Ethnobotanical Survey and Biological Screening of Medicinal Plants from Vanuatu

Dissertation

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Für meinen Opa.

Gewisse Bücher scheinen geschrieben zu sein, nicht damit man daraus lerne, sondern damit man wisse, daß der Verfasser etwas gewußt hat“

– J. W. von Goethe, *Maximen und Reflexionen* (1833)

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SUMMARY

Vanuatu, a Pacific archipelago, 2,000 km east of northern Australia, is the world's most diverse nation in terms of the number of actively spoken indigenous languages per head of population. The resulting cultural diversity and its great biodiversity compared to other islands in this region made it a unique target for an ethnobotanical survey.

During five months of fieldwork 130 plant species used in traditional medicine were documented together with 420 individual use reports. Along with the voucher specimen, information on treatment methods, healing concepts and diseases was collected, and subsequently qualitatively and quantitatively analysed. Dermatological and gastrointestinal complaints, followed by respiratory ailments and diseases related to the urogenital system were the categories most commonly indicated, reflecting a prevalence of these illnesses in the study areas.

18 plants with indications towards immunomodulatory effects were selected on site and material of 21 plant parts was collected and subsequently screened for antibacterial, antifungal, and antiprotozoal activities. In addition the extracts were subjected to a detailed analysis on cytotoxic effects towards human cancer cell lines, designed as a smaller version of the NCI60 screen. Patterns of relative drug sensitivity and resistance reflect possible mechanisms of drug action, which gives the opportunity for molecular-targeted anticancer drug discovery. In total the screenings yielded moderate antibacterial activity for one and antifungal for four extracts, five extracts were shown to be moderately active against *Trypanosoma brucei brucei*, three extracts have displayed good and specific activities against *Trypanosoma cruzi,* and three extracts significantly killed *Plasmodium falciparum*. Intriguingly 15 plant extracts exhibited strong cytotoxic effects specific for only one cancer cell line.

Also a phytochemical investigation was carried out for *Baccaurea stylaris* MUELL. ARG. (Phyllanthaceae) leading to the discovery of seven pure compounds, one of them a new diterpenoid with neoclerodane-skeleton.

SAMARI

Vanuatu, wan aelan long pasifik wanem i klosap ostrelia, hemia wan kantri wetem plante we plante derfen lanwis. Fromwe i gat fulap lanwis, i gat fulap defren kalja, tu mo i gat plante kaenkaen planem; olsem i no gat long narafala aelan long Saot si, taswe hemia wan gudfala ples blong mekem wan risej long lif meresin mo long Kastom blong kantri ia.

Long wan filwok kasem faef manis, tok save long 130 planem wanem oli yusum long kastom meresin i bin klektem long wan kleksen kasem 420 ripot. Olgeta planem oli bin draem, bin gluim long lif pepa mo bin givim nem long letin. Tugeta wetem wanem kaen sik i gat long

aelan, tok save long hao olgeta hila oli tritim evri kaen sik bin klektem finis. Folem se wan save faenemaot, taswe long Vanuatu i gat plante sik blong skin mo blong basket blong sitsit, afta i gat fulap sik blong lang mo basket blong pispis mo sik blong mama.
18 planem wanem oli save tritim ol kaen sik olsem fiva o kof bin jusumaot mo 21 pat blong planem nomo oli bin klektem mo wan skrin i bin mekem blong faenemaot sapos oli save hilim ol kaen sik long Vanuatu olsem kansa, fiva o kof. Blong faenem aot long kansa wan bigfala skrin i bin mekem mo difren kaen kansa oli bin jekem ap. Riseja i save faenem wan planem wanem yu save yusum blong tritim sora blong devel, fo blong sik olsem kof, faef planem oli save tritim wan sik long afrika oli singaotem sik blong slip long hem, tri planem oli save yusum sipos oli kasem wan sik wanem i nogud mo oli long saot amerika singaotem jagas long hem, tri planem oli gud taem we yu kasem malaria mo fiftin planem riseja oli save yusum blong mekem wan meresin blong kansa.
Wan planem nomo, olgeta long Aneityum oli singaotem niththschaub long hem, hemi bin putum long wan wota olsem alikol traem faenemaot, wanem kaen tingting blong planem ia i mekem hemia wan meresin.

