	
24ξ-ethyl-cholesta-5-en-3β-ol	TS	–	–	
24ξ-ethyl-5α-cholestan-3β-ol	TS	–	–	
24-ethyl-cholesta-5,24(28)-dien-3β-ol	TS	–	–	
24-propyl-cholesta-5,24(28)-dien-3β-ol	TS	–	–	
Salpa thompsoni				
(22E)-24-norcholesta-5,22-dien-3β-ol	TS	MO?	–	Mimura *et al.* (1986)
(22E)-24-nor-5α-cholest-22-en-3β-ol	TS	MO?	–	
sterol[19]	TS	–	–	
sterols[20,21]	TS	PC?	–	
cholesterol	TS	B	–	
cholestanol (5α-cholestan-3β-ol)	TS	PC?	–	
desmosterol (cholesta-5,24-dien-3β-ol)	TS	PC?	–	
(22E)-(24ξ)-24-methylcholesta-5,22-dien-3β-ol	TS	D?	–	
(22E)-(24ξ)-24-methyl-5α-cholest-22-en-3β-ol	TS	D?	–	
sterols[22,23]	TS	D?	–	
(22E)-(24ξ)-24-ethylcholesta-5,22-dien-3β-ol	TS	D?	–	
(22E)-(24ξ)-24-ethyl-5α-cholest-22-en-3β-ol	TS	D?	–	
fucosterol	TS	D?	–	

Table 1. (Continued)

Taxonomic group, species, natural products extracts and secretions, or body parts	Chemical structure	Origin	Activity	References
(24ξ)-24-ethylcholest-5-en-3β-ol	TS	D?	–	
(24ξ)-24-ethyl-5α-cholest-3β-ol	TS	D?	–	
fucostanol	TS	D?	–	
methanolic extract	–	–	H	
acetate extract	–	–	H	
sterols + fatty acids	–	–	H	
sterols	TS	–	H	
fatty acids	FA	–	H	
no mycosporine-like amino acids	–	–	–	Karentz *et al.* (1991)
PH. VERTEBRATES, CL. OSTEICHTHYES (FISH)				
Unidentified larvae of an ice-fish species				
palythine	MA	–	UV	Karentz *et al.* (1991)
porphyra-334	MA	–	UV	
shinorine	MA	–	UV	
mycosporine-glycine	MA	–	UV	
mycosporine-glycine:valine	MA	B?, MO?	UV	
palythene	MA	–	UV	
Lycodichthys dearborni				
no mycosporine-like amino acids	–	–	–	McClintock & Karentz (1997)
Trematomus bernacchii				
shinorine	MA	–	UV	McClintock & Karentz (1997)
palythine	MA	–	UV	

Codes are described in the text. Superscript numbers refer to long names and are reported here.
Long-named compounds: [1]: (2′E,6′E,10′E,14′E)-2-(8′-one-3′,7′,11′,15′-tetramethylhexadeca-2′,6′,10′,14′-tetraenyl)-6-methyl-1,4-benzoquinone; [2]: (2′E,6′E,10′E,14′E)-2-(8′,9′-dione-15′-formyl-3′,7′,11′-trimethylhexadeca-2′,6′,10′,14′-tetraenyl)-6-methyl-1,4-benzoquinone; [3]: 2,4-dichloro-trans-1-chlorovinyl-1-methyl-5-methylene-cyclohexane; [4]: 2-chloro-4-bromo-trans-1-chlorovinyl-1-methyl-5-methylene-cyclohexane; [5]: 2-chloro-trans-1-chlorovinyl-1-methyl-5-chloromethyl-4-cyclohexane; [6]: 2,5-dichloro-4-bromo-trans-1-chlorovinyl-1-methyl-5-bromomethyl-cyclohexane; [7]: methyl (22R,24E)-22-acetoxy-3-oxocholesta-1,4,24-trien-26-oate; [8]: methyl (22E)-3-oxo-24-norcholesta-1,4,22-trien-26-oate; [9]: (22E)-11β-hydroxy-24-norcholesta-1,4,22-trien-3-one; [10]: (20S,22E)-20-hydroxy-24-norcholesta-1,4,22-trien-3-one; [11]: 2′-acetoxyglyceryl (5R,10R,13R)-labda-8-en-15-oate; [12]: 3′-acetoxyglyceryl (5R,10R,13R)-labda-8-en-15-oate; [13]: (20R)-cholesta-5,24-diene-2β,3α,21-triol 2,21-disulphate; [14]: (20R)-5α-cholest-24-ene-2β,3α,21-triol 3,21-disulphate; [15]: (20R)-cholesta-5,24-diene-2α,3α,4β,21-tetrol 3,21-disulphate; [16]: (20R)-cholest-5-ene-2β,3α,21-triol 3,21-disulphate; [17]: (20R,22E)-cholesta-5,22-diene-2β,3α,21-triol 3,21-disulphate; [18]: (20R)-cholest-5-ene-3α,4β,21-triol 3,21-disulphate; [19]: (22E)-24-nor-(24ξ)-24-methylcholesta-5,22-dien-3β-ol; [20]: trans-22-dehydrocholesterol:(22E)-cholesta-5,22-dien-3β-ol; [21]: trans-22-dehydrocholestanol:(22E)-5α-cholest-22-en-3β-ol; [22]: 24-methylenecholesterol:24-methylene-cholest-5-en-3β-ol; [23]: 24-methylenecholestanol:24-methylene-5α-cholestan-3β-ol.

Chemical structure

AA, aromatic aldehydes; BA, brominated alkaloids; CA, carotenoids; CR, chromenes; DA, discorhabdin alkaloids; DK, diketopiperazine alkaloids; DT, diterpenes; FA, fatty acids and glyceryl derivatives; GS, glycosides and saponins; HP, halogenated products; IC, inorganic compounds; MA, mycosporine-like amino acids; MT, monoterpenes; NA, pyridinic alkaloids; NC, nitrogenated compounds; PA, phenazine alkaloids; PK, polyketides; PT, phlorotannins; PY, pyridopyrrolopyrimidine alkaloids; QA, quinolinic alkaloids; QN, quinones; SF, stilbene flavonoids; SQ, sesquiterpenes; ST, sesterterpenes; TS, triterpenes, sterols and steroids; VH, volatile halogenated organic compounds.

Origin

A, algae; B, *de novo* biosynthesis; C, cnidarians; D, diet in general (not specified); E, epibionts; M, molluscs; MI, associated microorganisms; MO, modification of an existing compound; P, plankton; PC, precursor of cholesterol; S, sea water sequestration.

Activity

A, antiviral; AV_S, avoidance behavior to sympatric species (*Nacella concinna*); B, antibacterial activity (undetermined); B_A, antibacterial activity against allopatric species; B_S, antibacterial activity against sympatric species; C, cytotoxicity (undetermined); C_A, cytotoxicity to allopatric

species; C_S, cytotoxicity to sympatric species (usually gametes or spermatozoa of *Sterechinus neumayeri*); CE, inhibition of cholesteryl ester transfer protein; CR, toxicity to crayfish (*Procambarus clarkii*); D_S, deterrent to sympatric species (undetermined); D_A, deterrent to allopatric species (undetermined); D_{AF}, deterrent to allopatric fish; D_{AI}, deterrent to allopatric insects; $D_{SA,}$ deterrent to sympatric anemone *Isotealia antarctica*; D_{SC}, deterrent to sympatric crustaceans; D_{SF}, deterrent to sympatric fish; D_{SS}, deterrent to sympatric sea stars; E_S, arm retraction in sympatric sea stars; F, antifungal activity; FO_S, antifouling against sympatric diatoms; F_T, antifungal activity applied to TLC plate; G_S, defended against grazing by sympatric grazers (undetermined); G_{SM}, defended against grazing by sympatric molluscs; H, hemolytic activity; I, ichthyotoxicity (undetermined); I_A, ichthyotoxicity to allopatric species; I_S, ichthyotoxicity to sympatric species; IN, insecticidal activity; L, inhibitor for embryos and/or larvae (undetermined); L_A, inhibitor for embryos and/or larvae in allopatric sea urchin bioassay; L_S, inhibitor for embryos and/or larvae in sympatric sea urchin bioassay; M_S, molt inhibition in sympatric crustaceans; MI, mating induction (pheromone) between cells of complementary strains; P_{SU}, phagostimulation in sympatric sea urchin *Sterechinus neumayeri*; PP_S, physical protection from the sympatric anemone *Isotealia antarctica*; R_S, rightening response in sympatric sea stars; S, antitumor; T_S, tube-foot retraction in sympatric species; UV, UV radiation protectant; X, antioxidative activity; Y, antiyeast activity; YM_S, chemo-avoidance in Y-maze experiment to sympatric species.

