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Marine cyanobacteria diversity and biotechnological potential in Caribbean waters

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ABSTRACT

Marine cyanobacteria are producers of structurally diverse secondary metabolites, many have intriguing biological properties. These compounds represent a series of different chemical entities, such as alkaloids, polyketides, peptides or mixed NRPS/PKS metabolites, exhibiting a variety of antifouling, anticancer, antimicrobial, allelopathic and anti-inflammatory properties. Nevertheless, cyanobacteria have been less used as sources of marine natural products when compared with sponges or macroalgae. Cyanobacteria studies in Caribbean marine waters are still scarce and scattered, but reveal an interesting diversity with a total of 76 genera and 119 species reported. The presence of cyanobacteria blooms in the Caribbean region has been observed with greater frequency, but their toxin profile and impact are scarcely understood. In the case of the Dominican Republic, there have been no reports on studies with cyanobacteria biotechnological applications. New strains are expected to be isolated from different Caribbean environments, contributing to our understanding of cyanobacterial biodiversity and their potential biotechnological applications.

KEY WORDS
Caribbean waters,
cyanobacteria,
biodiversity,
biotechnology.

RÉSUMÉ

Diversité des cyanobactéries marines et potentiel biotechnologique dans les eaux des Caraïbes.

Les cyanobactéries marines produisent des métabolites secondaires structurellement diversifiés, dont beaucoup ont des propriétés biologiques intrigantes. Ces composés représentent une série d'entités chimiques différentes, telles que des alcaloïdes, des polykétides, des peptides ou des métabolites NRPS/PKS mixtes, présentant une variété de propriétés antifouling, anticancéreuses, antimicrobiennes, allélopathiques et anti-inflammatoires. Néanmoins, les cyanobactéries ont été moins utilisées comme sources de produits naturels marins que les éponges ou les macroalgues. Les études sur les cyanobactéries dans les eaux marines des Caraïbes sont encore rares et parcellaires, mais elles révèlent une diversité intéressante avec un total de 76 genres et 119 espèces signalés. La présence d'efflorescences de cyanobactéries dans la région des Caraïbes a été observée plus fréquemment, mais le profil de leurs toxines et leur impact sont encore mal compris. Dans le cas de la République dominicaine, il n'y a pas eu de rapports d'études sur les applications biotechnologiques des cyanobactéries. De nouvelles souches devraient être isolées dans différents environnements des Caraïbes, contribuant ainsi à notre compréhension de la biodiversité des cyanobactéries et de leurs applications biotechnologiques potentielles.

MOTS CLÉS
Caraïbes,
cyanobactéries,
biodiversité,
biotechnologie.

INTRODUCTION

The exploration of the potential bioactivity of marine organisms is a remarkable tool for the development of new pharmacological products (Butler 2004). Marine cyanobacteria are producers of structurally diverse secondary metabolites. These compounds represent a series of different chemical entities such as alkaloids, polyketides, peptides or mixed NRPS/PKS metabolites, exhibiting a variety of biological properties (antifouling, anticancer, antimicrobial, allelopathic and anti-inflammatory) (Almeida *et al.* 2015; Costa *et al.* 2015; Ribeiro *et al.* 2017; Barreiro Felpeto *et al.* 2018). Cyanobacteria culture collections are a great source for discovering new chemodiversity (Ramos *et al.* 2018). Nevertheless, cyanobacteria have been less used as natural sources of marine natural products (NP) than sponges or macroalgae.

Most of the work on cyanobacteria natural products has been carried out by research groups in the United States and Japan (Cardellina *et al.* 1979; Han *et al.* 2006; Kwan *et al.* 2011; Hilborn *et al.* 2014; Ling *et al.* 2015), using cyanobacterial samples mainly from tropical regions.

The presence of cyanobacteria blooms in the Caribbean region has been observed with greater frequency (Puyana *et al.* 2015). The ideal conditions for the development of blooms of cyanobacteria include a high concentration of nutrients, high amount of biomass, high temperature and high irradiation (Vasconcelos & Pereira 2001). These conditions occur frequently in various Dominican environments, although no paper was published (Vásquez-Tineo pers. comm.), highlighting the need to study their bioactivity and biotechnological potential in the Dominican Republic.

The extensive fractionation of the crude organic extract from a Puerto Rican collection of *Lyngbya majuscula* Harvey ex Gomont, led to the discovery of three new secondary metabolites: a quinoline alkaloid, malyngamide T and a derivative of tryptophan (Nogle & Gerwick 2003). In another study carried out in La Parguera, Puerto Rico, several filamentous species of moderately cytotoxic marine cyanobacteria were found to have activity against H-460 human lung cancer cells, and from their extracts, two secondary metabolites, a linear acylamide (parguerene) and a lipopeptide (precarriebowmide), were isolated and structurally defined (Mevers *et al.* 2013).

In the case of the Dominican Republic, there have been no reports on studies with cyanobacteria biotechnological applications, but it is relevant to point out that over 25 years ago, at the Center for Marine Biology Research of the University State (CIBIMA-UASD), one of the first initiatives to research marine organisms with antibiotic potential was launched (Vásquez-Tineo pers. comm.).

Therefore, it is expected to discover more novel structures with powerful bioactivity from cyanobacteria. Some of these may have important pharmacological relevance, as in the case of three antibodies derived from natural products of cyanobacteria that are currently in clinical trials and have been approved by the Food and Drug Administration (FDA) (Gerwick *et al.* 1994). Small molecules of these potential therapeutic agents are derivatives of auristatins E and F, which have been isolated from sponges but are, in all likelihood, produced by cyanobacteria (Gerwick *et al.* 1994), highlighting the potential of these organisms for the discovery of powerful bioactive compounds.

MATERIAL AND METHODS

For the construction of the database, different search engines were used, especially Web of Science and Google Scholar, without time restrictions. Publications reporting the occurrence of cyanobacteria in the Caribbean were searched using a combination of keywords for cyanobacteria and location, such as "cyanobacteria", "cyanotoxins", "cyanophytes", "blue-green algae" and related terms, combined with "Caribbean Islands", "Caribbean", "Islas Mayores", "Islas Menores", "Cuba", "Jamaica", "Puerto Rico", "Haiti", "Curaçao", "Dominican Republic" and similar. We reviewed publications on search sites such as PUBMED, ISI, SCOPUS.

A total of 83 publications from 1979 to 2021 were analyzed. Species names were revised to the most recent nomenclature according to AlgaeBase (Guiry & Guiry 2020). Each entry, or taxa, had information on its origin (island, archipelago, country and region of the Atlantic Ocean), habitat, respective reference(s) and year of identification.

The database was analyzed using tools such as Excel for the construction of graphs (Oliveros 2007-2015) and Venn diagrams, and Inkscape 0.92.4 (https://inkscape.org/pt/) was used to draw graphics and edit images.

Fig. 1. — Map showing Caribbean countries were studies on cyanobacteria have been reported (**gray**) and those that have no reports yet (**white**).

Abbreviations

ATX	anatoxin-a;
BBD	black band disease;
CYN	cylindrospermopsin;
KS	ketosynthase;
MS	mass spectrometry;
NP	natural products;
NRPS	nonribosomal peptide synthetases;
PBP	phycobiliproteins;
PHA	polyhydroxyalkanoates;
PKS	polyketide synthase;
PSP	paralytic shellfish poisoning.

RESULTS AND DISCUSSION

Cyanobacteria in Caribbean marine waters

Cyanobacteria studies in Caribbean marine waters are still scarce and scattered but reveal an interesting diversity. A total of 76 genera and 119 species are listed with some genera, more associated with freshwaters such as *Aphanothece* C.Nägeli, *Coelosphaerium* C.Nägeli and *Microcystis* Kützing, also present in coastal waters (Table 1). Works on planktonic and benthic cyanobacteria carried out in the Caribbean region focus on their relationships with other organisms and their functions in this ecosystem (Gerwick *et al.* 1989; Villareal 1995; Orjala & Gerwick 1996, 1997; Hooper *et al.* 1998; Navarro *et al.* 2000; Jiménez & Scheuer 2001; Stielow & Ballantine 2003; Rejmánková *et al.* 2004; Paul *et al.* 2005; Chacón *et al.* 2006; Littler *et al.* 2006; Bernecker & Wehrtmann 2009; Linington *et al.* 2009; Morrow *et al.* 2011; Dobal *et al.* 2012; Hirose *et al.* 2012; Olson & Lesser 2013; Giles *et al.* 2013; Mevers *et al.* 2013; Tavera *et al.* 2013; Hernández-Becerril 2014; Den Haan *et al.* 2014; Guidi-Rontani *et al.* 2014; Brocke *et al.* 2015; Engene *et al.* 2015; Gutiérrez-Salcedo *et al.* 2015; Kiryu *et al.* 2015; Puyana *et al.* 2015; Comas-González & Moreira-González 2016; Comas-González *et al.* 2017; Couradeau *et al.* 2017; Luzzatto-Knaan *et al.* 2017).

Many reports are based on studies done in coral reef environments (Linington *et al.* 2009; Morrow *et al.* 2011; Olson & Lesser 2013; Den Haan *et al.* 2014; Engene *et al.* 2015; Puyana *et al.* 2015). Nevertheless, other types of substrates such as marshes and mangroves (Rejmánková *et al.* 2004; Guidi-Rontani *et al.* 2014), sea grasses (Stielow & Ballantine 2003), coastal shallow waters (Orjala & Gerwick 1996, 1997; Hooper *et al.* 1998; Jiménez & Scheuer 2001; Mevers *et al.* 2013) and association with invertebrates such as sponges (Giles *et al.* 2013) and ascidians (Hirose *et al.* 2012) are referred. Endolytic and carstic cyanobacteria have also being studied showing an interesting biodiversity still unexplored (Chacón *et al.* 2006; Tavera *et al.* 2013; Couradeau *et al.* 2017). Planktonic cyanobacteria show also an interesting biodiversity, with *Trichodesmium* spp. as the most referred in the Caribbean Sea region with report from Belize (Villareal 1995), Puerto Rico (Navarro *et al.* 2000), Mexico (Hernández-Becerril 2014) and Colombia (Gutiérrez-Salcedo *et al.* 2015; Puyana *et al.* 2015) (Table 2).

During the last three decades, natural products discovery efforts have successfully exploited collections of tropical marine cyanobacteria for biologically active secondary metabolites with potential pharmaceutical properties (Tidgewell *et al.* 2010). Tropical marine cyanobacteria are prolific producers of NP (Luesch *et al.* 2001; Thacker & Paul 2004; Engene *et al.* 2015). The massive blooms reported (Villareal 1995; Navarro *et al.* 2000; Hernández-Becerril 2014; Gutiérrez-Salcedo *et al.* 2015; Puyana *et al.* 2015) motivate to deepen

TABLE 1. — Cyanobacteria species and their habitats reported from the Caribbean region.