ZUSAMMENFASSUNG

Vanuatu, ein pazifischer Archipel, 2.000 km östlich von Nord-Australien gelegen, ist das Land mit der weltweit pro Kopf größten Vielfalt an aktiv gesprochenen indigenen Sprachen. Die daraus resultierende kulturelle zusammen mit einer im Vergleich zu anderen Inseln in dieser Region enormen Bio-Diversität, machte es zu einem einzigartigen Ziel für eine ethnobotanische Studie.
Während einer fünfmonatigen Feldstudie wurden 130 in der traditionellen Medizin Verwendung findende Pflanzenspezies zusammen mit 420 Einzel-Nutzungsberichten dokumentiert. Neben Herbarexemplaren wurden ebenfalls Informationen zu Behandlungsmethoden, Heilungskonzepten und Krankheiten gesammelt und die ethnobotanischen Daten anschließend qualitativ und quantitativ analysiert. Dermatologische und gastrointestinale Beschwerden, gefolgt von Erkrankungen des Respirationstraktes und Krankheiten, welche dem Urogenitalsystem zugeordnet werden können, waren die Kategorien, für welche die meisten Indikationen genannt wurden, welches eine Prävalenz dieser Krankheiten im Untersuchungsgebiet widerspiegelt.
18 Pflanzen mit Indikationen in Richtung immunmodulatorischer Aktivität wurden vor Ort ausgewählt und insgesamt 21 Pflanzenteile gesammelt. Daraus gewonnene Extrakte wurden anschließend auf antibakterielle, antifungale und antiprotozoale Eigenschaften hin gescreent. In einer kleinen Version des NCI60 Screenings wurden die Extrakte außerdem einer detaillierten Analyse ihrer cytotoxischen Aktivität gegenüber humanen Krebszell-Linien unterzogen. Sensitivitäts- und Resistenzmuster gegenüber einem Arzneistoff spiegeln dabei

mögliche Wirkungsmechanismen dieses Stoffes auf molekularer Ebene wider, was die gezielte molekülgerichtete Suche nach Antitumor-Wirkstoffen ermöglicht.

Insgesamt zeigten ein Extrakt moderate antibakterielle und vier Extrakte moderate antifungale Aktivitäten, fünf Extrakte wiesen moderate Aktivität gegenüber *Trypanosoma brucei brucei* auf, drei Extrakte zeigten gute und spezifische Aktivität gegenüber *Trypanosoma cruzi* und drei Extrakte waren sehr effektiv gegenüber *Plasmodium falciparum*. 15 Extrakte zeigten gute cytotoxische Effekte spezifisch für nur eine Zell-Linie.

Für die Pflanze *Baccaurea stylaris* MUELL. ARG. (Phyllanthaceae) wurde außerdem eine phytochemische Untersuchung durchgeführt, welche zur Isolierung von sieben Reinsubstanzen führte, eine davon ein neues Diterpenoid mit Neoclerodanskelett.

ABBREVIATIONS

$[\alpha]_D$	specific optical rotation
µg	microgram
µL	microliter
^{13}C NMR	carbon 13 NMR spectroscopy
^{1}H NMR	proton NMR spectroscopy
2D	two dimensional
786-0	human renal adenocarcinoma cell line
A2780	human ovarian cancer cell line
A549	human epithelial lung carcinoma cell line
Aβ	amyloid *beta*
ACh	acetylcholine
AChE	acetylcholinesterase
ACN	acetonitrile
AD	*Alzheimer's* disease
AIDS	Acquired Immune Deficiency Syndrome
ANOVA	analysis of variance
ATCC	American Type Culture Collection
BChE	butyrylcholinesterase
BSA	bovine serum albumin
Ca	*Candida albicans*
$CDCl_3$	deuterated chloroform
CFU	colony forming unit
ChAT	choline acetyltransferase
CHN	Chinese Herb Nephropathy
CML	chronic myelogenous leukaemia
CNS	Central Nervous System
COSY	correlated spectroscopy (2D NMR method)
COX	cyclooxygenase
CPRG	chlorophenolred ß-D-galactopyranoside
DCM	dichloromethane
DMSO	dimethylsulfoxide
E. coli	*Escherichia coli*
EGF	epidermal growth factor
EGFR	epidermal growth factor receptor
EI-MS	electron impact-mass spectrometry