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Antitumoural activity in Antarctic and sub-Antarctic benthic organisms

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Abstract: A prospecting search for antitumoural activity in polar benthic invertebrates was conducted on Antarctic and sub-Antarctic benthos in three different areas: Bouvet Island (sub-Antarctic), eastern Weddell Sea (Antarctica) and the South Shetland Islands (Antarctica). A total of 770 benthic invertebrate samples (corresponding to at least 290 different species) from 12 different phyla were assayed to establish their pharmacological potential against three human tumour cell lines (colorectal adenocarcinoma, lung carcinoma and breast adenocarcinoma). Bioassays resulted in 15 different species showing anticancer activity corresponding to five different phyla: Tunicata (5), Porifera (4), Cnidaria (3), Echinodermata (2) and Annelida (1). This appears to be the largest pharmacological study ever carried out in Antarctica and it shows very promising antitumoural activities in the Antarctic and sub-Antarctic benthos.

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Introduction

Modern marine pharmacology starts with the work by Bergmann & Feeney (1951) who studied the chemical activity of a Caribbean sponge and reported the first marine chemical compounds displaying antitumoural activity. This discovery shifted part of the attention from terrestrial organisms to marine organisms and expanded the research conducted in the marine environment to the pharmacological field. Since then, *c*. 21 500 structurally diverse natural products with different activities have been discovered from marine natural sources (MarinLit database - http://www.chem.canterbury.ac.nz/marinlit/marinlit.shtml, accessed 2009), many of them providing the basis for the investigation of new compounds for human use.

During the past 15 years, despite the promising results in the search for new natural drugs, there has been a decrease in the investment of large companies in natural products research (Lam 2007). Against this trend in downgrading the effort invested in exploring nature, the percentage of new leads currently and over the last century with direct or indirect origins in naturally occurring compounds is still very high, always exceeding in importance the synthetically derived compounds (Paterson & Anderson 2005, Mayer & Gustafson 2006, Harvey 2007, Lam 2007, Newman & Cragg 2007). As an example, an investigation reviewing the new drugs from 1981 to 2006 stated that only 22.2% of the total number of anticancer drugs were synthetic (Newman & Cragg 2007). Interestingly, several of these future anticancer leads are originally from marine-derived compounds currently in clinical and preclinical trials (Simmons *et al*. 2005, Mayer & Gustafson 2006).

Marine environments are considered to be the largest potential sources of biodiversity on Earth. Experts estimate that biodiversity in certain marine ecosystems is higher than in tropical rain forests (Haefner 2003). This is probably due to the fact that seas cover about 70% of the Earth surface as well as that life had its origin in the primordial oceans. Furthermore, seas harbour a greater proportion of phyla - some of them exclusively marine - when compared with terrestrial habitats (Clarke & Johnston 2003). This appears to be strongly correlated with the possibility of finding new compounds since when searching across phyla, the probability of finding unique classes of compounds is higher than when sampling different species within one phylum (Devlin 1997, Munro *et al*. 1999).

Many marine organisms are sessile and have no physical mechanism of defence. This could have led them to develop strategies to chemically defend themselves from predators and/or competitors (Amsler *et al*. 2001, Simmons *et al*. 2005). Evidence for the connection between marine biodiversity and the field of marine natural products are well documented. In 2005, 812 new marine compounds were described, an increase of *c*. 13% on the number of compounds reported the previous year. Interestingly, this increasing trend in the number of new marine chemical compounds has been steady since 1965 (Blunt *et al*. 2007).

Antarctica is amongst the regions that are likely to harbour many new and promising chemical products.

Evidence for chemical defensive compounds exist in many Antarctic invertebrate phyla (Blunt *et al*. 1990, McClintock & Baker 1997, Lebar *et al*. 2007, Avila *et al*. 2008). There are only a few examples in the Antarctic literature of interesting antitumoural/cytotoxic compounds in sponges (Perry *et al*. 1994, Trimurtulu *et al*. 1994, Fontana *et al*. 1999), cnidarians (Mellado *et al*. 2004, 2005), echinoderms (De Marino *et al*. 1998), bryozoans (Winston & Bernheimer 1986) and tunicates (Diyabalanage *et al*. 2006, Reyes *et al*. 2008). However, very few Antarctic specimens have been tested to date from the *c*. 4000 currently described invertebrate species in the Southern Ocean (Clarke & Johnston 2003, Avila *et al*. 2008). Since it was recently predicted that there must be more than 17 000 macrozoobenthic species inhabiting the entire Antarctic Shelf in the Southern Ocean (Gutt *et al*. 2004), it is reasonable to assume that high percentages of chemical activity may exist in these waters.

We collected and analysed 770 benthic animals (corresponding to at least 290 different species) from 12 different phyla in order to investigate the antitumoural potential of the invertebrates inhabiting the Southern Ocean and adjacent waters,. In this study we present the results of an extensive antitumoural pharmacological screening performed with marine invertebrates from the eastern Weddell Sea, the South Shetland Islands (Antarctica) and the Bouvet Island (sub-Antarctic) areas. The aim of this work is to highlight the antitumoural possibilities that these geographic areas can provide, considering macrozoobenthic organisms from a wide bathymetric range.

Material and methods

Study area and field sampling

Invertebrate benthic marine samples were collected on two different Antarctic cruises: ANTXXI/2 (November 2003–January 2004) and ECOQUIM-2 (January 2006). ANTXXI/2 expedition surveyed mostly the eastern Weddell Sea area (Antarctic) but also the vicinity of Bouvet Island (sub-Antarctic waters). Sampling was performed on board the RV *Polarstern*, from the Alfred Wegener Institute for Polar and Marine Research (Bremenhaven, Germany), using seven different sampling devices: Agassiz trawl, bongo net, bottom trawl, epibenthic sledge, giant box corer, plankton multinet and Rauschert dredge. A total of 55 stations were sampled ranging from 0–1866 m depth (see Arntz & Brey 2005 for details). Sorting of the samples was carried out on deck, and invertebrates from different phyla were selected based on the availability of the specimens, the required biomass for the pharmacological tests, and the *in situ* observations of feasible characters related to the presence of chemical natural products (i.e. absence of physical defences, particular colour and/or smell, absence of epibionts, …). Each sample corresponded to one invertebrate species and every specimen to be chemically analysed was immediately frozen to -20°C.

Table I. Taxonomic list of the species of this survey grouped by phylum. Number of samples used and geographic area in brackets: B = Bouvet Island, S = South Shetland Islands, W = Weddell Sea. + two species tested together, * antitumoral activity detected.

Phylum: Porifera	
Anoxycalyx ijimai	1(W)
Antho (*Acarnia*) *gaussiana*	1(W)
Astrophorida sp.	8(W)
Axinellidae sp.	1(S)
Bubaris sp.	1(B)
Cinachyra barbata	2(W), 1(S)
Cinachyra vertex	7(W), 1(S)
Cinachyra sp.	4(W)
Clathria (*Axosuberites*) *nidificata*	2(W)
Clathriidae sp.	1(W)
Dendrilla antarctica	1(S)
Hadromerida sp.	7(W)
Haplosclerida sp.	8(W)
Gellius sp.	1(W)
? *Gellius* sp.	1(W)
Homaxinella balfourensis	1(S)
Homaxinella cf. *balfourensis*	1(W)
Iophon unicorne	2(W)
Iophon cf. *unicorne*	4(W)
Iophon cf. *unicorne* or *Isodictya* sp.	1(W)
Iophon sp. 1	2(W), 3(S)
Iophon sp. 2	5(W)
Iophon sp. 3	1(W)
Isodictya bentarti	4(S)
Isodictya erinacea	5(W)
Isodictya kerguelenensis	4(W)
Isodictya lankesteri	1(W), 1(S)
Isodictya setifera	3(W)
Isodictya toxophila	4(W), 1(S)
Isodictya cf. *verrucosa*	1(W)
Isodictya sp. 1 & 2	1(W) of each
*Latrunculia biformis**	2(W)
*Latrunculia brevis**	2(W), 1(B)
Lissodendoryx (*Ectyodoryx*) *anacantha*	1(W)
Lissodendoryx (*Ectyodoryx*) cf. *ramilobosa*	1(W)
Mycale (*Mycale*) sp.	2(W)
Mycale (*Oxymycale*) *acerata*	5(W), 2(S)
Mycale (*Oxymycale*) cf. *acerata*	6(W)
Mycale sp.	2(W)
Myxilla (*Burtonanchora*) *asigmata*	1(W)
Myxilla (*Burtonanchora*) *lissostyla*	1(W), 2(S)
Myxilla (*Burtonanchora*) sp.	1(W)
Myxilla sp.	5(W)
Myxillidae sp.	8(W)
Phorbas glaberrima	1(W)
Poecilosclerida sp.	5(W)
Polymastia sp.	2(W)
Pyloderma latrunculioides	2(W)
Rossella cf. *antarctica*	3(W)
Rossella fibulata	3(W)
Rossella cf. *fibulata*	1(W)
Rossella nuda	1(W)
Rossella cf. *nuda*	2(W)
Rossella cf. *vanhoffeni*	4(W)
Rossella sp. 1*	1(W)
Rossella sp. 2*	1(W)
Rossella sp.	10(W), 2(B)
Scolymastra cf. *joubini*	6(W)
Sphaerotylus antarcticus	1(S)
Stylocordyla sp.	4(W), 2(S)