Species	Habitat	Country	Methods of identification	References
Hormothamnion enteromorphoides	Bottom tuffs	Puerto Rico	Morphological	Gerwick *et al.* 1989
Lyngbyopsis willei, *Cylindrospermum minutissimum* var. *rinoi*, *C. zonatum*, *C. bourrellyi*, *C. desikacharyi*, *C. breve*, *C. minutissimum*, *C. michailovskoense*, *C. muscicola* var. *kashmiriense*, Gomphosphaerioideae species, *Phormidium* cf. *formosum* dominated in 13 localities from 16 samples, *Oscillatoria* cf.*annae*, *Phormidium ambiguum* and *Anabaena ablonga*	Mountain creeks	Cuba	Morphological	Komárek 1989
Trichodesmium	Plankton	Belize	Morphological	Villareal 1995
Lyngbya majuscula	Shallow coastal waters	Curaçao		Orjala & Gerwick 1996, 1997
Lyngbya majuscula	Shallow waters	Curaçao		Hooper *et al.* 1998
Trichodesmium sp.	Phytoplankton	Puerto Rico	Morphological	Navarro *et al.* 2000
Lyngbya majuscula	Shallow waters	Panama		Jiménez & Scheuer 2001
Microcoleus lyngbyaceus	Sea grasses	Puerto Rico		Stielow & Ballantine 2003
Aphanocapsa venezuelae, *Aphanothece bacilloidea*, *A. comasii*, *A. cylindracea*, *A. hardersii*, *A. granulosa*, *A. opalescens*, *A. variabilis*, *Arthrospira*, *Asterocapsa*, *Chlorogloea gardneri*, *C. gessneri*, *Chroococcus minutissimus*, *C.aeruginosus*, *C. minutus*, *C. subsphaericus*, *C. major*, *C. mipitanensis*, *C. ocidentalis*, *C. polyedriformis*, *C. pulcherrimus*, *Coelomoron microcystoides*, *Coelosphaerium evidenter-marginatum*, *Cyanobium* sp., *Cyanosarcina* sp., *C. bourrellyi*, *C. breve*, *Fortiea*, *Geitlerinema splendidum*, *Gloeocapsa ovalis*, *Gloeothece interspersa*, *G. Opalothecata*, *Gomphosphaeria semen-vitis*, *Hapalosiphon*, *Hassalia*, *Johannesbaptistia pellucida*, *Komvophoron*, *Lemmermanniella*, *Leptolyngbya angustissima*, *L. mucosa*, *L. perelegans*, *Limnothrix*, *Lyngbya maior*, *L. minor*, *L. martensiana*, *merismopedia*, *Nostoc*, *Onkonema*, *Oscillatoria miniata*, *O. Jenensis*, *O. levis*, *Phormidium granulatum*, *Pseudanabaena*, *Rhabdogloea*, *Scytonema*, *Schizothrix*, *Spirulina tenerrima*, *Stigonema*, *Synechococcus*, *Synechocystis willei*, *Tolypothrix willei*, *Trichocoleus*, *Trichormus protoricencis*	Inland marshes	Belize	Morphological and ecological characters	Rejmánková *et al.* 2004
Lyngbya confervoides, *L. polychroa*	Coral reefs	United States	Microscopical analyses and molecular genetic techniques	Paul *et al.* 2005
Nodularia spumigena	Low salinity water conducts	Bahamas	Morphological and microscopical analyses	Littler *et al.* 2006
Lythophilum, *Matteia conchicola*, *Plectonema terebrans*, *Calothrix*, *Fischerella*, *Phormodium*, *Leptolyngbya*, *Microcoleus*, *Halomicronema*	Endolythic	Puerto Rico	Microscopical analyses and molecular genetic techniques	Chacón *et al.* 2006
Lyngbya confervoides	n.s.	Costa Rica	Morphological and microscopical analyses	Bernecker & Wehrtmann 2009
Schizothrix	Coral reefs	Panama	–	Linington *et al.* 2009
Lyngbya majuscula, *L. polychroa*	Coral reefs	Virgin Islands, Belize	Molecular analyses	Morrow *et al.* 2011
Oscillatoria, *Symploca*	Coral reefs and sand	Curaçao	Morphological and microscopical analyses	Den Haan *et al.* 2014
Synechoccocus	Sponges	Bahamas	Molecular analyses	Giles *et al.* 2013

Table 1. — Continuation.

Species	Habitat	Country	Methods of identification	References
Prochloron	Ascidians	Panama	Molecular analyses	Hirose *et al.* 2012
Aphanothece cf. *stagnina*, *A. variabilis*, *A. marina*, *A. smithii*, *Cyanothece halobia*, *Lemmermanniella pallida*, *Synechococcus mundulus*, *Synechocystis minuscula*, *S. aquatilis*, *S. setentrionalis*, *Coealosphaerium dubium*, *Chroococcus prescottii*, *C. minutus*, *Gloeocapsopsis dvorakii*, *Spirulina tenerrima*, *Leptolyngbya ectocarpii*, *Komvophoron* cf. *minutum*, *K. breve*, *Hormoscilla* cf. *fragmentosa*, *Oscillatoria leonardii*	Plankton	Cuba	Morphological and microscopical analyses	Dobal *et al.* 2012
Moorea producens	Shallow waters	Puerto Rico	Molecular analyses	Mevers *et al.* 2013
Synechoccocus spongiarium	Coral reefs	United States, Little Cayman Island, Bahamas	Molecular analyses	Olson & Lesser 2013
Asterocapsa xcaamalensis, *Chlorogloea halkab*, *C. epiphytica*, *C. gardneri*, *Cyanosarcina caribeana*, *Synechococcus socialis*, *Aphanocapsa elachista*, *A. holsatica*, *A. intertexta*, *A. incerta*, *A. nubilum*, *A. venezuelae*, *Coelomoron microcystoides*, *C. tropicale*, *C. vestitum*, *Aphanothece comasii*, *A. conglomerata*, *A. granulosa*, *A. hardersii*, *A. stagnina*, *A. variabilis*, *Radiocystis geminata*, *Rhabdoderma tenuissimum*, *Rhabdogloea subtropica*, *R. yucatanensis*, *Chroococcus mipitanensis*, *Microcystis comperei*, *M. protocystis*, *M. preudofilamentosa*, *Geitlerinema unigranulatum*, *Limnothrix borgertii*, *Pseudanabena voronichinii*, *Spirulina subtilissima*, *Leptolyngbya lagerheimii*	Carstic environments	México	Molecular analyses	Tavera *et al.* 2013
Oscillatoria, *Planktothricoides niger*, *P. rosea*	Tuffs in Mangle roots	Guadeloupe	Molecular analyses	Guidi-Rontani *et al.* 2014
Trichodesmium thiebautii, *Prochlorococcus*, *Synechococcus*, *Richelia intracellularis*	Phytoplankton	Mexico	Morphological and microscopical analyses	Hernández-Becerril 2014
Plankthotricoides sp.	mangroves	Guadeloupe	Molecular analyses	Guidi-Rontani *et al.* 2014
Lyngbya, *Oscillatoria*, *Richelia*, *Synechoccocus*, *Trychodesmium*	Phytoplankton	Colombia	Morphological and microscopical analyses	Gutiérrez-Salcedo *et al.* 2015
Trichodesmium, *Okeania erythroflocculosa*, *Symploca hydnoides*, *Phormidium submembranaceum*, *P. gracile*, *Oscillatoria acuminata*, *Spirulina subsalsa*, *Lyngbya*, *Symploca*	Water, Coral reef	Colombia	Morphological and microscopical analyses	Puyana *et al.* 2015
Oscillatoria bonnemaisonii, *Hydrocolium glutinosum*	Mats	Curaçao	–	Brocke *et al.* 2015
Caldora penicilatta	Coral reefs	Belize, Bonaire, Curaçao, Florida Keys, Honduras	Molecular analyses	Engene *et al.* 2015
Anabaenopsis elenkinii, *Glaucospira*, *Geitlerinema*, *Merismopedia tenuissima*, *Phormidium*, *Pseudanabaena catenata*, *Spirulina labyrinthiformis*, *S. major*, *Synechocystis salina*	Shrimp farm	Cuba	Morphological and microscopical analyses	Comas-González & Moreira-González 2016
Rivularia, *Cyanothece*, *Mastigocoleus*, *Hyela*, *Halomicronema*, *Chroococcidiopsis polansiana*, *Pleurinema perforans*	Endolythic	Puerto Rico	Molecular analyses	Couradeau *et al.* 2017
Limnoraphis robusta	Plankton	Cuba	Morphological and microscopical analyses	Comas-González *et al.* 2017

Table 2. — Harmful cyanobacteria found in Caribbean waters and associated diseases.

Species	**Habitat/Disease**	**Location**	**Country**	**References**
Roseofilum reptotaenium	Coral reefs, increasing blooms	Culebra Natural Reserve	Puerto Rico	Ballantine *et al.* 2008
Phormidium corallyticum	BBD	South coast	Curaçao	Frias-Lopez *et al.* 2003
Oscillatoria, *Geitlerinema*	Coral reef BBD, MC-LR producers	St. Croix and the northern Florida Keys	United States	Stanić *et al.* 2011
Limnothrix, *Plectonema*, *Leptolyngbya*, *Synechococcus*, *Prochlorococcus*	Sponges orange BD	Florida Keys	United States	Angermeier *et al.* 2011
	Sponges BBD	Lee Stocking Island	Bahamas	Lesser *et al.* 2016
Roseofilum reptotaenium	Coral BBD	St. Croix	United States	Casamata *et al.* 2012
Geitlerinema, *Leptolyngbya*	Coral BBD	Lee Stocking Island	Bahamas	Voss *et al.* 2007
Roseofilum reptotaenium	Coral BBD	St. Croix	United States	Richardson *et al.* 2014
Oscillatoriales	Sea fans	Gulf Stream Reef, Florida	United States	Kiryu *et al.* 2015

these studies as they affect the stability of this ecosystem. The main species of cyanobacteria involved in the massive blooms are *Schizothrix mexicana* Gomont and the red alga *Metapeyssonnelia corallepida* Ballesteros & Antonius (Ballantine *et al.* 2008), strains of *Cyanothece* Komárek, related to the genus *Synechococcus* Nägeli, and *Bradyrhizobium jicamae* Ramírez-Bahena *et al.* (Olson & Lesser 2013).

Most reports of cyanobacteria in Caribbean islands are associated with black band disease (BBD), a very common disease in Caribbean coral reefs, caused by a consortium of microorganisms (e.g. *Leptolyngbya* Anagnostidis & Komárek). This type of phenomenon is common in the Caribbean but little reported as in other coral reefs such as the Great Barrier Reef in Australia (Page & Willis 2006), in the Indo-Pacific reefs around Palau (Sussman *et al.* 2006) and Okinawa coral reefs in Japan (Hutabarat *et al.* 2018).