EtOAc	ethyl acetate
EtOH	ethanol
F_{IC}	factor of informant consensus
FID	free induction decay
FAO	Food and agriculture organization of the United Nations
HCMV	human cytomegalovirus
HeLa	human cervical cancer cell line
HepG2	human liver cancer cell line
HIV	human immunodeficiency virus
HL-60	human promyelocytic leukaemia cell line
HMBC	heteronuclear multiple bond correlation (2D NMR method)
HONE-1	human nasopharyngeal cancer cell line
HPLC	high performance liquid chromatography
HREIMS	high resolution electron impact mass spectrometry
HSQC	heteronuclear single quantum correlation (2D NMR method)
HSV	Herpes simplex virus
HT-29	human colorectal adenocarcinoma cell line
IC_{50}	50% inhibition concentration
IPCB	International Program of Cooperation for Biodiversity
K-562	human CML cell line
KB	human HeLa contaminant cell line
LaCiTo	Laboratoire de Langues et civilisations à tradition orale
LDH	lactate dehydrogenase
Li	*Leishmania infantum*
LREIMS	low resolution electron impact mass spectrometry
min.	minute
m.p.	melting point
Mc	*Microsporum canis*
MCF7	human breast adenocarcinoma cells (metastatic site: pleural effusion)
MeOH	methanol
MHz	megahertz
MIC	minimum inhibitory concentration
MRC-5 SV2	immortal (SV40-transformed) human foetal lung fibroblast cell line
MRSA	methicillin-resistant *Staph. aureus*
MTT	3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide
NCI	National Cancer Institute, Bethesda, MD, USA
NCI-H522	human non-small lung cancer cell line

No.	number
NSCLL-N6	human non-small lung bronchiopulmonary cancer cell line
NUCG	human stomach cancer cell line
NMDA	*N*-methyl-*D*-aspartate
NMR	nuclear magnetic resonance
NOESY	nuclear Overhauser enhanced spectroscopy (2D NMR method)
NP	normal phase
OD	optical density
ORSTOM,	L'institut français de recherché scientifique pour le développement
OVCAR-3:NIH	human ovarian adenocarcinoma cell line
p.	page
P-388	murine lymphoma cell line
PC-3	human prostate adenocarcinoma cell line (metastatic site: bone)
PE	petrol ether
Pf GHA	*Plasmodium falciparum* 1/GHA strain
PNG	Papua New Guinea
ROESY	rotating frame NOESY (2D NMR method)
RSV	respiratory syncytial virus
RT	room temperature
Sa	*Staph*(*ylococcus*) *aureus*
SD	standard derivation
SDS	Sodium dodecyl sulphate
SK-Mel-28	human malignant melanoma cell line
SK-OV-3	human ovarian adenocarcinoma cell line
SKVLB-1	human ovarian cancer cell line
SNB-19	human glioblastoma cell line
sp.	species
spp.	species (plural)
Staph.	*Staphylococcus*
SV40	Simian virus 40
Tb	*Trypanosoma brucei*
Tc	*Trypanosoma cruzi*
TCM	Traditional Chinese Medicine
TLC	thin layer chromatography
Tr	*Trichophyton rubrum*
TSA	Tryptone soy agar
TSB	Tryptone soy broth

UO-31	human renal cancer cell line
UR	use report
UV	ultraviolet
VIS	visible
VLC	vacuum liquid chromatography
VSV	vesicular stomatitis virus
WHO	World Health Organization

INTRODUCTION

1. PLANTS IN TRADITIONAL AND MODERN MEDICINE

The empirical use of plants as medicine can be traced back over five millennia to ancient documents of early civilizations such as in China, Egypt, India, and the Near East, but is certainly as old as mankind.[1] These medicines initially took the form of crude drugs such as tinctures, teas, poultices, powders, and other herbal formulations.[2]