Table I. Continued

Tedania (*Tedaniopsis*) *charcoti*	1(W)
Tedania (*Tedaniopsis*) *oxeata*	3(W)
Tedania (*Tedaniopsis*) *tantula*	4(W), 2(B)
Tedania sp.	1(W), 1(B), 2(S)
Tetilla leptoderma	1(W)
Calcarea sp.	3(W)
Demospongiae sp.	2(W)
Hexactinellida sp.	18(W)
Porifera sp. 1–7	1(W) of each
Phylum: Cnidaria	
Ainigmaptilon cf. *antarcticum*	1(W)
Alcyonium grandis	2(W)
Alcyonium cf. *roseum*	1(W)
Antarctoscyphus elongatus	2(W)
Antarctoscyphus sp.	1(W)
Echinisis spicata	3(W)
Eudendrium sp.	1(W)
Fannyella aurora	5(W)
*Fannyella mawsoni**	1(W)
Fannyella rossii	2(W)
Hormathia sp.	2(S)
Isididae sp.	6(W)
Oswaldella billardi	3(W)
Primnoisis ambigua	1(W)
Primnoisis antarctica	9(W)
Staurotheca antarctica	1(W)
Staurotheca dichotoma	1(W)
Staurotheca glomulosa	1(W)
Staurotheca sp.	1(S)
Symplectoscyphus cf. *glacialis*	1(W)
Symplectoscyphus sp.	1(S)
Thauroprimnoa cf. *austasensis*	1(W)
Thouarella cf. *laxa*	2(W)
Thouarella cf. *minuta*	1(W)
Thouarella sp. 1	3(W)
Thouarella sp.2	17(W)
Thouarella sp. 2 + *Primnoisis antarctica*	1(W)
Thouarella sp. 2 + *Thouarella* sp. 5	1(W)
Thouarella sp. 3	1(W)
Thouarella sp. 4	4(W)
Thouarella sp. 5	12(W)
Thouarella sp. 6	5(W)
Thouarella sp. 7	2(W)
Thouarella sp. 8	1(W)
?*Thouarella* sp.	8(W)
Cnidarian sp. 1 & 2	1(W) of each
Cnidarian sp.	5(W)
Gorgonacea sp. 1 & 2*	1(W) of each
Hydrozoa sp.	4(W)
Unidentified cnidarians	14(W)
Phylum: Nemertea	
Parborlasia corrugatus	5(S)
Nemertean sp. 1 & 2	1(B) of each
Nemertean sp. 3–5	1(W) of each
Unidentified nemerteans	1(W)
Phylum: Priapulida	
Priapulus cf. *tuberculatospinosus*	4(S)
Phylum: Mollusca	
Austrodoris kerguelenensis	2(W), 1(S)
A. kerguelenensis (eggs)	1(W)
Lamellaria sp.	2(S)
Nacella concinna	2(S)

Table I. Continued

Philine sp.	3(S)
Thracia meridionalis	1(S)
Tritonia challengeriana	1(B)
Yoldia eightsi	2(S)
Solenogastres sp.	2(S)
Phylum: Annelida	
Aglaophamus trissophyllus	1(S)
Aglaophamus cf. *trissophyllus*	1(W)
Amphitrite sp.	1(S)
Antarctinoe spicoides	1(B)
Flabelligera mundata	1(B), 1(S)
Laetmonice sp.	1(B)
Pista sp.	1(S)
Polyeunoa cf. *laevis*	13(W)
Polynoidae sp. 1 & 2	1(B) of each
Terebellidae sp. 1*	1(W)
Phylum: Crustacea	
Glyptonotus cf. *antarcticus*	1(S)
Phylum: Bryozoa	
Alcyonidium flabelliforme	1(W)
Alcyonidium cf. *flabelliforme*	1(W)
Alcyonidium sp.	4(W), 1(S)
Austroflustra vulgaris	1(W), 1(B)
Bostrychopora dentata	13(W)
Camptoplites angustus	3(W)
Camptoplites bicornis	3(W)
Camptoplites tricornis	2(W), 1(S)
Carbasea curva	2(W)
Carbasea ovoidea	3(S)
Cellaria diversa	2(W), 2(S)
Cellaria incula	1(W)
Cellaria sp. 1 & 2	1(S) of each
Cellarinella nutti	8(W)
Cellarinella sp.	1(W)
Cornucopina polimorpha	1(B)
Dakariella dabrowni	4(W)
Himantozoum antarcticum	1(W), 2(S)
Hornera sp.	1(W)
Isoschizoporella secunda	2(W)
Isoschizoporella tricuspis	2(W)
Isoschizoporella sp.	1(W)
Isosecuriflustra tenuis	2(W)
Isosecuriflustra sp.	1(W)
Klugella echinata	2(W)
Melicerita obliqua	2(W)
Nematoflustra flagellata	5(W), 1(S)
Notoplites drygalskii	5(W)
Osthimosia curtioscula	5(W), 1(B)
Paracellaria wandeli	1(W)
Pemmatoporella marginata	1(W)
Reteporella antarctica	1(W)
Reteporella frigida	4(W)
Reteporella hippocrepis	1(W), 1(B)
Reteporella lepralioides	1(W)
Reteporella sp.	2(W)
Smittina antarctica	1(W)
Smittoidea albula	1(W)
Smittoidea sp.	1(W)
Staurotheca sp.	1(W)
Stystenopora contracta	2(W)
Bryozoa sp. 1	2(W)
Bryozoa sp. 2–10	1(W) of each

Table I. Continued

Unidentified bryozoans	13(W)
Phylum: Brachiopoda	
Brachiopoda sp.	1(W)
Liothyrella uva	1(S)
Phylum: Echinodermata	
Abatus sp.	1(S)
Abyssocucumis liouvillei	1(B)
Achlyonice violaecuspidata	2(W)
Cidaridae sp.	1(W)
Chiridota weddellensis	1(W)
Diplasterias cf. *brucei*	1(S)
Diplopteraster sp.	1(W)
Echinopsolus acanthocola	1(W)
Ekmocucumis steineri	3(W)
Ekmocucumis cf. *steineri*	1(W), 1(S)
Ekmocucumis sp. 1	2(W)
Ekmocucumis sp. 2	1(W)
Ekmocucumis sp. 3	2(W)
Encrinus liliformis	1(W)
Labidiaster annulatus	3(S)
Lysasterias hemiora	2(W)
Lysasterias sp.	1(S)
Macroptychaster sp.	1(W)
Odontaster validus	2(S)
Ophionotus victoriae	3(S)
Ophiurolepis sp. + *Iophon* cf. *unicorne*	1(W)
Ophiurolepis sp.	1(W)
Ophionotus victoriae	1(B)
Peniagone vignioini	1(W)
Porania antarctica	1(B)
Porania antarctica glabra	1(B)
Pseudostichopus villosus	1(W)
Psolus charcoti	7(W)
Psolus ephipiffer	1(W)
*Psolus paradubiosus**	1(B)
Psolus sp.	1(W)
Sterechinus neumayeri	3(S)
*Taeniogytus contortus**	4(W)
Crinoidea sp.	1(W)
Holothuroidea sp. 1	1(W)
Holothuroidea sp. 2	1(W), 1(B)
Holothuroidea sp. 3 & 4	1(B) of each
Holothuroidea sp. 5–7	1(W) of each
Ophiuroidea sp. 1	2(B)
Ophiuroidea sp. 2	1(B)
Phylum: Hemichordata	
Cephalodiscus cf. *nigrescens*	9(W)
Cephalodiscus sp. 1	9(W)
Cephalodiscus sp. 2	4(W)
Cephalodiscus sp. 3	3(W)
Cephalodiscus sp. 4	6(W)
Cephalodiscus sp. 5	7(W)
Cephalodiscus sp. 6	1(W)
Phylum: Tunicata	
Agnezia biscoei	1(S)
*Aplidium cyaneum**	2(W)
*Aplidium falklandicum**	2(W), 2(B), 1(S)
Aplidium millari	1(W), 1(S)
Ascidia challengeri	4(S)
Caenagnesia schmitti	1(S)
Cnemidiocarpa verrucosa	10(W), 4(S)

Table I. Continued

Corella eumyota	3(S)
Distaplia cylindrica	1(W)
Distaplia cf. *cylindrica*	1(W)
Molgula pedunculata	1(W), 4(S)
Molgula cf. *pedunculata*	1(W)
Paraeugyrioides arnbackae	1(W)
*Polysyncraton trivolutum**	3(S)
Pyura obesa	2(S)
Styela wandeli	1(S)
Synoicum adareanum	9(W), 3(S)
Synoicum cf. *adareanum*	1(W)
*Tylobranchion speciosum**	2(S)
Ascidiacea sp. 1*	1(W)
Ascidiacea sp. 2	2(W)
Ascidiacea sp. 3	3(W)
Ascidiacea sp. 4 & 5	1(W) of each
Ascidiacea sp. 6	3(W)
Ascidiacea sp. 7	1(W)
Ascidiacea sp. 8	3(W)
Ascidiacea sp.9	6(W)
Ascidiacea sp. 10	2(W)
Ascidiacea sp. 11	4(W)
Ascidiacea sp. 12	1(W)
Ascidiacea sp. 13	12(W)
Ascidiacea sp. 14–19	1(W) of each

Some individuals from each of the corresponding samples were fixed for later taxonomic identification in the laboratory by specialists on each of the different phyla. In addition, images of live animals were taken when possible for the same purpose.