Many studies attempt to determine the phylogenetic identity of the cyanobacteria associated with the black band disease (Table 3). Cyanobacteria may affect tropical organisms, in special corals, causing the BBD (Ballantine *et al.* 2008). Several species of cyanobacteria are associated with this disease, that may kill extensive areas of coral, among them: *Phormidium corallyticum* Rützler & Santavy, *Roseofilum reptotaenium* Casamatta, Stanic, Gantar & Richardson and other species of *Oscilatoria* Vaucher ex Gomont, *Geitlerinema* Anagnostidis, *Limnothrix* Meffert, *Plectonema* Thuret ex Gomont, *Leptolyngbya*, *Synechococcus* and *Prochlorococcus* Chisholm *et al.* (Table 3). Most of the reports of coral BBD are from the eastern coast of the United States, namely in the Bahamas (e.g. Voss *et al.* 2007; Lesser *et al.* 2016) and Florida (Kiryu *et al.* 2015), but there are also cases reported in the Caribbean area, e.g. US Virgin Islands, Puerto Rico and Curaçao (Frias-Lopez *et al.* 2003; Ballantine *et al.* 2008; Stanić *et al.* 2011; Richardson *et al.* 2014). Although hard corals seem to be the most impacted organisms, sponges may also be affected by the BBD (Angermeier *et al.* 2011; Lesser *et al.* 2016). In all these cases, the toxins involved in the disease are not yet known.

CIANOTOXINS IN CARIBEAN CYANOBACTERIA

The progress in analytical chemistry has allowed the isolation and structural identification of a diverse array of cyanotoxins. These include three neurotoxins with quite different modes of blocking neuronal signal transmission (anatoxin-a, anatoxin-a (s) and saxitoxins), a general cytotoxin that inhibits synthesis of proteins (cylindrospermopsin), and a group of hepatotoxins called microcystins and nodularines (in brackish water) that inhibit protein phosphatases (Vasconcelos 2015).

These cyanotoxins were named after the organism from which they were first isolated, but most have been found in a wide range of genera, and some species contain more than one toxin, or both microcystins and neurotoxins (Sivonen & Jones 1999). Cylindrospermopsin (CYN) is an alkaloid that causes cytotoxic, hepatotoxic, neurotoxic and general effects in mammals (Pearson *et al.* 2010). The production of CYN was detected for the first time in the cyanobacterium *Cylindrospermopsis raciborskii* (Woloszynska) Seenayya & Subba Raju (Ohtani *et al.* 1992). Later, a series of species of cyanobacteria, *Umezakia natans* Watanabe (Harada *et al.* 1994), *Aphanizomenon ovalisporum* Forti (Banker *et al.* 1997), *Raphidiopsis curvata* Fritsch & Rich (Li *et al.* 2001), *Lyngbya wollei* (Farlow ex Gomont) Speziale & Dyck (Seifert *et al.* 2007) and *Anabaena lapponica* Borge (Spoof *et al.* 2006) were reported as CYN producers. The mysterious disease of Palm Island (Queensland, Australia), which has been linked to CYN poisoning, affected 148 people in 1979 (Griffiths & Saker 2003). Anatoxin-a (ATX) is one of the neurotoxic compounds produced by several species of cyanobacteria. It is a potent agonist of the nicotinic acetylcholine receptor and can cause neurotoxic effects in vertebrates, including muscle fasciculation, wheezing, convulsions and death from respiratory arrest (Carmichael 1992). The production of anatoxin-a has been observed in several strains of *Aphanizomenon* spp. (Sivonen *et al.* 1990; Rantala-Ylinen *et al.* 2011).

Toxic cyanobacteria are found throughout the world in inland and coastal waters. It has been shown that at least 46 species caused toxic effects in vertebrates (Sivonen & Jones 1999). The most common toxic cyanobacteria are *Microcystis* spp., *Cylindrospermopsis raciborskii*, *Planktothrix rubescens* (De Candolle ex Gomont) Anagnostidis & Komárek, *Synechococcus* spp., *Planktothrix agardhii* (Gomont) Anagnostidis & Komárek, *Gloeotrichia* spp., *Anabaena* spp., *Lyngbya* spp., *Aphanizomenon* spp., *Nostoc* spp., *Oscillatoria* spp., *Schizothrix* spp. and

TABLE 3. — Blooms of *Trichodesmium* species in the Caribbean marine waters.

Species	Country	Date	Cell density	References
Trichodesmium sp.	Belize	1993-1994	–	Villareal 1995
Trichodesmium sp.	Puerto Rico	1995-1997	Max 23.5 g/cm^3	Navarro *et al.* 2000
Trichodesmium tiebautii	Mexico	Before 2009	–	Hernández-Becerril 2014
Trichodesmium sp.	Colombia	2009-2010	–	Puyana *et al.* 2015
Trichodesmium sp.	Colombia	2011	–	Gutiérrez-Salcedo *et al.* 2015

Synechocystis spp. (Sivonen & Jones 1999; Vasconcelos 2015). Populations of the genus *Microcystis* are the most common bloom-forming and almost always toxic (Carmichael 1995). It has been shown that the toxicity of a strain depends on whether it contains the gene for microcystin production (Rouhiainen *et al.* 1995; Kurmayer *et al.* 2002).

As the research expands and covers more regions around the world, it is likely that more toxin producing species will be found. Therefore, it is prudent to assume a toxic potential in any population of cyanobacteria. The conditions that lead to the proliferation of cyanobacteria are well known (physiological or biochemical function of the toxins) (Chorus & Bartram 1999).

Around the world, *c.* 60% of the samples of cyanobacteria investigated contain toxins (Sivonen & Jones 1999). There are numerous cases of lethal poisoning of animals that drink water with massive developments of cyanobacteria. Documented reports refer back to at least 1853. The first detailed scientific account of toxic cyanobacteria appeared in 1878. In a perceptive and prescient paper in *Nature*, the Adelaide assayer and chemist George Francis reported on stock deaths at Milang on the shores of Lake Alexandrina in South Australia (Codd *et al.* 2015). There is also a human risk associated with exposure to toxic cyanobacteria; several deaths have been reported following renal dialysis (Jochimsen *et al.* 1998), as well as health implications due to the use or absorption of drinking water and/or during recreational activities such as irritation of the skin, membranes, mucous membranes (Teixeira *et al.* 1993). It is likely that different cyanobacterial metabolites are involved in the evocation of symptoms associated with these exposure routes.

So far, the production of paralytic shellfish poisoning (PSP) toxin has been found in filamentous cyanobacterial species belonging to the Nostocal order (*Dolichospermum circinale* (Rabenhorst ex Bornet & Flahault) Wacklin, Hoffmann & Komárek, *Anabaena circinalis* Rabenhorst ex Bornet & Flahault, *Aphanizomenon gracile* Lemmermann, *Cuspidothrix issatschenkoi* (Usachev) Rajaniemi, Komárek, Willame, Hrouzek, Kastovská, Hoffmann & Sivonen, *Cylindrospermopsis raciborskii*, *Raphidiopsis brookii* Fritsch & Rich, *Scytonema* sp.) among others (Wiese *et al.* 2010; Borges *et al.* 2015).

Although cell density is not referred in these studies, *Trichodesmium* Ehrenberg ex Gomont blooms have been recorded since 1993, without any information on potential toxicity or toxin profiles (Table 3).

In the Caribbean waters, the cyanotoxins reported so far are mostly microcystins (Table 4) although the reported blooms of *Trichodesmium* in Belize, Puerto Rico, Mexico and Colombia (Table 2) may have associated other toxins such as palytoxins and analogues (Kerbrat *et al.* 2011).

Microcystin-LR has been associated with episodes of *Geitlerinema* and *Oscillatoria* blooms with concentrations ranging from 0.02 to 0.04 mg/g (Stanić *et al.* 2011). Nodularins were also found in Bahamas, associated with a bloom of *Nodularia spumigena* Mertens ex Bornet & Flahault, but no quantification was done (Littler *et al.* 2006). A cytotoxin and fish toxic toxin called Hormothamnin A was isolated from a bloom of *Hormothamnion enteromorphoides* Setchell & Gardner in Puerto Rico (Gerwick *et al.* 1989), and unknown toxic effects in *Artemia* Grochowski were registered from a sample of *Plankthotricoides* Suda & Watanabe from Guadaloupe (Guidi-Rontani *et al.* 2014) (Table 2). Despite the large number of cyanobacteria species found in Caribbean waters (Table 1) there is still limited knowledge related to cyanotoxin diversity, seasonality and concentration.

BIOTECHNOLOGICAL POTENTIAL OF CYANOBACTERIA

The marine environment is extraordinarily rich in biological and chemical diversity. Marine organisms are recognized as a rich source of new chemical entities. Cyanobacteria are an example of these organisms, since hundreds of chemical products of interest synthesized by them have been discovered since the 1970s. Cyanobacteria's biological activities include anticancer, anti-inflammatory, antibacterial, antiparasitic, neuromodulatory and antiviral (Leão *et al.* 2012).

The cyanobacterial natural products that are under investigation for anticancer applications include the cyclodepsipeptides apratoxin A and F, the A lipid-containing nitrogen and the lipopeptides dolastatin 10 and carmaphycin B (Blokhin *et al.* 1995; Luesch *et al.* 2001; Tidgewell *et al.* 2010; Pereira *et al.* 2012). Collections of tropical marine cyanobacteria identified as *Symploca hydnoides* Kützing ex Gomont and *Symploca* sp. have produced several pharmaceutical NP with promising potential, including the metabolites: symplostatin 1 (Harrigan *et al.* 1998), dolastatin 10 (Luesch *et al.* 2001), largazole (Taori *et al.* 2008), janthielamide A, kimbeamides AC and Kimbelactone A (Nunnery *et al.* 2012). Cyanobacteria are prokaryotic photoautotrophs found in almost every plausible habitat on Earth (Nübel *et al.* 2000; Garcia-Pichel & Pringault 2001). Existing knowledge about the diversity and physiology of cyanobacteria provides an excellent basis for exploring their applications in biotechnology (Cirés *et al.* 2014).

The phycobiliproteins (PBP) can have a wide range of applications: paints; textiles, mainly clothing; body products such

Table 4. — Species of toxic cyanobacteria reported in the Island of Cuba. Potential for the production of cyanotoxins (analytical identification in environmental samples or by molecular methods).