Although indigenous knowledge systems rapidly disappear under the influence of Western culture, the World Health Organization (WHO) estimates that even today 80% of the world's population exclusively rely on traditional medicine; especially in developing countries resources to build up a primary health care system are still lacking.[3] In industrialised countries medicinal plant research had its ups and downs in the last decades. It was not until the early 19th century that the isolation of active principles marked a new era in the use of medicinal plants and one particular landmark, the discovery of the alkaloid quinine from *Cinchona* bark by the French scientists Caventou and Pelletier in 1820 led to a new attention towards plants from the New World. An interesting fact is that *Cinchona* was once provided by Peruvian indigenous people to Spanish conquerors. The Peruvians used it as a treatment of intermittent fever or malaria since generations and quinine and the later discovered quinidine and their analogues, isomers and (semi)synthetics are still widely used due to their ability to treat malaria, heart conditions, and other ailments, being a blessing for millions suffering.[4] In the following "expedition boom" researchers dispersing all over the world scoured almost impenetrable jungles in search of new medicines in journeys sometimes lasting for years. The industrial revolution and progress made in organic chemistry somehow slowed this development causing a preference of synthetic drugs in western communities. These soon got an excellent reputation, originating from the fact that pure compounds could easily be obtained and structural modifications yielding in more active and less toxic and therefore safer drugs could simply be performed. But in recent years the tide has turned and the interest in alternative medicine and natural products, especially of plant origin revived due to several reasons, namely conventional medicine can cause strong side effects or can be inefficient if incorrectly used and the term "natural" products falsely pretends that they are generally harmless.[5] The WHO considers that in Germany for example 90% of the population have used a natural remedy at least once in their life and the global market for herbal medicines currently stands at over US$ 60 billion per annum (2003) and is growing steadily. But the organization also cautions against the dangers of unregulated or inappropriate use of complementary medicine and stresses the need for more stringent controls of herbal preparations by pointing out two examples: in Belgium at least 100 female patients

developed Chinese Herb Nephropathy (CHN), an extensive intestinal fibrosis of the kidneys after having followed a weight-loss regimen that included the use of a herbal preparation made from the wrong species. The prescribed Chinese herb “Fangji” (*Stephania tetrandra,* Menispermaceae) was, in fact, inadvertently replaced by another Chinese herb, namely “Guang fangji” (*Aristolochia fangchi*, Aristolochiaceae) containing aristolochic acid, a well known nephrotoxic. In the second example, the herb “Ma Huang” (*Ephedra sinica*, Ephedraceae), widely used in Traditional Chinese Medicine (TCM) to treat respiratory congestion, was marked as a dietary aid in the US. Over-dosage led to at least a dozen deaths, heart attacks, and strokes.[6]

However at least 119 chemical substances from 90 plant species are important drugs used all over the world, many of them containing compounds derived from or modelled after naturally occurring lead molecules[7] and 74% of these come from traditional medicinal plants.[3] Of the 252 drugs considered as basic and essential by the WHO, 11% are exclusively of plant origin e.g. digoxin from *Digitalis spp*. (Plantaginaceae), quinine and quinidine from *Cinchona spp*. (Rubiaceae), vincristine and vinblastine from *Catharanthus roseus* (Apocynaceae), or morphine and codeine from *Papaver somniferum* (Papaveraceae), furthermore a significant number are synthetic drugs obtained from natural precursors.[5]

It is further estimated that 60% of anti-cancer and anti-infectious drugs already on the market or under clinical trials are of natural origin.[8] Indeed the already mentioned *Catharanthus*-alkaloids are two of the most important cancer chemotherapeutic agents currently in use, followed by the podophyllotoxin-derivative etoposide, isolated from *Podophyllum peltatum* (Berberidaceae). In 2000 worldwide over ten million new cases of cancer occurred and six million suffering died. A 22% increase was observed for cancer incidence as well as mortality since 1990,[9] making it to the second leading cause of death in high income countries, surpassed only by cardiovascular diseases (WHO fact-sheet No. 310, The top ten causes of death, 2007). There have been several efforts to discover new anticancer agents of plant origin, the most prominent is the National Cancer Institute (NCI) program initiated by Dr. Jonathan Hartwell. It was him too, who between 1969 and 1971 assembled a list containing over 3,000 different species of plants traditionally used against cancer describing their uses in considerable detail, remaining today as the only compilation of the ethnomedicinal use of anticancer plants.[10-18] Altogether, the NCI, Bethesda, MD, U.S.A. has screened 33,000 plant samples for anti-tumour and more than 50,000 for anti-HIV activity but they have not been screened for other pharmacological activities yet.[1] However, of the estimated 350,000 plant species worldwide only a small percentage has been investigated phytochemically and an even smaller percentage has been properly studied in terms of their pharmacological properties.[5]

But what makes plants produce biologically active secondary metabolites? As entrenched organisms with no escapism, plants had to develop other mechanisms to defend themselves against microbial attack and predators, including morphological adaptations such as thorns or spikes, as well as chemical such as toxic or irritant secondary metabolites. Competition for light, space, pollinators, and nutritients also influences the spectrum of these substances. Lacking a growth pause as in winter in temperate zones, tropical plants always have to be defensive and due to the greater biodiversity in tropical regions plants are more exposed to competition. For these reasons a greater portion of tropical plants contains potentially useful compounds,[19] so tropical forests are most likely the best source of potentially active natural products.