The ECOQUIM-2 cruise was carried out around Deception Island, Livingston Island and their vicinities (South Shetland Islands) on board the Spanish RV *BIO-Hespérides*. Two different sampling devices (Agassiz trawl and rocky dredge) were used to obtain the samples at depths from 25–215 m. Dredging range in all stations was not higher than a few metres except for a station where it started at 65 m and finished at 215 m depth. Sorting was performed as described above. Also in this case, specimens to be chemically analysed were frozen at -20°C and the procedure for the later identification of animals with the fixed material was the same as described before.

In vitro *tests*

All frozen samples from invertebrates collected from both expeditions were analysed by the biopharmaceutical company PharmaMar SA to search for antitumoural activity. Two grammes of frozen samples were extracted in distilled water using an ultraturrax homogenizer. The aqueous extract was decanted and stored at -30°C. The remaining solid pellet was dried using a speed-vac centrifuge and extracted in 1:1 dichloromethane/methanol. The organic extract was also decanted and stored at -30°C. To analyse the putative pharmacological potential of the extracts, equal

Table II. Percentage of cell growth for the active samples against three human tumor cell lines (HT-29, A-549 and MDA-MB 231) at three concentrations (50, 15 and 5 $\mu g\,ml^{-1}$)

(Phylum[a])/Active species name	Station code [b]	Fraction[c]	Tumour cell lines		
			HT-29*	A-549*	MDA-MB 231*
			50/15/5	50/15/5	50/15/5
(POR) *Latrunculia biformis*	PS65/259-1	A	-86/-80/-16	-74/-83/71	-88/-48/-18
		DM	-90/-45/24	-90/-34/89	-88/-53/67
(POR) *Latrunculia biformis*	PS65/274-1	A	-78/3/99	-84/80/100	-91/-35/78
		DM	-86/-61/-35	-81/-87/-42	-86/-71/-56
(POR) *Latrunculia brevis*	PS65/019-1	A	-83/-29/13	-87/-65/107	-87/-37/35
		DM	-81/-79/-43	-85/-85/-36	-83/-76/-59
(POR) *Latrunculia brevis*	PS65/253-1	A	-89/-66/58	-90/-66/29	-87/-76/47
		DM	-84/-74/-41	-79/-86/44	-87/-68/-61
(POR) *Latrunculia brevis*	PS65/265-1	A	-88/-82/-43	-66/-83/-82	-92/-90/-77
		DM	-84/-73/-30	-76/-85/80	-75/-81/-21
(POR) *Rossella* sp. 1	PS65/253-1	DM	-76/-81/-73	-12/-1/3	-14/-30/-30
(POR) *Rossella* sp. 2	PS65/253-1	DM	-69/-75/-68	-4/-1/1	-15/-21/-21
(CNI) *Fannyella mawsoni*	PS65/232-1	DM	-88/-49/65	-83/-60/89	-97/-75/93
(CNI) Gorgonacea sp. 1	PS65/121-1	A	-96/-26/-8	-96/-14/23	-91/-72/-69
		DM	-92/-11/42	-90/21/75	-91/2/66
(CNI) Gorgonacea sp. 2	PS65/166-1	A	-94/2/29	-89/33/64	-93/18/57
(ANN) Terebellidae sp. 1	PS65/166-1	DM	-58/3/134	-72/71/115	-75/-18/123
(ECH) *Psolus paradubiosus*	PS65/020-1	A	-90/-66/58	-90/-66/29	-87/-76/47
		DM	-83/49/89	-85/11/97	-83/-5/113
(ECH) *Taenyogytus contortus*	PS65/265-1	A	-90/-51/28	-87/18/4	-90/11/57
(TUN) *Aplidium cyaneum*	PS65/148-1	A	-58/-48/42	8/12/65	-62/-1/11
		DM	-45/-39/-19	-4/19/22	-70/-57/-5
(TUN) *Aplidium cyaneum*	PS65/280-1	A	-68/-55/50	1/5/64	-30/-10/21
		DM	-59/-27/3	6/15/78	-65/-25/4
(TUN) *Aplidium falklandicum*	AGT-6	DM	-29/2/37	-80/-60/21	-64/-71/11
(TUN) *Polysyncraton trivolutum*	AGT-5	A	-54/-32/25	-47/-34/11	-89/-44/18
(TUN) *Tylobranchion speciosum*	AGT-5	A	-45/-30/-3	-59/-36/-15	-83/-19/2
(TUN) Ascidiacea sp. 1	PS65/166-1	DM	-80/18/121	-88/85/88	-90/-3/113

[a] ANN = Annelida, CNI = Cnidaria, ECH = Echinodermata, POR = Porifera, TUN = Tunicata.
[b] See Fig. 4 for details.
[c] A = aqueous extract, DM = dichloromethane/methanol extract.
*active extracts are considered when the percentage of cell growth < 50% at least at two concentrations in one of the cell lines. Positive values, in the range between +100 and 0, represent samples with no activity or some degree of cytostatic activity. Negative values, in the range between 0 and -100, represent samples with cytotoxic activity (net cell death).

"weight/volume" amount of each tissue homogenate was assayed *in vitro*, using three different final concentrations (50, 15 and 5 $\mu g\,ml^{-1}$), against the following human tumour cell lines: HT-29 (ATCC HTB-38) colorectal adenocarcinoma; A-549 (ATCC CCL 185) lung carcinoma; and MDA-MB 231 (ATCC HTB-26) breast adenocarcinoma. Briefly, cells were

Table III. Total number of samples (N spls.) and species (N sps.) analysed by phylum in each surveyed area with the number of active species in brackets

Geographic area		Phylum[a]										
		POR	CNI	BRY	TUN	ECH	HEM	ANN	MOL	NEM	OTH*	Total
Bouvet Island	N spls.	7	-	4	2	11	-	5	1	2	-	32
	N sps.	5(1)	-	4	1	10(1)	-	5	1	2	-	28(2)
Weddell Sea	N spls.	202	128	116	76	42	39	15	3	4	1	626
	N sps.	70(4)	39(3)	49	30(2)	27(1)	7	3(1)	2	4	1	232(11)
South Shetlands	N spls.	23	4	12	30	15	-	4	13	5	6	112
	N sps.	14	3	8	13(3)	8	-	4	7	1	3	61(3)
Total	N spls.	232	132	132	108	68	39	24	17	11	7	770
	N sps.[b]	76(4)	42(3)	53	38(5)	43(2)	7	11(1)	9	7	4	290(15)

[a] ANN = Annelida, BRY = Bryozoa, CNI = Cnidaria, ECH = Echinodermata, HEM = Hemichordata, MOL = Mollusca, NEM = Nemertina, OTH = others, POR = Porifera, TUN = Tunicata
*This category includes the following phyla: Priapulida, Brachiopoda and Arthropoda
[b] The total number of species for every phylum does not correspond to the sum of species for the three geographic areas since some species are shared in the different areas

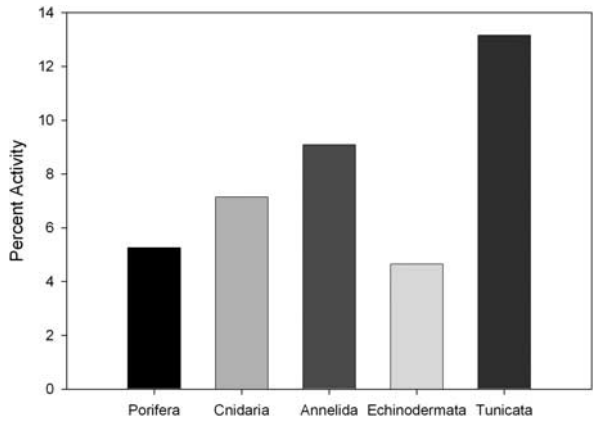

Fig. 1. Percentages of antitumoural activity (number of species with antitumoural activity respect to the total of species tested) within each active phyla.