Reported species	Cyanotoxins	References
Aphanizomenon flos-aque	Cylindrospermopsin, microcystin	Brient *et al.* 2008; Osswald *et al.* 2009
Dolichospermum planctonicum	Anatoxin-a, cylindrospermopsin	Park *et al.* 1993; Brient *et al.* 2008
Kamptonema formosum	Homoanatoxin-a	Skulberg *et al.* 1992
Oscillatoria	Cylindrospermopsin, homoanatoxin-a, microcystin	Cadel-Six *et al.* 2007; Osswald *et al.* 2009; Mazmouz *et al.* 2010; Stanić *et al.* 2011
Phormidium	Anatoxin-a, homoanatoxin-a, microcystin	Cadel-Six *et al.* 2007; Gantar *et al.* 2009
Synechococcus	Microcystin	Gantar *et al.* 2009
Planktothrix	Microcystin	Ernst *et al.* 2001

as cosmetics, bath powders, body lotions, toothpastes, soaps; food products such as jellies, frostings; and beverages such as beer, wine, champagne, soft drinks, among others (Sekar & Muruganandham 2007). In recent years, cyanobacteria have been shown to be one of the most promising groups of organisms that produce a large number of bioactive compounds such as anticancer, antibacterial, antifungal, antiplasmodial, algicide and immunosuppressive properties (Bhadury & Wright 2004; Dahms *et al.* 2006; Abed *et al.* 2008). It has been found that some cyanobacteria accumulate intracellular polyhydroxyalkanoates (PHA) that can be used in the production of biodegradable plastic products (Steinbüchel *et al.* 1997).

Cyanobacterial biotechnological applications may comprise agriculture, mariculture, biomedical, food, fuel and dyes (Capone *et al.* 2005; Dutta *et al.* 2005; Rastogi *et al.* 2010), vitamins such as vitamins B and E, phycobiliproteins, toxins and pharmaceuticals (Carmichael *et al.* 2001; Plavsic *et al.* 2004). In our teal we have unraveled new cyanobacterial natural compounds with allelopathic activity (Leão *et al.* 2010), anticancer activity (Ribeiro *et al.* 2017), antimicrobial (Costa *et al.* 2015) and antifouling (Almeida *et al.* 2015; Martins *et al.* 2018; Antunes *et al.* 2019).

During the last decades, NP discovery efforts have successfully exploited collections of tropical marine cyanobacteria with biologically active metabolites such as symplostatin 1 (Harrigan *et al.* 1998), dolastatin 10 (Luesch *et al.* 2001), largazole (Taori *et al.* 2008), janthielamide A, kimbeamides AC and kimbelactone A (Luesch *et al.* 2001; Taori *et al.* 2008; Nunnery *et al.* 2010; Tidgewell *et al.* 2010; Engene *et al.* 2015). Morrow *et al.* (2011) developed an important study to analyze the allelochemicals produced by cyanobacteria and macroalgae of the Caribbean, and the specific effect in the prevention of bacterial and fungal colonization. In this sense macroalgae and cyanobacteria were collected from coral reefs between 2003 (*Dictyota pulchella* Hörnig & Schnetter), July 2005 (*Dictyota menstrualis* (Hoyt) Schnetter, Hörnig & Weber-Peukert), and between May and August 2008 (*Acanthophora spicifera* (Vahl) Børgesen, *Dictyota menstrualis* (Hoyt) Schnetter, Hörnig & Weber-Peukert, *D. pulchella* Hörnig & Schnetter, *Dictyota* sp., *Lobophora variegata* Lamouroux, *Halimeda tuna* (Ellis & Solander) J.V.Lamouroux, *Lyngbya majuscula* and *L. polychroa* (Meneghini) Rabenhorst), and extracts of macroalgae and cyanobacteria were found exhibiting broad spectrum antibacterial activity and broad spectrum stimulating activity.

Bioactive compounds from cyanobacteria

The enormous diversity of cyanobacteria and related species and the amount of synthesized secondary metabolites provide a great opportunity for research, denoting much more expectation in these little explored environments. Currently, more than 60 cyanobacterial genome sequencing projects are underway (Guiry & Guiry 2020). This group of microalgae receives significant attention since its representatives also produce a significant amount of bioactive compounds, which represent a great resource of high interest for biotechnological applications (Rosales *et al.* 2006), such as antiviral, antibacterial, antitumor and anti-inflammatory (Leonard *et al.* 2010). Antioxidant properties have also been identified in several of these sulfated polysaccharides, which are mainly composed of galactose, methylated sugars, and anhydrides (Ferreira *et al.* 2012).

A study presented by the Costa-Leal group analyzed 5286 marine natural products discovered between 2000 and 2010. Of the 5286 NP considered in the study, 40.5% were terpenes, 22.1% alkaloids, 13.0% aliphatic compounds not coming from the isoprene pathway, 7.5% steroids, 6.3% carbohydrates and finally 5.4% corresponded to peptides/amino acids. We can observe that the amount of terpenes discovered increased during the second half of the decade, while for the alkaloids the opposite occurred. The study also showed that most of the natural products came from samples belonging to Asian regions (55.1%). This undoubtedly reflects the little attention that has been paid by research groups to the Americas and the Caribbean, which account for just 14.6% of the total (Costa-Leal *et al.* 2012).

Future needs

The structural and functional diversity increases due to the composition, geographical location and extraction methods used (Rohani-Ghadikolaei *et al.* 2012). Although cyanobacteria are commonly found in tropical regions, including the Caribbean and Central America, and some of the most potent natural products of cyanobacteria known to date have been revealed there (Gerwick *et al.* 1994; Edwards *et al.* 2004; Tidgewell *et al.* 2010), little is known about the bioactive potential of Dominican cyanobacteria.

Mass spectrometry (MS) imaging methodologies (Watrous & Dorrestein 2011) have an increasing role in chemoecology studies (Lane *et al.* 2009; Esquenazi *et al.* 2011) and, combined with the analysis of the genome and/or groups of genes,

TABLE 5. — Toxins in marine cyanobacteria found in Caribbean waters.

Species	Location	Toxicity/Toxin	Assay	Concentration	References
Blennothrix lyngbyacea	Brazil coastal islands	Homoanatoxin-a	GC-MS and NMR	–	Méjean *et al.* 2009
Lyngbya majuscula	Hawaii	Lyngbyatoxin-a, lyngbyatoxin-b, lyngbyatoxin-c	Cytotoxic to several human cell lines	4ng/ml, 7ng/ml, and 700ng/ml	Fujiki *et al.* 1981; Aimi *et al.* 1990
Geitlerinema	Florida Keys	Microcystin-LR	ELISA	10 µg/ml	Gantar *et al.* 2009
Oscillatoria	Virgin Islands	Microcystin-LR	UPLC/MS	0.02-0.04 mg/g	Stanić *et al.* 2011
Hormothamnion enteromorphoides	Puerto Rico	Hormothamnin-a	Fish assay, cytotoxic to several human cell lines	–	Gerwick *et al.* 1989
Plankthotricoides sp.	Guadeloupe	Unknown	Artemia	–	Guidi-Rontani *et al.* 2014
Nodularia spumigena	Bahamas	Nodularin	Not measured	–	Littler *et al.* 2006

are an important tool in the study of cyanobacteria, to infer relevant ecological, physiological and biotechnological characteristics. Given the almost null information on the diversity and bioactive potential of cyanobacteria in the country, we could identify molecules that could potentially become viable alternatives as a source of pharmaceutical products.

The availability of bioactive compounds derived from cyanobacteria can be optimized to produce sustainable yields. Genetic engineering for the improvement of cyanobacterial strains is also being established. In the future, a multidisciplinary effort to support the use of more sensitive and rapid bioactive compound detection methods will accelerate the discovery of new compounds from cyanobacteria.

A single strain of cyanobacteria is capable of producing a series of secondary metabolites with different chemical arrangements and interesting bioactivities. As an example, a strain of *Lyngbya majuscula* collected in Granada was found to produce two new halogenated fatty acid amides (granadamid B and C), two depsipeptides (itralamides A and B) and two lipopeptides (hectochlorin and desacetylhectochlorin) (Jiménez *et al.* 2009).

Although there are bioanalytical methods designed to detect known metabolites early in the process of isolation (such as MS-based replication) (Gaudêncio & Pereira 2015), the ideal approach is to avoid rediscovery altogether. With this in mind, modern research approaches in natural products should be based on one or more of the following strategies:

1) using metagenomics for the study of the chemical diversity of the strains;

2) obtaining the production of new metabolites by limiting abiotic nutrients or biotic factors, for example co-culture;

3) developing methods to grow strains that were previously non-culturable organisms;

4) exploring unexploded organisms, based on the phylogenetic distance estimation of organisms already studied;

5) exploring organisms from unexploited places that very often are also eligible for the strategy.

With recent advances in nucleic acid sequencing technologies and bioinformatics, the biosynthetic richness of environmental microbiomes and non-cultured bacteria has come to light (Libis *et al.* 2019; Rego *et al.* 2020). Despite the fact that the ocean covers more than 70% of the Earth's surface, the marine environment is still considered one of the least studied ecosystems (Ambrosino *et al.* 2019). Molecular markers targeting biosynthetic genes, such as the ketosynthase (KS) domain of PKS, have been instrumental in assessing the diversity and distribution of bacterial biosynthetic genes in complex microbial communities (Kallifidas *et al.* 2012; Charlop-Powers *et al.* 2014).

The difference in morphological, physiological and genetic traits make cyanobacteria produce different biologically active metabolites in accordance with their habitat and exposed environmental conditions (Kini *et al.* 2020).

It is clear that the field of cyanobacterial research has been the most productive approach to discovering and characterizing chemoecological interactions and it is hoped that, with advances in omic sciences, we will be able to shift the paradigm of natural products discovery from microorganisms to predict interesting chemical scaffolds with subsequent functional expression in heterologous hosts, even for groups or clusters of genes (Hertweck 2009).

Recent trends in drug discovery from marine microalgae with antibacterial, antifouling and anticancer activities draw attention, as bioactive compounds such as dolastatins, carrageenan, apratoxins, cryptophycin and their derivatives are showing interesting results in clinical trials, providing an excellent opportunity for new drug discovery (Kumar *et al.* 2020).

Cyanobacteria and microalgae harvested and/or isolated from these Caribbean environments may provide a large chemical diversity with many different biotechnological applications. The deposit of newly isolated strains in established culture collections will be very important to maximize the potential for new discoveries, taking into account the application of the Nagoya protocol principles.

CONCLUSION

Cyanobacteria studies in Caribbean marine waters are still scarce and scattered, but cyanobacteria biodiversity indicates great potential for biotechnological exploitation. Toxin producing species have also being registered but comprehensive studies are still lacking. The isolation of strains and the collection of bloom material is a good approach to unravel novel molecules with biotechnological potential with pharmaceutical, agricultural and other industrial applications.