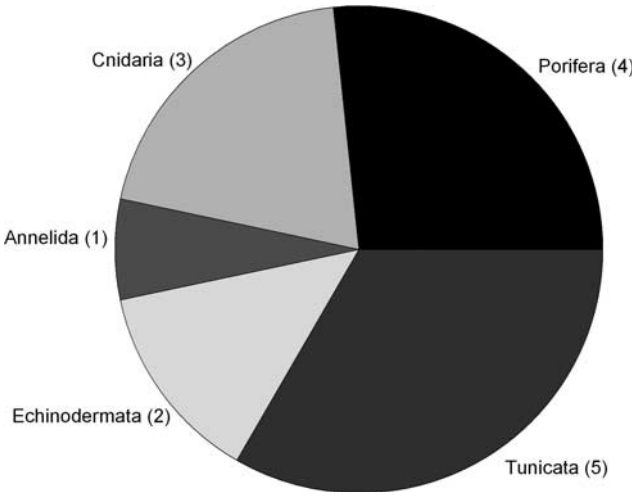

Fig. 3. Relative proportions of antitumoural activity for each active phylum considering species number.

seeded in 96-well microtitre plates and allowed to stand for 24 h in a drug-free medium before treatment with vehicle alone or test extracts for 72 h period. For viability quantification, a colorimetric assay (sulphurhodamine B, SRB) was used. Cells were washed twice with PBS, fixed for 15 min in 1% glutaraldehyde solution, rinsed twice in PBS, and stained in 0.4% SRB solution for 30 min at room temperature. Cells were then rinsed several times with 1% acetic acid solution and air-dried. SRB was then extracted in 10 mM trizma base solution and the absorbance measured at 490 nm. The cytostatic or cytotoxic effect of the compounds was estimated applying the algorithm developed by the American National Cancer Institute (NCI). Being Tz the number of control cells at time zero, C the number of cells in control wells at 72 h, and T the number of cells in the test wells at 72 h then: if $Tz < T < C$ (no effect or growth inhibition), cell survival is $100 \times ([T - Tz]/[C - Tz])$; if $T < Tz$ (net cell killing), cell survival is $100 \times ([T - Tz]/Tz)$. Three dose response parameters were calculated for each experimental agent: i) GI50, or compound concentration that produces 50% inhibition on cell growth compared to control cells, ii) TGI, or compound concentration that produces total growth inhibition as compared to control cells, iii) LC50, or compound concentration that produces 50% net cell killing. GI50 is used as reference value. Results represented the mean of at least three independent experiments.

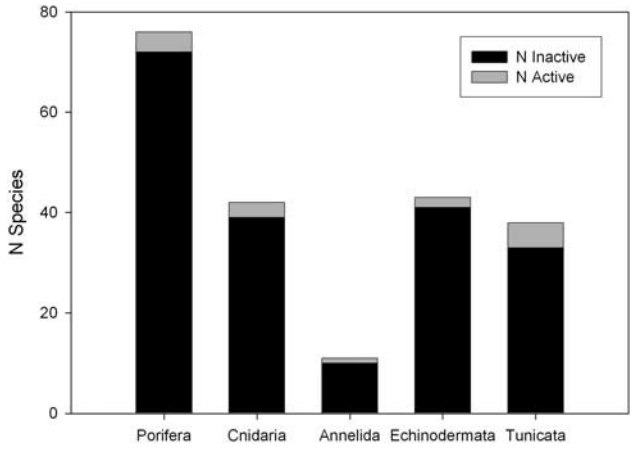

Fig. 2. Number of active versus inactive species in phyla presenting activity (N = number of species).

Results

A total of 770 samples (corresponding to at least 290 different species) were collected, 658 from the ANTXXI/2 expedition and 112 from the ECOQUIM-2 cruise. To date, the number of species identified is 260 for the ANTXXI/2 expedition and 61 for the ECOQUIM-2 cruise. A taxonomic list of these species and the number of samples for any given species is reported in Table I. Samples consisted of benthic invertebrates belonging to 12 different phyla: Porifera, Cnidaria, Nemertina, Priapulida, Mollusca, Annelida, Arthropoda, Bryozoa, Brachiopoda, Echinodermata, Hemichordata and Tunicata. Results from the *in vitro* tests carried out against the three different human tumour cell lines indicated that 19 samples (corresponding to 15 different species) presented relevant antitumoural activity (Tables II & III). This represents the 2.47% of the total number of tested samples, and 5.17% when considering the number of assayed species (290) versus the number of active species (15). In every active sample detected in the study, the three tumour cell lines tested presented a similar behaviour, in the sense that a similar effect for every tumour cell line was detected, except for the tunicate *Aplidium cyaneum*. In this specific case, the antitumoural effects of the tested fractions were mild for A-549 lung carcinoma and strong for the other two tumour cell lines (HT-29 colorectal

Table IV. Data from the stations where active samples were collected.

Geographic area	Station code	Coordinates		Gear[a]	Depth (m)	(Phylum[b])	Active species name
Bouvet Island	PS65/019-1	54°30.01'S	003°13.97'E	AT	259.7	(POR)	*Latrunculia brevis*
Bouvet Island	PS65/020-1	54°36.95'S	003°12.42'E	AT	553.4	(ECH)	*Psolus paradubiosus*
Weddell Sea	PS65/121-1	70°50.08'S	010°34.76'W	AT	274.0	(CNI)	Gorgonacea sp. 1
Weddell Sea	PS65/148-1	70°56.67'S	010°32.05'W	BT	302.4	(TUN)	*Aplidium cyaneum*
Weddell Sea	PS65/166-1	70°56.83'S	010°32.61'W	BT	338.0	(CNI)	Gorgonacea sp. 2,
						(ANN)	Terebellidae sp. 1
						(TUN)	Ascidiacea sp. 1
Weddell Sea	PS65/232-1	71°18.61'S	013°56.12'W	ES	910.0	(CNI)	*Fannyella mawsoni*
Weddell Sea	PS65/253-1	71°04.30'S	011°33.92'W	BT	308.8	(POR)	*Latrunculia brevis,*
							Rossella sp. 1 & sp. 2
Weddell Sea	PS65/259-1	70°57.00'S	010°33.02'W	BT	332.8	(POR)	*Latrunculia biformis*
Weddell Sea	PS65/265-1	70°52.75'S	010°51.24'W	BT	294.8	(POR)	*Latrunculia brevis,*
						(ECH)	*Taenyogytus contortus*
Weddell Sea	PS65/274-1	70°52.16'S	010°43.69'W	BT	290.8	(POR)	*Latrunculia biformis*
Weddell Sea	PS65/280-1	71°07.15'S	011°26.23'W	AT	228.4	(TUN)	*Aplidium cyaneum*
South Shetlands	AGT-5	62°40.56'S	60°42.41'W	AT	25.1	(TUN)	*Polysyncraton trivolutum*,
							Tylobranchion speciosum
South Shetlands	AGT-6	62°43.12'S	60°43.68'W	RD	94.9	(TUN)	*Aplidium falklandicum*

[a] AT = Agassiz trawl, BT = Bottom trawl, ES = Epibenthic sledge, RD = Rocky dredge.
[b] ANN = Annelida, CNI = Cnidaria, ECH = Echinodermata, POR = Porifera, TUN = Tunicata.

adenocarcinoma and MDA-MB 231 breast adenocarcinoma). For the remaining cases, there was no significant difference among the results in the different tumour cell lines assays for every analysed sample (Table II). Antitumour activity was detected in both the aqueous and organic extracts in some of the cases (five out of the 15 species showed activity in both fractions) indicating a distribution of the active metabolites between both extracts, probably due to medium polarity compounds being responsible for the bioactivity. In the rest of the cases, the bioactivity was found only in one of the fractions, most probably indicating that the antitumour properties are due to the presence of very polar compounds (activity found only in aqueous extracts) or non-polar compounds (activity found in organic extracts) (Table II).

Samples with antitumoural activity belonged to only five phyla: Porifera, Cnidaria, Annelida, Echinodermata and Tunicata. Considering just the number of species, Tunicata is the group with the higher relative percentage of activity (13.16%), followed by Annelida with more than 9% activity. The last three phyla, in decreasing order of antitumoural activity, are Cnidaria, Porifera and Echinodermata with 7.14%, 5.26% and 4.65% activity, respectively (Fig. 1). A comparison of the relative number of active versus inactive species is shown for each phyla possessing antitumoural activity in Fig. 2. In the analysis of activity by phyla, Tunicata (with five species) contains the largest number of active species, representing more than 33% of the total activity observed in the whole screening. Porifera reaches more than 25% of the activity observed with four active species, while Cnidaria and Echinodermata are the following groups in order of importance, with three and two active species, respectively. Finally, just one Annelid species was found to show antitumoural activity (Table III; Fig. 3).

Bouvet Island (*sub-Antarctica*)

The four sampling stations studied from the Bouvet Island area yielded 28 different species (32 samples when considering the replicates). Specimens analysed were from seven different phyla (Porifera, Nemertina, Mollusca, Annelida, Bryozoa, Echinodermata and Tunicata) with the Echinodermata the most represented phylum in our survey, with 10 species. The rest of phyla presented five or less species each (Table III). Antitumoural activity was observed in two species: one holothurian (*Psolus paradubiosus*) and one sponge (*Latrunculia brevis*). Both samples were collected using Agassiz trawl at depths of 553 and 259 m, respectively (Table IV; Fig. 4). About 50% of the samples analysed in this area were collected at *c*. 260 m depth. The rest of the samples were collected at three different depths, with the highest percentage of samples concentrated at depths around 375 m and 550 m (Fig. 5).

Eastern Weddell Sea (*Antarctica*)

The eastern Weddell Sea was the largest area sampled, as well as being the most surveyed region. A total of 232 different species (626 samples when considering the replicates) were collected from 51 different sampling stations. Specimens from ten phyla were tested (Porifera, Cnidaria, Nemertina, Mollusca, Annelida, Bryozoa, Brachiopoda, Echinodermata, Hemichordata, and Tunicata). From these, Porifera (4 active species), Cnidaria (3), Tunicata (2), Echinodermata (1) and Polychaeta (1) presented antitumoural activity (Table III).

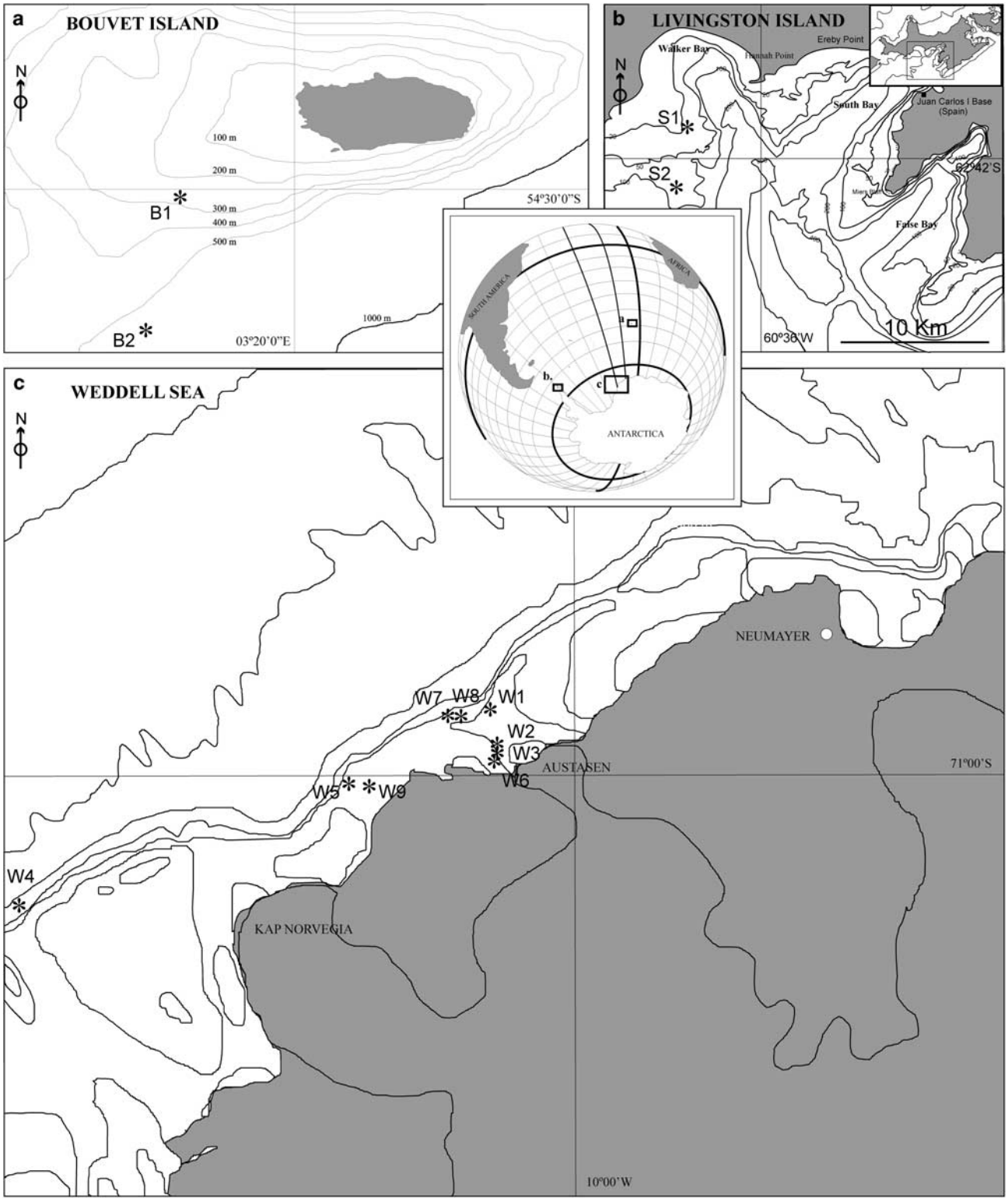

Fig. 4. Map representing the stations that presented active samples at the three different surveyed areas: **a.** Bouvet Island (B1-2), **b.** South Shetland Islands-Livingston Island (S1-2), and **c.** eastern Weddell Sea (W1-9).

Although the bathymetry of stations ranged from 0 to more than 1800 m, most of the active samples were collected from depths *c*. 300 m. Only in one deeper station, more than 900 m deep, the cnidarian *Fannyella mawsoni* presented antitumoral activity (Table IV; Fig. 4). Most samples in this area (> 80%) were collected at depths ranging between 200–400 m (Fig. 5).

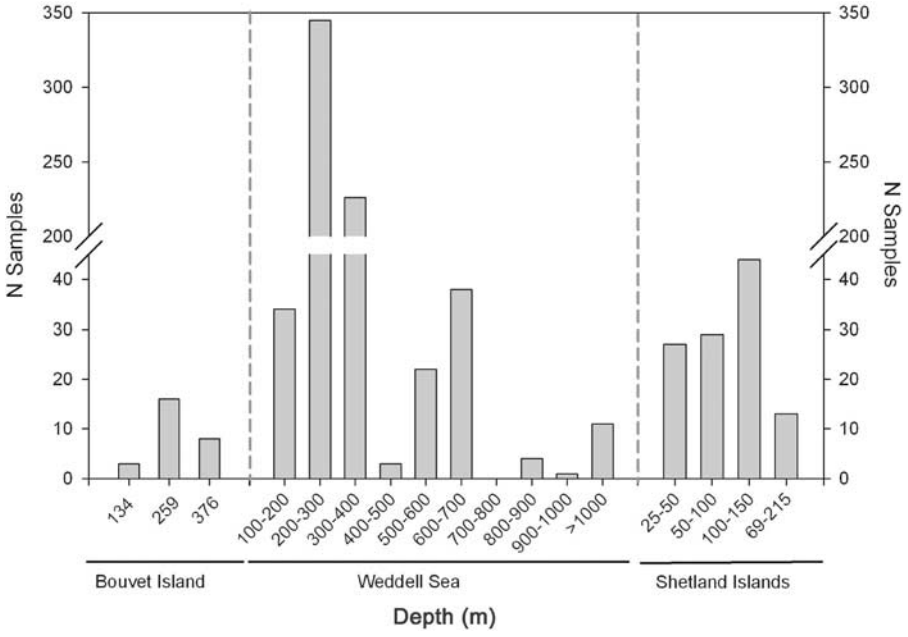

Fig. 5. Number of samples analysed in the stations from the Bouvet Island, the Weddell Sea and the South Shetland Islands area at different depths.

South Shetland Islands (*Antarctica*)

Sampling in the South Shetland Islands yielded 61 different species (112 samples when considering the replicates) belonging to 11 phyla (Porifera, Cnidaria, Nemertina, Priapulida, Mollusca, Annelida, Arthropoda, Bryozoa, Brachiopoda, Echinodermata and Tunicata). A total of 13 sampling stations, ranging from a few metres to more than 200 m depth were surveyed. Only two stations - both in the vicinity of Livingston Island - presented organisms with antitumoural activity; in particular three different tunicate species: *Polysyncraton trivolutum*, *Tylobranchion speciosum* and *Aplidium falklandicum*. These sampling stations were at relatively shallow depths, in the very first 100 m depth (Table IV; Fig. 4). Most of the samples from the South Shetland Islands area were obtained from the first 150 m depth. Only 13 samples were collected from a deeper station that ranged from 69–215 m deep (Fig. 5).