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REFERENCES

Abed R. M. M., Dobretsov S. & Sudesh K. 2008. — Applications of cyanobacteria in biotechnology. *Journal of Applied Microbiology* 106: 1-12. https://doi.org/10.1111/j.1365-2672.2008.03918.x

Aimi N., Odaka H., Sakai S., Fujiki H., Suganuma M., Moore R. E. & Patterson G. M. L. 1990. — Lyngbyatoxin-B and lyngbyatoxin-C, 2 new irritants from *Lyngbya majuscula*. *Journal of Natural Products* 53 (6): 1593-1596. https://doi.org/10.1021/np50072a035

Almeida J., Freitas M., Cruz S., Vasconcelos V. & Cunha I. 2015. — Acetylcholinesterase in Biofouling Species: characterization and Mode of Action of Cyanobacteria-Derived Antifouling Agents. *Toxins* 7 (8): 2739-2756. https://doi.org/10.3390/toxins7082739

Ambrosino L., Tangherlini M., Colantuono C., Esposito A., Sangiovanni M., Miralto M., Sansone C. & Chiusano M. L. 2019. — Bioinformatics for marine products: an overview of resources, bottlenecks, and perspectives. *Marine Drugs* 17 (10): 576. https://doi.org/10.3390/md17100576

Angermeier H., Kamke J., Abdelmohsen U. R., Krohne G., Pawlik J. R., Lindquist N. L. & Hentschel U. 2011. — The pathology of sponge orange band disease affecting the Caribbean barrel sponge *Xestospongia muta*. *FEMS Microbiology Ecology* 75 (2): 218-230. https://doi.org/10.1111/j.1574-6941.2010.01001.x

Antunes J., Pereira S., Ribeiro T., Plowman J. E., Thomas A., Clerens S., Campos A., Vasconcelos V. & Almeida J. 2019. — A multi-bioassay integrated approach to assess the antifouling potential of the cyanobacterial metabolites portoamides. *Marine Drugs* 17 (2): 111. https://doi.org/10.3390/md17020111

Ballantine D. L., Appeldoorn R. S., Yoshioka P., Weil E., Armstrong R., Garcia J. R., Otero E., Pagan F., Sherman C., Hernandez-Delgado E. A., Bruckner A. & Lilyestrom C. 2008. — Biology and Ecology of Puerto Rican Coral Reefs, *in* Riegl B. M. & Dodge R. E. (eds), *Coral Reefs of the USA*. Springer Science, Dordrecht: 375-406. https://doi.org/10.1007/978-1-4020-6847-8_9

Banker R., Carmeli S., Hadas O., Teltsch B., Porat R. & Sukenik A. 1997. — Identification of cylindrospermopsin in *Aphanizomenon ovalisporum* (Cyanophyceae) isolated from Lake Kinneret, Israel. *Journal of Phycology* 33: 613-616.

Barreiro Felpeto A., Śliwinska-Wilczewska S., Zloch I. & Vasconcelos V. 2018. — Light-dependent cytolysis in the allelopathic interaction between picoplanktonic and filamentous cyanobacteria. *Journal of Plankton Research* 40 (2): 165-177. https://doi.org/10.1093/plankt/fby004

Bernecker A. & Wehrtmann I. S. 2009. — New records of benthic marine algae and Cyanobacteria for Costa Rica, and a comparison with other Central American countries. *Helgoland Marine Research* 63: 219-229. https://doi.org/10.1007/s10152-009-0151-1

Bhadury P. & Wright P. C. 2004. — Exploitation of marine algae: biogenic compounds for potential antifouling applications. *Planta* 219: 561-578.

Blokhin A. V., Yoo H. D., Geralds R. S., Nagle D. G., Gerwick W. H. & Hamel E. 1995. — Characterization of the interaction of the marine cyanobacterial natural product curacin A with the colchicine site of tubulin and initial structure-activity studies with analogues. *Molecular Pharmacology* 48: 523-531.

Borges H. L. F., Branco L. H. Z., Martins M. D., Lima C. S., Barbosa P. T., Lira G. A. S. T., Bittencourt-Oliveira M. C. & Molica R. J. R. 2015. — Cyanotoxin production and phylogeny of benthic cyanobacterial strains isolated from the northeast of Brazil. *Harmful Algae* 43: 46-57. https://doi.org/10.1016/j.hal.2015.01.003

Brient E., Gugger M., Franlois J.-J., Bernard C., Humbert J.-F. & Quiblier C. 2008. — Temporal Variations in the Dynamics of Potentially Microcystin-Producing Strains in a Bloom-Forming *Planktothrix agardhii* (Cyanobacterium) Population. *Applied and Environmental Microbiology* 74: 3839-3848. https://doi.org/10.1128/AEM.02343-07

Brocke H. J., Polerecky L., De Beer D., Weber M., Claudet J. & Nugues M. M. 2015. — Organic Matter Degradation Drives Benthic Cyanobacterial Mat Abundance on Caribbean Coral Reefs. *PLOS ONE* 10 (5): e0125445. https://doi.org/10.1371/journal.pone.0125445

Butler M. S. 2004. — The Role of Natural Product Chemistry in Drug Discovery. *Journal of Natural Products* 67 (12): 2141-2153. https://doi.org/10.1021/np040106y

Cadel-Six S., Peyraud-Thomas C., Brient L., Tandeau De Marsac N., Rippka R. & Méjean A. 2007. — Different genotypes of anatoxin-producing cyanobacteria coexist in the Tarn River, France. *Applied and Environmental Microbiology* 73: 7605-7614. https://doi.org/10.1128/AEM.01225-07

Capone D. G., Burns J. A., Montoya J. P., Subramaniam A., Mahaffey C., Gunderson T., Michaels A. F. & Carpenter E. J. 2005. — Nitrogen fixation by *Trichodesmium* spp.: an important source of new nitrogen to the tropical and subtropical North Atlantic Ocean. *Global Biogeochemestry Cycles* 19 (2): GB2024. https://doi.org/10.1029/2004GB002331

Cardellina J. H., Marner F. J. & Moore R. E. 1979. — Seaweed dermatitis structure of Lyngbyatoxin A. *Science* 204 (4389): 193-195. https://doi.org/10.1126/science.107586

Carmichael W. W. 1992. — Cyanobacteria secondary metabolites – the cyanotoxins. *Journal of Applied Bacteriology* 72 (6): 445-459. https://doi.org/10.1111/j.1365-2672.1992.tb01858.x

Carmichael W. W. 1995. — Cyanobacterial toxins, *in* Hallegraeff G. M., Anderson D. M. & Cembella A. D. (eds), *Manual on Harmful Marine Microalgae*. UNESCO, Paris: 163-169. http://unesdoc.unesco.org/images/0012/001220/122021eo.pdf

Carmichael W. W., Azevedo S. M., An J. S., Molica R. J., Jochimsen E. M., Lau S., Rinehart K. L., Shaw G. R. & Eaglesham G. K. 2001. — Human fatalities from cyanobacteria: chemical and biological evidence for cyanotoxins. *Environmental Health Perspectives* 109 (7): 663-668.

Casamata D., Stanic D., Gantar M. & Richardson L. L. 2012. — Characterization of *Roseofilum reptotaenium* (Oscillatoriales, Cyanobacteria) gen. et sp. nov. isolated from Caribbean black band disease. *Phycologia* 51 (5): 489-499. https://doi.org/10.2216/11-10.1

Chacón E., Berrendero E. & Garcia Pichel F. 2006. — Biogeological signatures of microboring cyanobacterial communities in marine carbonates from Cabo Rojo, Puerto Rico. *Sedimentary Geology* 185 (3-4): 215-228. https://doi.org/10.1016/j.sedgeo.2005.12.014

Charlop-Powers Z., Owen J. G., Reddy B. V. B., Ternei M. A. & Brady S. F. 2014. — Chemical-biogeographic survey of secondary metabolism in soil. *Proceedings of the National Academy of Sciences of the United States of America* 111 (10): 3757-3762. https://doi.org/10.1073/pnas.1318021111

Chorus I. & Bartram J. 1999. — *Toxic Cyanobacteria in Water – A guide to their public health consequences, monitoring and management.* Spon Press, London, 440 p.

Cirés S., Roa C. A., Wood S. & Heimann K. 2014. — First report of microcystin-producing *Fischerella* sp (Stigonematales, Cyanobacteria) in tropical Australia. *Toxicon* 88: 62-66. https://doi.org/10.1016/j.toxicon.2014.06.010

Codd G. A., Morton H. & Baker P. D. 2015. — George Francis: a pioneer in the investigation of the quality of South Australia's drinking water sources (1878-1883). *Transactions of the Royal Society of South Australia* 139 (2): 164-170. https://doi.org/10.1080/03721426.2015.1057093

Comas-González A. & Moreira-González A. R. 2016. — Novedades para la flora de algas y cianobacterias de Cuba: *Strombomonas borysteniensis* (Roll) Popova (Euglenophyceae), *Anabaenopsis elenkinii* Miller y *Glaucospira* sp. (Cyanobacteria). *Anales de Biología* 38: 1-8. http://dx.doi.org/10.6018/analesbio.38.01

Comas-González A., Labaut-Betancourt Y. & Peraza-Escarra R. 2017. — Ocurrencia de *Limnoraphis robusta* (Parakutty) Komárek *et al.* (Oscillatoriales, Cyanobacteria) en el embalse Hanabanilla (Cuba Central). *Anales de Biología* 39: 1-6. http://dx.doi.org/10.6018/analesbio.39.01

Costa S., Costa M., Ramos V., Leão P., Barreiro A., Vasconcelos V. & Martins R. 2015. — Picocyanobacteria from a clade of marine Cyanobium revealed bioactive potential againts microalgae, bacteria and marine invertebrates. *Journal of Toxicology and Environmental Health*, Part A, 78 (7): 432-442. https://doi.org/10.1080/15287394.2014.991466

Costa-Leal M. C., Madeira C., Brandão C. A., Puga J. & Calado R. 2012. — Bioprospección de invertebrados marinos para nuevos productos naturales: una perspectiva química y zoogeográfica. *Moléculas* 17 (8): 9842-9854.

Couradeau E., Roush D., Scott Guida B. & Garcia-Pichel F. 2017. — Diversity and mineral substrate preference in endolithic microbial communities from marine intertidal outcrops (Isla de Mona, Puerto Rico). *Biogeosciences* 14 (2): 311-324. https://doi.org/10.5194/bg-14-311-2017

Dahms H.-U., Xu Y. & Pfeiffer C. 2006. — Antifouling potential of cyanobacteria: a mini-review. *Biofouling* 22: 317-327.

Den Haan J., Visser P. M., Ganase A. E., Gooren E. E., Stal L. J., van Duyl F. C., Vermeij M. J. A. & Huisman J. 2014. — Nitrogen fixation rates in algal turf communities of a degraded versus less degraded coral reef. *Coral Reefs* 33: 1003-1015.

Dobal V., Lugioyo G. M., Álamo B. & Loza Álvarez S. 2012. — New reports of planktonic cyanobacteria in Jigüey Bay, Cuba. *Serie Oceanológica* 11: 103-106.