Discussion

The present work is, to the best of our knowledge, the largest pharmacological study ever carried out on Antarctic and sub-Antarctic marine benthic invertebrates. Different studies conducted on sessile marine invertebrates from other areas of the world have proved these organisms to have the highest probability of providing compounds with cytotoxic properties (Schmitz *et al*. 1993, Munro *et al*. 1999). In this sense, our results from the Antarctic and sub-Antarctic areas are consistent with this general trend, since the majority of the pharmacologically active hits (80%) correspond to strict sessile invertebrates belonging to the phyla Porifera, Cnidaria and Tunicata.

There is only one previous study in a comparable geographic area dealing with pharmacological activity in marine invertebrates. Blunt *et al*. (1990) investigated a different region (Ross Sea) and restricted their bathymetry range of study to shallow waters (SCUBA diving). Although in their analysis they considered jointly the incidence of antiviral and cytotoxic activity of the different Antarctic phyla, and the number of surveyed benthic species was relatively small (59), it is remarkable that the main active phyla are coincident with our results.

In our survey, two main geographical areas were sampled: sub-Antarctic (Bouvet Island) and Antarctic (eastern Weddell Sea and South Shetland Islands). In the sub-Antarctic area, two different species out of the 28 analysed (7.4%) presented antitumoural properties. In contrast, the percentage of active samples in the Antarctic area reached 5.1% (14 active species out of the 277 species analysed). However, these differences cannot lead us to hypothesize any trend, since there is a significant difference in the sampling effort when comparing both areas. Further analysis should be conducted in order to compare, from the pharmacological point of view, Bouvet Island with the rest of Antarctic samples. This could be especially relevant since this island, situated just south of the Polar Front, is a transitional area considered to be a linking point between the High Antarctic and the adjacent temperate Atlantic ecosystems (Arntz *et al*. 2006).

As stated above, the majority of active species (*c*. 90%) came from the Antarctic area (eastern Weddell Sea and the South Shetland Islands) and this area included also the largest number of bioassayed species (> 90%). The Antarctic benthos is commonly characterized by presenting a very rich and diverse community of sessile suspension feeders (Arntz *et al*. 1994, Orejas *et al*. 2000, Clarke & Johnston 2003).

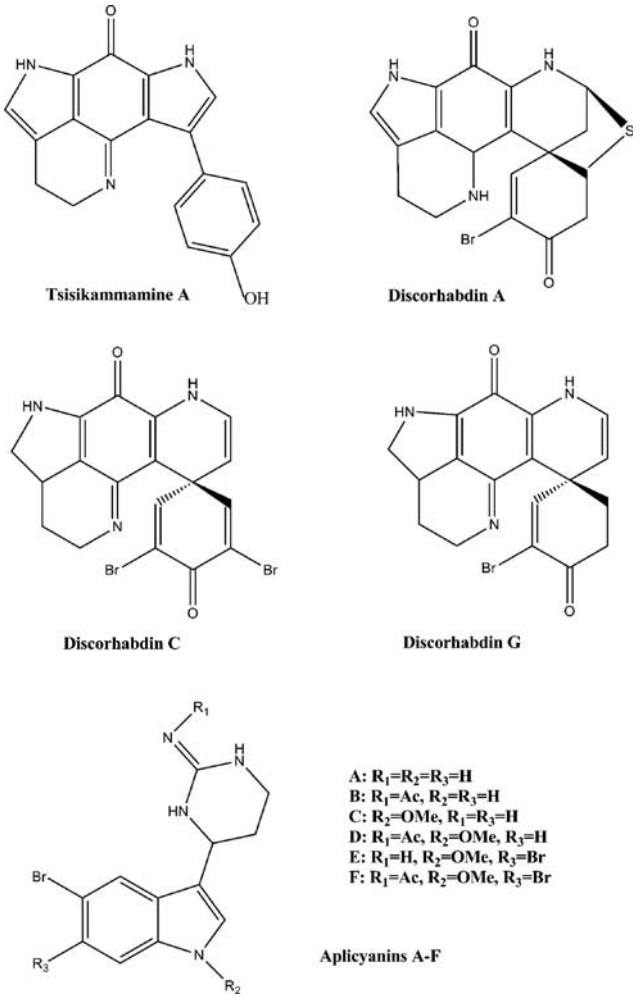

Fig. 6. Chemical compounds found in the samples analysed in the present survey.

This community has been quite well surveyed in our case, despite the fact that our sampling was qualitative; the Porifera, Cnidaria, Bryozoa and Tunicata in our study represent > 70% of the whole survey. The environment, below the area of ice scouring, believed to be very old and stable and with a high degree of physical environment predictability, is postulated to be ruled by biological factors (Dayton *et al*. 1974). Accordingly, it could be expected that marine benthic Antarctic invertebrates (mostly sessile) develop chemical means to defend themselves from predation, inhibition of settling, and prevention of fouling and overgrowth of other species (Amsler *et al*. 2001, Avila *et al*. 2008). These chemical compounds could be hypothesized to be involved in the antitumoural activity described here.

In our study, Porifera yielded the highest number of pharmacological hits (seven), although it is also true that it was the group with the highest percentage of tested samples (*c*. 30% of our samples were sponges) and the highest percentage of tested species (*c*. 30%) (Table II & III; Fig. 2). Among the species found to possess antitumoural activity, there are two species from the genus *Latrunculia* (*L. biformis* and *L. brevis*). Analysis of the biochemical composition of one of our *L. brevis* specimens (Table IV, PS/65-265-1 station code) confirmed the occurrence of discorhabdins A, C and G and also tsitsikammamine A (Fig. 6; unpublished results from the authors), an alkaloid firstly described in a South African latrunculid sponge (Hooper *et al*. 1996). Similarly, specimens of *L. brevis* with its origin in New Zealand and Argentinean waters yielded some antitumoural alkaloids, discorhabdins A, D, L and I (Perry *et al*. 1988, Reyes *et al*. 2004). In addition, an Antarctic congeneric species, *Latrunculia apicalis*, was found to possess discorhabdin G located preferentially in the outermost layer of the sponge, where it could cause deterrence against predatory sea stars (Furrow *et al*. 2003). Apart from the latrunculids, two specimens of the genus *Rossella* (*Rossella* sp. 1 and sp. 2), still under taxonomic study, also displayed antitumoural activity. To the best of our knowledge, this is the first time that any specimen from the class Hexactinellida (glass sponges provided with long siliceous spicules that can act as a physical defence) is reported to show antitumoural activity. Porifera are one of the major targets of chemical investigations in marine environments due to their high biomass and their well-documented ability to possess interesting natural products (McClintock *et al*. 2005, Blunt *et al*. 2007, Avila *et al*. 2008, Peters *et al*. 2009). There are several examples in the literature providing evidence of pharmacologically active compounds from sponges presenting relevant antitumoural effects from tropical (e.g. Bergmann & Feeney 1951) and temperate waters (e.g. Burres & Clement 1989). As shown in this work, a similar pattern can be expected in the Southern Ocean since this group of invertebrates constitutes a basic element in the benthic ecosystem, both in terms of abundance and in number of described species (Orejas *et al*. 2000, Clarke & Johnston 2003). Actually, Antarctic sponges represent the group of invertebrates with the highest number of natural compounds described to date and have been extensively studied in terms of chemical compounds, when compared with the rest of invertebrate groups (McClintock *et al*. 2005, Avila *et al*. 2008). Interestingly, some Antarctic sponges have been previously found to present antitumoural activity, with variolin-B, a new alkaloid described from *Kirkpatrickia variolosa*, (Perry *et al*. 1994, Trimurtulu *et al*. 1994), and flabellatene A, a new antiproliferative cembrane isolated from *Lissodendoryx flabellata* (Fontana *et al*. 1999), the most remarkable ones.

In our pool of tested cnidarians three different species were active against the tumour cell lines assayed. The Gorgonacea *Fannyella mawsoni* is reported for the first time as possessing interesting pharmacological activity. The other two cnidarians (order Gorgonacea) presenting activity are still under taxonomic study. As in sponges, cnidarians also play an important ecological role in Antarctic marine benthic ecosystems (Orejas *et al*. 2000). Although very few species have been studied so far from

the chemical point of view (Avila *et al*. 2008), there are examples of two different species pertaining to the orders Gorgonacea and Alcyonacea with compounds presenting cytotoxic activity against human tumour cell lines (Mellado *et al*. 2004, 2005). Cnidarians are one of the major sources of marine natural products in other geographical areas as well (Schmitz *et al*. 1993, Munro *et al*. 1999).