Dutta D., De D., Chaudhuri S. & Bhattacharya S. K. 2005. — Hydrogen production by Cyanobacteria. *Microbial Cell Factories* 4: 36. https://doi.org/10.1186/1475-2859-4-36

Edwards D. J., Marquez B. L., Nogle L. M., McPhail K., Goeger D. E., Roberts M. A. & Gerwick W. H. 2004. — Structure and biosynthesis of the jamaicamides, new mixed polyketide-peptide neurotoxins from the marine cyanobacterium *Lyngbya majuscula*. *Chemistry & Biology* 11 (6): 817-833. https://doi.org/10.1016/j.chembiol.2004.03.030

Engene N., Tronholm A., Salvador-Reyes L. A., Luesch H. & Paul V. J. 2015. — *Caldora penicillata* gen. nov., comb. nov. (Cyanobacteria), a pantropical marine species with biomedical relevance. *Journal of Phycology* 51 (4): 670-681. https://doi.org/10.1111/jpy.12309

Ernst B., Hitzfeld B. C. & Dietrich D. R. 2001. — Presence of *Planktothrix* sp. and cyanobacterial toxins in Lake Ammersee Germany and their impact on whitefish (*Coregonus lavaretus* L.). *Environmental Toxicology* 16: 483-488. https://doi.org/10.1002/tox.10006

Esquenazi E., Jones A. C., Byrum T., Dorrestein P. C. & Gerwick W. H. 2011. — Dinámica temporal de la biosíntesis de productos naturales en cianobacterias marinas. *Actas de la Academia Nacional de Ciencias* 108 (13): 5226-5231.

Ferreira L. G., Noseda M. D., Gonçalves A. G., Ducatti D. R. B., Fujii M. T. & Duarte M. E. R. 2012. — Chemical structure of the complex pyruvylated and sulfated agaran from the red seaweed *Palisada flagellifera* (Ceramiales, Rhodophyta). *Carbohydrate Research* 347 (1): 83-94. https://doi.org/10.1016/j.carres.2011.10.007

Frias-Lopez J., Bonheyo G. T., Jin Q. & Fouke B. W. 2003. — Cyanobacteria Associated with Coral Black Band Disease in Caribbean and Indo-Pacific Reefs. *Applied and Environmental Microbiology* 69: 2409-2413.

Fujiki H., Mari M., Nakayasu M., Tereda M., Sugimura T. & Moore R. E. 1981. — Indole alkaloids: dihydroteleocidin B, teleocidin and lyngbyatoxin A as members of a new class of tumor promoters. *Proceedings of the National Academy of Sciences of the United States of America* 78 (6): 3872-3876. https://doi.org/10.1073/pnas.78.6.3872

Gantar M., Sekar R. & Richardson L. L. 2009. — Cyanotoxins from black band disease of corals and from other coral reef environments. *Microbial Ecology* 58: 856-864. https://doi.org/10.1007/s00248-009-9540-x

Garcia-Pichel F. & Pringault O. 2001. — Cyanobacteria track water in desert soils. *Nature* 413: 380-381. https://doi.org/10.1038/35096640

Gaudêncio S. P. & Pereira F. 2015. — Dereplication: Racing to speed up the natural products discovery process. *Natural Product Reports* 32 (6): 779-810. https://doi.org/10.1039/c4np00134f

Gerwick W. H., Mrozek C., Moghaddam M. F. & Agarwal S. K. 1989. — Novel cytotoxic peptides from the tropical marine cyanobacterium *Hormothamnion enteromorphoides*. 1. Discovery, isolation and initial chemical and biological characterization of the hormothamnins from wild and cultured material. *Experientia* 45 (2): 115-21.

Gerwick W. H., Proteau P. J., Nagle D. G., Hamel E., Blokhin A. & Slate D. L. 1994. — Structure of curacin A, a novel antimitotic, antiproliferative, and brine shrimp toxic natural product from the marine cyanobacterium *Lyngbya majuscula*. *The Journal of Organic Chemistry* 59 (6): 1243-1245. https://doi.org/10.1021/jo00085a006

Giles E. C., Kamke J., Moitinho-Silva L., Taylor M. W., Hentschel U., Ravasi T. & Schmitt S. 2013. — Bacterial community profiles in low microbial abundance sponges. *FEMS Microbiology Ecology* 83 (1): 232-241. https://doi.org/10.1111/j.1574-6941.2012.01467.x

Griffiths D. J. & Saker M. L. 2003. — The Palm Island mystery disease 20 years on: a review of research on the cyanotoxin cylindrospermopsin. *Environmental Toxicology* 18 (2): 78-93. https://doi.org/10.1002/tox.10103

Guiry M. D. & Guiry G. M. 2020. — Algaebase. Worldwide Electronic Publication, National University of Ireland, Galway.

Guidi-Rontani C., Jean M. R. N., Gonzalez-Rizzo S., Bolte-Kluge S. & Gros O. 2014. — Description of new filamentous toxic Cyanobacteria (Oscillatoriales) colonizing the sulfidic periphyton mat in marine mangroves. *FEMS Microbiology Letters* 359 (2): 173-181. https://doi.org/10.1111/1574-6968.12551

Gutiérrez-Salcedo J. M., Cabarcas-Mier A. & Suárez-Mozo N. 2015. — First Chraracterization of the planktonic community in the northern sector of the joint regime area Jamaica-Colombia. *Boletín de Investigaciones Marinas y Costeras* 44 (2): 343-368.

Han B. N., Gross H., Goeger D. E., Mooberry S. L. & Gerwick W. H. 2006. — Aurilides B and C, cancer cell toxins from a Papua New Guinea collection of the marine cyanobacterium *Lyngbya majuscula*. *Journal of Natural Products* 69 (4): 572-575. https://doi.org/10.1021/np0503911

Harrigan G. G., Luesch H., Yoshida W. Y., Moore R. E., Nagle D. G., Paul V. J., Mooberry S. L., Corbett T. H. & Valeriote F. A. 1998. — Symplostatin 1: a dolastatin 10 analogue from the marine cyanobacterium *Symploca hydnoides*. *Journal of Natural Products* 61: 1075-1077. https://doi.org/10.1021/np980321c

Harada K.-I., Ohtami I., Iwamoto K., Suzyuki M., Watanabe M. F., Watanabe M. & Terao K. 1994. — Isolation of cylindrospermopsin from a cyanobacterium *Umezakia natans* and its screening method. *Toxicon* 32: 73-84.

Hernández-Becerril D. 2014. — Biodiversity of marine planktonic algae (Cyanobacteria, Prasinophyceae, Euglenophyta, Chrysophyceae, Dictyochophyceae, Eustigmatophyceae, Parmophyceae, Raphidophyceae, Bacillariophyta, Cryptophyta, Haptophyta, Dinoflagellata) in Mexico. *Revista Mexicana de Biodiversidad* 85 (1): 44-53. https://doi.org/10.7550/rmb.32037

Hertweck C. 2009. — Hidden biosynthetic treasures brought to light. *Nature Chemical Biology* 5: 450-452.

Hilborn E., Roberts V. A., Backer L., DeConno E., Egan J. S., Hyde J. B., Nicholas D. C., Wieger E. J., Billing L. M., Diorio M., Mohr M. C., Hardy J., Wade T. J., Yoder J. S. & Hlavsa M. C. 2014. — Algal Bloom-Associated Disease Outbreaks Among Users of Freshwater Lakes – United States, 2009-2010. *Morbidity and Mortality Weekly Report* 63 (1): 11-15.

Hirose E., Turon X., López-Legentil S., Erwin P. M. & Hirose M. 2012. — First records of didemnid ascidians harbouring Prochloron from Caribbean Panama: genetic relationships between Caribbean and Pacific photosymbionts and host ascidians. *Systematics and Biodiversity* 10 (4): 435-445. https://doi.org/10.1080/14772000.2012.735716

Hooper G. J., Orjala J., Schatzman R. C. & Gerwick W. H. 1998. — Carmabins A and B, new Lipopeptides from the Caribbean Cyanobacterium *Lyngbya majuscula*. *Journal of Natural Products* 61 (4): 529-533. https://doi.org/10.1021/np970443p

Hutabarat P. U. B., Nguyen X. H. & Suda S. 2018. — Black Band disease-related (BBD) *Cyanobacterium* from Okinawan corals. *Journal of Applied Phycology* 30 (6): 3197-203. https://doi.org/10.1007/s10811-018-1507-1

Jiménez J. I. & Scheuer P. J. 2001. — New Lipopeptides from the Caribbean Cyanobacterium *Lyngbya majuscula*. *Journal of Natural Products* 64 (2): 200-203. https://doi.org/10.1021/np000462q

Jiménez J. I., Vansach T., Yoshida W. Y., Sakamoto B., Pörzgen P. & Horgen F. D. 2009. — Halogenated Fatty Acid Amides and Cyclic Depsipeptides from an Eastern Caribbean Collection of the Cyanobacterium *Lyngbya majuscule*. *Journal of Natural Products* 72 (9): 1573-1578. https://doi.org/10.1021/np900173d

Jochimsen E. M., Carmichael W. W., An J. S., Cardo D. M., Cookson S. T., Holmes C. E., Antunes M. B., De Melo Filho D. A., Lyra T. M., Barreto V. S., Azevedo S. M. & Jarvis W. R. 1998. — Liver failure and death after exposure to microcystins at a hemodialysis center in Brazil. *The New England Journal of Medicine* 338 (13): 873-878. https://doi.org/10.1056/NEJM199803263381304

Kallifidas D., Kim J. H., Charlop-Powers Z., Feng Z. & Brady S. F. 2012. — Natural product biosynthetic gene diversity in geographically distinct soil microbiomes. *Applied and Environmental Microbiology* 78 (10): 3744-3752. https://doi.org/10.1128/aem.00102-12

Kerbrat A. S., Amzil Z., Pawlowiez R., Golubic S., Sibat M., Darius H. T., Chinain M. & Laurent D. 2011. — First Evidence of Palytoxin and 42-Hydroxy-palytoxin in the Marine Cyanobacterium *Trichodesmium*. *Marine Drugs* 9 (4): 543-560.

Kini S., Divyashree M., Mani M. K. & Mamatha B. S. 2020. — Algae and cyanobacteria as a source of novel bioactive compounds for biomedical applications, *in* Singh P. K., Kumar A., Singh V. K. & Shrivastava A. K. (eds), *Advances in Cyanobacterial Biology*. Academic Press, Cambridge: 173-194.

Kiryu Y., Landsberg J. H., Peters E. C., Tichenor E., Burleson C. & Perry N. 2015. — Pathological effects of cyanobacteria on sea fans in southeast Florida. *Journal of Invertebrate Pathology* 129: 13-27. https://doi.org/10.1016/j.jip.2015.04.007

Komárek J. 1989. — Studies on the cyanophytes of Cuba 7-9. *Folia Geobotanica et Phytotaxonomica* 24: 171-206. https://doi.org/10.1007/BF02853041

Kumar D., Kumari K., Jayaraj A., Kumar V., Kumar R. V., Dass S. K., Chandra R. & Singh P. 2020. — Understanding the binding affinity of noscapines with protease of SARS-CoV-2 for COVID-19 using MD simulations at different temperatures. *Journal of Biomolecular Structure and Dynamics* 39 (7): 1-14. https://doi.org/10.1080/07391102.2020.1752310

Kurmayer R., Dittmann E., Fastner J. & Chorus I. 2002. — Diversity of microcystin genes within a population of the toxic cyanobacterium *Microcystis* spp. in Lake Wannsee (Berlin, Germany). *Microbial Ecology* 43: 107-118.

Kwan J. C., Meickle T., Ladwa D., Teplitski M., Paul V. & Luesch H. 2011. — Lyngbyoic acid, a “tagged” fatty acid from a marine cyanobacterium, disrupts quorum sensing in *Pseudomonas aeruginosa*. *Molecular BioSystems* 7: 1205-1216. https://doi.org/10.1039/c0mb00180e

Lane A. L., Nyadong L., Galhena A. S., Shearer T. L., Stout E. P., Parry R. M., Kwasnik M., Wang M. D., Hay M. E., Fernández F. M. & Kubanek J. 2009. — Desorption electrospray ionization mass spectrometry reveals surface-mediated antifungal chemical defense of a tropical seaweed. *Proceedings of the National Academy of Sciences of the United States of America* 106 (18): 7314-7319. https://doi.org/10.1073/pnas.0812020106

Leão P. N., Pereira A. R., Liu W.-T., König G. M., Dorrestein P. C., Vasconcelos V. M. & Gerwick W. H. 2010. — Synergistic allelochemicals from a freshwater cyanobacterium. *Proceedings of the National Academy of Sciences* 107 (25): 11183-11188. https://doi.org/10.1073/pnas.0914343107

Leão P. N., Engene N., Antunes A., Gerwick W. H. & Vasconcelos V. 2012. — The chemical ecology of cyanobacteria. *Natural Products Reports* 29: 372-391. https://doi.org/10.1039/c2np00075j

Lesser M. P., Fiore C., Slattery M. & Zaneveld J. 2016. — Climate change stressors destabilize the microbiome of the Caribbean barrel sponge, *Xestospongia muta*. *Journal of Experimental Marine Biology and Ecology* 475: 1-18. https://doi.org/10.1016/j.jembe.2015.11.004

Leonard S. G., Sweeney T., Pierce K. M., Bahar B., Lynch B. P. & O’Doherty J. V. 2010. — The effects of supplementing the diet of the sow with seaweed extracts and fish oil on aspects of gastrointestinal health and performance of the weaned piglet. *Livestock Science* 134 (1-3): 135-138. https://doi.org/10.1016/j.livsci.2010.06.118

Li R., Carmichael W. W., Brittain S., Eaglesham G. K., Shaw G. R., Mahakhant A., Noparatnaraporn N., Yongmanitchai W., Kaya K. & Watanabe M. M. 2001. — Isolation and identification of the cyanotoxin cylindrospermopsin and deoxy-cylindrospermopsin from a Thailand strain of *Cylindrospermopsis raciborskii* (Cyanobacteria). *Toxicon* 39: 973-980.

Libis V., Antonovsky N., Zhang M., Shang Z., Montiel D., Maniko J., Ternei M. A., Calle P. Y., Lemetre C., Owen J. G. & Brady S. F. 2019. — Uncovering the biosynthetic potential of rare metagenomic DNA using co-occurrence network analysis of targeted sequences. *Nature Communications* 10: 3848. https://doi.org/10.1038/s41467-019-11658-z

Ling L. L., Schneider T., Peoples A. J., Spoering A. L., Engels I., Conlon B. P., Mueller A., Schäberle T. F., Hughes D. E., Epstein S., Jones M., Lazarides L., Steadman V. A., Cohen D. R., Felix C. R., Fetterman K. A., Millett W. P., Nitti A. G., Zullo A. M., Chen C. & Lewis K. 2015. — A new antibiotic kills pathogens without detectable resistance. *Nature* 517: 455-459. https://doi.org/10.1038/nature14098

Linington R. G., Clark B. R., Trimble E. E., Almanza A., Ureña L.-D., Kyle D. E. & Gerwick W. R. 2009. — Antimalarial Peptides from Marine Cyanobacteria: Isolation and Structural Elucidation of Gallinamide A. *Journal of Natural Products* 72 (1): 14-17. https://doi.org/10.1021/np8003529

Littler M. M., Littler D. S., Lapointe B. E. & Barile P. J. 2006. — Toxic Cyanobacteria (blue-green algae) associated with groundwater conduits in the Bahamas. *Coral Reefs* 25: 186.

Luesch H., Moore R. E., Paul V. J., Mooberry S. L. & Corbett T. H. 2001. — Isolation of dolastatin 10 from the marine cyanobacterium *Symploca* species VP642 and total stereochemistry and biological evaluation of its analogue symplostatin 1. *Journal of Natural Products* 64: 907-910. https://doi.org/10.1021/np010049y

Luzzatto-Knaan T., Garg N., Wang M., Glukhov E., Peng Y., Ackermann G., Amir A., Duggan B. M., Ryazanov S., Gerwick L., Knight R., Alexandrov T., Bandeira N., Gerwick W. H. & Dorrestein P. C. 2017. — Digitizing mass spectrometry data to explore the chemical diversity and distribution of marine cyanobacteria and algae. *eLife* 6: e24214. https://doi.org/10.7554/eLife.24214

Martins J., Leikoski N., Wahlsten M., Azevedo J., Antunes J., Jokela J., Sivonen K., Vasconcelos V., Fewer D. P. & Leão P. N. 2018. — Sphaerocyclamide, a prenylated cyanobactin from a *Sphaerospermopsis* sp. LEGE 00249. *Scientific Reports* 8: 1453739. https://doi.org/10.1038/s41598-018-32618-5

Mazmouz R., Chapuis-Hugon F., Mann S., Pichon V., Méjean A. & Ploux O. 2010. — Biosynthesis of Cylindrospermopsin and 7-Epicylindrospermopsin in *Oscillatoria* sp. Strain PCC 6506: Identification of the cyr Gene Cluster and Toxin Analysis. *Applied and Environmental Microbiology* 76: 4943-4949. https://doi.org/10.1128/AEM.00717-10

Medina R. A., Goeger D. E., Hills P., Mooberry S. L., Huang N., Romero L. I., Ortega-Barría E., Gerwick W. H. & McPhail K. L. 2008. — Coibamide A, a potent antiproliferative cyclic depsipeptide from the panamanian marine cyanobacterium *Leptolyngbya* sp. *Journal of the American Chemical Society* 130 (20): 6324-6325. https://doi.org/10.1021/ja801383f

Méjean A., Mann S., Maldiney T., Vassiliadis G., Lequin O. & Ploux O. 2009. — Evidence that biosynthesis of the neurotoxic alkaloids anatoxin-a and homoanatoxin-a in the cyanobacterium *Oscillatoria* PCC 6506 occurs on a modular polyketide synthase initiated by l-proline. *Journal of the American Chemical Society* 131 (22): 7512-7513. https://doi.org/10.1021/ja9024353

Mevers E., Byrum T. & Gerwick W. H. 2013. — Parguerene and precarriebowmide, two classes of lipopeptides from the marine cyanobacterium moorea producens. *Journal of Natural Products* 76 (9): 1810-1814. https://doi.org/10.1021/np400347f

Morrow K. M., Paul V. J., Liles M. R. & Chadwick N. E. 2011. — Allelochemicals produced by Caribbean macroalgae and cyanobacteria have species-specific effects on reef coral microorganisms. *Coral Reefs* 30: 309-320. https://doi.org/10.1007/s00338-011-0747-1

Navarro A., Corredor J. E., Moreil J. & Armstrong R. A. 2000. — Distribution of tbe cyanophyte *Trichodesmium* (Oscillatoriaceae) in the eastern Caribbean Sea: infuence of the Orinoco River. *Revista de Biología Tropical* 48 (Sup. 1): 115-124.

Nogle L. M. & Gerwick W. H. 2003. — Diverse Secondary Metabolites from a Puerto Rican Collection of *Lyngbya majuscula. Journal of Natural Products* 66 (2): 217-220. https://doi.org/10.1021/np020332c

Nübel U., Garcia-Pichel F. & Muyzer G. 2000. — The halotolerance and phylogeny of cyanobacteria with tightly coiled trichomes (*Spirulina* Turpin) and the description of *Halospirulina tapeticola* gen. nov., sp. nov. *International Journal of Systematic and Evolutionary Microbiology* 50: 1265-1277.

Nunnery J. K., Mevers E. & Gerwick W. 2010. — Biologically active secondary metabolites from marine cyanobacteria. *Current Opinion in Biotechnology* 21 (6): 787-793. https://doi.org/10.1016/j.copbio.20

Nunnery J. K., Engene N., Byrum T. & Gerwick W. 2012. — Biosynthetically Intriguing Chlorinated Lipophilic Metabolites from Geographically Distant Tropical Marine Cyanobacteria. *The Journal of Organic Chemistry* 77 (9): 4198-4208. https://doi.org/10.1021/jo300160e

Ohtani I., Moore R. E. & Runnegar M. T. C. 1992. — Cylindrospermopsin, a potent hepatotoxin from the blue-green-alga *Cylindrospermopsis raciborskii. Journal of the American Chemical Society* 114: 7941-7942.

Olson N. D. & Lesser M. P. 2013. — Diazotrophic diversity in the Caribbean coral, *Montastraea cavernosa. Archives of Microbiology* 195: 853-859. https://doi.org/10.1007/s00203-013-0937-z

Orjala J. & Gerwick W. H. 1996. — Barbamide, a chlorinated metabolite with molluscicidal activity from the Caribbean cyanobacterium *Lyngbya majuscula. Journal of Natural Products* 59 (4): 427-430. https://doi.org/10.1021/np960085a

Orjala J. & Gerwick W. H. 1997. — Two quinoline alkaloids from the Caribbean cyanobacterium *Lyngbya majuscule. Phytochemistry* 45 (5): 1087-1090.