After the results of our survey, Antarctic Tunicata represent a much more important potential source for pharmacological purposes than previously. In fact, this is the group with the highest percentage of activity in our tests (Fig. 1). Among these interesting results there is one that stands out from the rest: aplicyanins A–F (Fig. 6), new compounds from the ascidian *Aplidium cyaneum* yielding strong antitumoural activity (Reyes *et al*. 2008). Other examples with a similar relevance such as didemnin B (Rinehart *et al*. 1981) or Ecteinascidin (Rinehart *et al*. 1990), both derived from tropical ascidians, highlight the importance of these animals in the context of the marine drug discovery field. In our study, two of the tunicates found to be active against tumour cell lines, belong to the genus *Aplidium* (*A. cyaneum* and *A. falklandicum*). This genus has been widely recognized as a source of antitumoural compounds in different areas of the world (McKee *et al*. 1998, Le Tourneau *et al*. 2007). Another species to highlight is *Polysyncraton trivolutum*, from the family Didemnidae. This family is also recognized as a source of chemical products with potent biological properties (e.g. Rinehart *et al*. 1981) and a congeneric species from the Fiji Islands, *P. lithostrotum*, also displays relevant antitumoural effects (McDonald *et al*. 1996). On the other hand, this is the first time that the ascidian *Tylobrachion speciosum* is reported as a source for antitumoural activity. Tunicates, together with bryozoans and the above-mentioned sponges and cnidarians, all of them being sessile suspension feeders, conform the basis of the Antarctic benthic ecosystems (Orejas *et al*. 2000). Nevertheless, little chemical work has been conducted to date in tunicates from the Southern Ocean (Avila *et al*. 2008). It is also worth mentioning the antitumoural activity described in the Antarctic ascidian *Synoicum adareanum* (Diyabalanage *et al*. 2006).

Only bryozoans seem not to follow the suggestion that sessile marine invertebrates have a high probability of showing cytotoxic activities (Schmitz *et al*. 1993, Munro *et al*. 1999), since none of the 53 species assayed here showed any activity (this group was the second in number of tested species and also the second in number of samples analysed; see Table III). Although they are very speciose and abundant in Antarctic waters (Orejas *et al*. 2000, Clarke & Johnston 2003), they have been little studied from a chemical perspective (Avila *et al*. 2008) and, to the best of our knowledge, there is only one reported case of Antarctic cytotoxic activity (haemolytic activity against erythrocytes from man and dog) in the bryozoan *Carbasea curva* (Winston & Bernheimer 1986). Nevertheless, there are examples from other marine geographical areas such as the cosmopolitan *Bugula neritina*, which possesses bryostatin 1, one of the strongest naturally derived antitumoural compounds known to date (Pettit *et al*. 1982).

Non-sessile invertebrates are usually considered less likely groups in which to find cytotoxic compounds (Munro *et al*. 1987). However, in our survey, there were some vagile invertebrates showing interesting antitumoural activity. Two echinoderm species (holothurians), *Psolus paradubiosus* and *Taenyogytus contortus*, presented antitumoural activity. These are not exceptional cases for these slow and soft-bodied organisms since echinoderms have been reported to have a remarkable incidence in cytotoxic activity in other areas of the world (Schmitz *et al*. 1993, Munro *et al*. 1999). This highly diverse group of Antarctic invertebrates (Clarke & Johnston 2003) has also been extensively studied for their chemical ecology (Amsler *et al*. 2001, Avila *et al*. 2008) yielding a large number of natural products. Among them, at least one of the species analysed (an unidentified sea star from the family Asteriidae) has been observed to possess compounds with cytotoxic activity against human carcinoma cells (De Marino *et al*. 1998).

Annelids are the other group of invertebrates presenting antitumoural activity in this study. The active species belongs to the family Terebellidae. Terebellids are sessile deposit feeders that live attached to the substrate protected by a tube. We know of only one precedent of an annelid with antitumoural activity: the case of *Terebella* sp. (also from the family Terebellidae) showing a mild antitumour activity against P388 murine leukaemia cell line (Battershill *et al*. 1989). As reported for echinoderms, annelids also represent a high percentage of the invertebrate biodiversity in Antarctica; actually, they are the most speciose group in the Antarctic benthos (Clarke & Johnston 2003). However, they have been barely studied from the chemical point of view (Lebar *et al*. 2007, Avila *et al*. 2008), and it seems probable that further positive results may appear for this group.

Other phyla have also displayed antitumoural activity in other marine areas. Examples such as dolastatins in molluscs (Pettit *et al*. 1987) or cephalostatins in pterobranchs (Pettit *et al*. 1994) are just two of the many examples that can be found in the literature. Thus, we may hypothesize that the chances of finding interesting active chemicals in these and other groups in future analyses in Antarctica are reasonably high.

Sampling depth is also an important variable to take into account when bioprospecting. It was mentioned that there seems to be a greater probablility of finding cytotoxicity in animals at depths greater than 30 m (Munro *et al*. 1987). In our survey, samples showing antitumoural activity were predominately found in depths ranging from 250–500 m in the eastern Weddell Sea area and the Bouvet Island vicinities, and *c.* 100 m depth in the South Shetland Islands area (Fig. 5). Since our study was qualitative and the sampling

effort was clearly biased to some depths (Fig. 5), in our case no further inferences can be drawn when evaluating depth as a factor related to bioactivity.

As explained above, the collection of our samples was supported by a qualitative sampling design in order to maximize the return for the effort invested. Although the sampling effort was, therefore, clearly biased to some particular groups, we believe that results in terms of pharmacological activity are similar to what could be expected after a quantitative sampling, since samples tested were, in general, the most representative organisms in each station. In a similar way, the different number of hits registered in the three major areas studied are proportionally correlated with the sampling effort (eastern Weddell Sea > South Shetland Islands > Bouvet Island); this leads us to hypothesize that the study area was not a decisive factor in our survey.

In our study, two samples identified as the same species (*Latrunculia brevis*) had a similar pharmacological behaviour although they were collected in different areas - Bouvet Island and eastern Weddell Sea (Table II). This species has also been reported to display antitumoural effects in other nearby geographical areas such as South America and New Zealand (Perry *et al*. 1988, Reyes *et al*. 2004). It is common that individuals from the same species possess similar activity regardless of the geographical area, as it is the case of the ascidian *Ecteinascidia turbinata* (Munro *et al*. 1987). However, occasionally, individuals of the same species but from different geographical locations may possess distinctly different activity. An example is *Bugula neritina*, a bryozoan only found to present bryostatin 1 in certain geographical areas (Pettit 1991). In our survey, we also found species that showed antitumoural activity in one sampling station and did not display any antitumoural effect in the rest of the stations where they were collected. These are the cases of the holothurian *Taeniogytus contortus* (only one out of four replicates analysed showed antitumoural activity), and the tunicates *Aplidium falklandicum* (only the sample collected in the South Shetland Islands displayed antitumoural activity), *Polysincraton trivolutum* (one replicate out of the three with activity) and *Tylobranchion speciosum* (one replicate out of the two with activity) (Table I). Whether this situation is common or rare in nature is still to be established, and it could be related, among other reasons, to the presence of symbionts (Faulkner *et al*. 2000, König *et al*. 2006). We suggest, therefore, that it is important to bioprospect different areas even when sampling similar or the same species, since unexpected results may be obtained.

Since the beginnings of marine pharmacological studies in the 1950s, this discipline has mainly focused on tropical areas and, to a lesser extent, on temperate regions (Bergmann & Feeney 1951, Dietzman 1996, Avila *et al*. 2008). Polar regions have received much less attention, in part due to the difficulties of prospecting in these remote areas and in part also due to the traditional and incorrect belief that they hold low marine chemical diversity (challenged by Amsler *et al*. 2000). Results of this and previous works in the field of chemical ecology are uncovering a very promising future in the search for new leads in the Southern Ocean (Lebar *et al*. 2007, Avila *et al*. 2008). Since only *c*. 25% of Antarctic fauna has been described so far (Gutt *et al*. 2004) and just a tiny part of it has been tested for biological activity (Avila *et al*. 2008), it can be assumed that natural products in this area will continue providing novel bioactive chemical structures. Furthermore, due to the particular characteristics of the Southern Ocean, which has been physically isolated from the surrounding oceans for 34 million years (Tripati *et al*. 2005), the chances of finding totally novel natural products seem to be higher in this area than in other parts of the world. Natural products are proving to be the most reliable way to find solutions to current and future human diseases (Amsler *et al*. 2001, Newman & Cragg 2007) and many new compounds wait to be discovered. As in an iceberg, which we believe to be very appropriate in this context, for chemical studies in general and pharmacological studies in particular, one could say that only the tip has been discovered so far.

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