Osswald J., Rellán S., Gago A. & Vasconcelos V. 2009. — Production of anatoxin-a by cyanobacterial strains isolated from Portuguese fresh water systems. *Ecotoxicology* 18: 1110-1115. https://doi.org/10.1007/s10646-009-0375-5

Page C. & Willis B. 2006. — Distribution, host range and large-scale spatial variability in black band disease prevalence on the Great Barrier Reef, Australia. *Diseases of Aquatic Organisms* 69 (1): 41-51. https://doi.org/10.3354/dao069041

Park H.-D., Watanabe M. F., Harada K.-I., Nagai H., Suzuki M. & Hayashi H. 1993. — Hepatotoxin (microcystin) and neurotoxin (anatoxin-a) contained in natural blooms and strains of cyanobacteria from Japanese freshwaters. *Natural Toxins* 1: 353-360. https://doi.org/10.1002/nt.2620010606

Paul V. J., Thacker R. W., Banks K. & Golibic S. 2005. — Benthic cyanobacterial bloom impacts the reefs of South Florida (Broward County, USA). *Coral Reefs* 24: 693-697. https://doi.org/10.1007/s00338-005-0061-x

Pearson L., Mihali T., Moffitt M., Kellmann R. & Neilan B. 2010. — On the chemistry, toxicology and genetics of the cyanobacterial toxins, microcystin, nodularin, saxitoxin and cylindrospermopsin. *Marine Drugs* 8 (5): 1650-1680. https://doi.org/10.3390/md8051650

Pereira A. R., Kale A. J., Fenley A. T., Byrum T., Debonsi H. M., Gilson M. K., Valeriote F. A., Moore B. S. & Gerwick W. H. 2012. — The carmaphycins: new proteasome inhibitors exhibiting an α, β-epoxyketone warhead from a marine cyanobacterium. *ChemBioChem* 13 (6): 810-817. https://doi.org/10.1002/cbic.201200007

Plavsic M., Terzic S., Ahel M. & Van Den Berg C. M. G. 2004. — Folic acid in coastal waters of the Adriatic Sea. *Marine and Freshwater Research* 53 (8): 1245-1252. https://doi.org/10.1071/MF02044

Puyana M., Acosta A., Bernal-Sotelo K., Velásquez-Rodríguez T. & Ramos F. 2015. — Spatial scale of cyanobacterial blooms in Old Providence Island, Colombian Caribbean. *Universitas Scientiarum* 20 (1): 83-105. https://doi.org/10.11144/Javeriana.SC20-1.sscb

Ramos V., Morais J., Castelo-Branco R., Pinheiro A., Martins M., Regueiras A., Pereira A. L., Lopes V., Frazão B., Gomes D., Moreira C., Costa M. S., Brûle S., Faustino S., Martins R., Saker M., Osswald J., Leão P. N. & Vasconcelos V. 2018. — Cyanobacterial diversity held in mBRCs as a promising biotechnological asset: the case study of the newly established LEGE Culture Collection. *Journal of Applied Phycology* 30: 1437-1451. https://doi.org/10.1007/s10811-017-1369-y

Rantala-Ylinen A., Känä S., Wang H., Rouhiainen L., Wahlsten M., Rizzi E., Berg K., Gugger M. & Sivonen K. 2011. — Anatoxin-a synthetase gene cluster of the cyanobacterium *Anabaena* sp. strain 37 and molecular methods to detect potential producers. *Applied and Environmental Microbiology* 77 (20): 7271-7278. https://doi.org/10.1128/AEM.06022-11

Rastogi R. P., Richa Singh R. P., Singh S. P. & Häder D.-P. 2010. — Photoprotective compounds from marine organisms. *Journal of Industrial Microbiology and Biotechnology* 37 (6): 537-558. https://doi.org/10.1007/s10295-010-0718-5

Rego A., Sousa A. G. G., Santos J. P., Pascoal F., Canário J., Leão P. N. & Magalhães C. 2020. — Diversity of bacterial biosynthetic genes in maritime antarctica. *Microorganisms* 8 (2): 279. https://doi.org/10.3390/microorganisms8020279

Rejmánková E., Komárek J. & Komárková J. 2004. — Cyanobacteria a neglected component of biodiversity: patterns of species diversity in inland marshes of northern Belize (Central America). *Diversity and Distributions* 10 (3): 189-199. https://doi.org/10.1111/j.1366-9516.2004.00077.x

Ribeiro T., Lemos F., Preto M., Azevedo J., Leão P., Campos A., Vitorino R., Vasconcelos V. & Urbatzka R. 2017. — Cytotoxicity of portoamides in human cancer cells and analysis of the molecular mechanisms of action. *PLOS ONE* 12 (12): e0188817. https://doi.org/10.1371/journal.pone.0188817

Richardson L. L., Stanić D., May A., Brownell A., Gantar M. & Campagna S. R. 2014. — Ecology and Physiology of the Pathogenic Cyanobacterium *Roseofilum reptotaenium*. *Life* 4 (4): 968-987. https://doi.org/10.3390/life4040968

Rohani-Ghadikolaei K., Abdulalian E. & Ng W. K. 2012. — Evaluation of the proximate, fatty acid andmineral composition of representative green, brown and red seaweeds from the Persian Gulf of Iran aspotential food and feed resources. *Journal of Food Science and Technology* 49: 774-780.

Rosales N., Jonte L. & Morales E. 2006. — Crecimiento y composiciónbioquímica de *Synechococcus* sp. modulados por el nitratode sodio. *Boletín del Centro de Investigaciones Biológicas* 40 (2): 120-132.

Rouhiainen L., Sivonen K., Buikema W. J. & Haselkorn R. 1995. — Characterization of toxin-producing cyanobacteria by using an oligonucleotide probe containing a tandemly repeated heptamer. *Journal of Bacteriology* 177: 6021-6026.

Seifert M., Mcgregor G., Eaglesham G., Wickramasinghe W. & Shaw G. 2007. — First evidence for the production of cylindrospermopsin and deoxy-cylindrospermopsin by the freshwater benthic cyanobacterium, *Lyngbya wollei* (Farlow ex Gornont) Speziale and Dyck. *Harmful Algae* 6: 73-80.

Sekar S. & Muruganandham C. 2007. — Phycobiliproteins as a commodity: trends in applied research, patents and commercialization. *Journal of Applied Phycology* 20 (2): 113-136. https://doi.org/10.1007/s10811-007-9188-1

Sivonen K. & Jones G. 1999. — Toxinas de cianobacterias. Cianobacterias tóxicas en el agua: una guía sobre sus consecuencias para la salud pública. *Seguimiento y Gestión* 1: 43-112.

Sivonen K., Niemelä S., Niemi R. M., Lepistö L., Luoma T. H. & Räsänen L. A. 1990. — Toxic cyanobacteria (blue-green algae) in Finnish fresh and coastal waters. *Hydrobiologia* 190: 267-275.

Skulberg O. M., Carmichael W. W., Anderson R. A., Matsunaga S., Moore R. E. & Skulberg R. 1992. — Investigations of a neurotoxic oscillatorialean strain (cyanophyceae) and its toxin. Isolation and characterization of homoanatoxin-a. *Environmental Toxicology and Chemistry* 11: 321-329. https://doi.org/10.1002/etc.5620110306

Spoof L., Berg K. A., Rapala J., Lahti K., Lepisto L., Metcalf J. S., Codd G. A. & Meriluoto J. 2006. — First observation of cylindrospermopsin in *Anabaena lapponica* isolated from the boreal environment (Finland). *Environmental Toxicology* 21: 552-560.

Stanić D., Oehrle S., Gantar M. & Richardson L. L. 2011. — Microcystin production and ecological physiology of Caribbean black band disease cyanobacteria. *Environmental Microbiology* 13 (4): 900-910. https://doi.org/10.1111/j.1462-2920.2010.02388.x

Steinbüchel A., Fuchtenbusch B., Gorenflo V., Hein S., Jossek R., Langenbach S. & Rehm B. H. A. 1997. — Biosynthesis of polyesters in bacteria and recombinantorganisms. *Polymer Degradation and Stability* 59: 177-182.

Stielow S. & Ballantine D. L. 2003. — Benthic cyanobacterial, *Microcoleus lyngbyaceus*, blooms in shallow, inshore Puerto Rican seagrass habitats, Caribbean Sea. *Harmful Algae* 2 (2): 127-133. https://doi.org/10.1016/S1568-9883(03)00007-6

Sussman M., Bourne D. G. & Willis B. L. 2006. — A single cyanobacterial ribotype is associated with both red and black bands on diseased corals from Palau. *Diseases of Aquatic Organisms* 69 (1): 111-118. https://doi.org/10.3354/dao069111

Taori K., Paul V. J. & Luesch H. 2008. — Structure and activity of largazole, a potent antiproliferative agent from the floridian marine cyanobacterium *Symploca* sp. *Journal of the American Chemical Society* 130: 1806-1807. https://doi.org/10.1021/ja7110064

Tavera R., Novelo E. & López S. 2013. — Cyanoprokaryota (Cyanobacteria) in karst environments in Yucatán, Mexico. *Botanical Sciences* 91 (1): 27-52. https://doi.org/10.17129/botsci.401

Teixeira M. Da G., Costa M. Da C., De Carvalho V. L. P., Pereira M. Dos S. & Hage E. 1993. — Gastroenteritis epidemic in the area of the Itaparica Dam, Bahia, Brazil. *Bulletin of the Pan American Health Organization* 27: 244-253.

Thacker R. W. & Paul V. J. 2004. — Morphological, chemical, and genetic diversity of tropical marine cyanobacteria *Lyngbya* spp. and *Symploca* spp. (Oscillatoriales). *Applied and Environmental Microbiology* 70 (6): 3305-3312. https://doi.org/10.1128/AEM.70.6.3305-3312.2004

Tidgewell K., Clark B. R. & Gerwick W. H. 2010. — The natural products chemistry of cyanobacteria. *Comprehensive Natural Products* II: 141-181.

Vasconcelos V. 2015. — Global changes and the new challenges in the research on cyanotoxin risk evaluation. *Limnetica* 34 (1): 149-158. https://doi.org/10.23818/limn.34.12

Vasconcelos V. M. & Pereira E. 2001. — Cyanobacteria diversity and toxicity in a wastewater treatment plant (Portugal). *Water Research* 35 (5): 1354-1357. https://doi.org/10.1016/S0043-1354(00)00512-1

Villareal T. A. 1995. — Abundance and photosynthetic characteristics of *Trichodesmium* spp. along the Atlantic barrier reef at carrie bow cay, Belize. *Marine Ecology* 16 (3): 259-271. https://doi.org/10.1111/j.1439-0485.1995.tb00410.x

Voss J. D., Mills D. K., Myers J. L., Remily E. R. & Richardson L. L. 2007. — Black Band Disease Microbial Community Variation on Corals in Three Regions of the Wider Caribbean. *Microbial Ecology* 54: 730-739. https://doi.org/10.1007/s00248-007-9234-1

Watrous J. D. & Dorrestein P. C. 2011. — Imaging mass spectrometry in microbiology. *Nature Reviews Microbiology* 9 (9): 683-694. https://doi.org/10.1038/nrmicro2634

Wiese M., D'agostino P. M., Mihali T. K., Moffitt M. C. & Neilan B. A. 2010. — Neurotoxic alkaloids: saxitoxin and its analogs. *Marine Drugs* 8 (7): 2185-2211. https://doi.org/10.3390/md8072185

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