2. SCOPE AND OBJECTIVES OF THE PRESENT WORK

The aims of this project were to collect and preserve ethnobotanical knowledge and to screen some selected plants whose ethnobotanical use, and/or taxonomic affiliation suggested promising immunomodulatory activities in several biological assays, and a detailed phytochemical investigation of a selected plant.

Vanuatu has been chosen as study area due to its large linguistic and cultural diversity combined with a great biodiversity compared to other islands in this region. In addition, only little ethnobotanical research has been conducted in this place yet, the ethnopharmacopoeia of some islands has actually never been studied so far.

The screening regimen performed in this thesis included:

(1) Antibacterial, antifungal, and antiprotozoal assays,

(2) a cytotoxicity screening on a variety of cell lines, a smaller version of the NCI60 disease oriented screening program developed by the National Cancer Institute (NCI),

(3) a screening for drugs which may be effective against *Alzheimer's* disease, and

(4) assays targeting at various anti-inflammatory processes (ongoing).

THEORETICAL PART

1. VANUATU

1.1 GEOGRAPHY, GEOLOGY, AND CLIMATE

Vanuatu (meaning “our land”; the word for land *vanua*, *fanua* or *fenua* is one of the most common Pacific words) is a Y-shaped archipelago about 2,000 km east of Northern Australia located between latitude 12° and 23° south and longitude 166° (Fig. 2) (

Fig. 1 Map of Vanuatu. Research areas are marked with arrows (from LaCiTo). Its closest neighbours are the Solomon Islands (170 km north), New Caledonia (230 km south), and Fiji (800 km east). The total area of Vanuatu is approximately 860,000 km^2, of which only 12,334 km2 (1.4%) are land, consisting of about 80 islands and numerous islets of which 67 are inhabited. Only twelve islands can be regarded as significant in terms of economy and population and the eight largest islands contribute 87% of the total land area.[20, 21] The capital city, Port Vila, is located on the island of Efate.

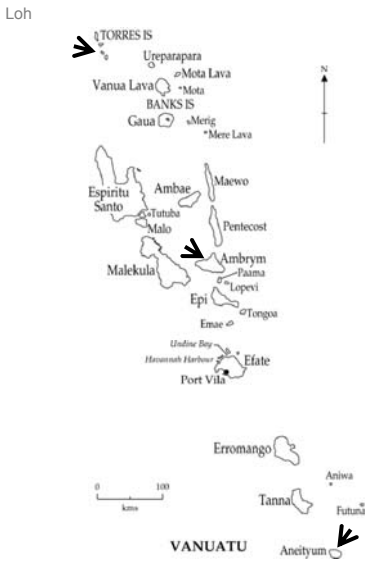

Fig. 1 Map of Vanuatu. Research areas are marked with arrows (from LaCiTo)

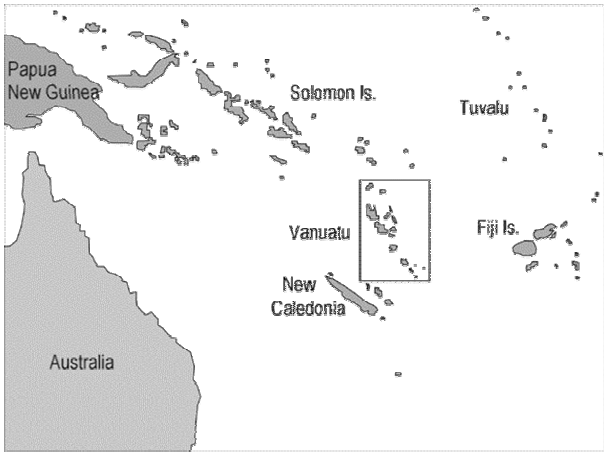

Fig. 2 Location of Vanuatu in the Pacific (from LaCiTo)

Geologically young, the islands mainly comprise volcanic mountains, but some raised reef islands and a few low coral islands and reefs are also found. Vanuatu is part of the Pacific ring of fire and is an island arc, a result of tectonic activity, as a subduction zone of around 1,500 km long marks the convergence of the Indian-Australian tectonic plate and the Pacific plate. Corollaries of the tectonic activity are the numerous volcanoes which contribute to the very active seismicity experiences in this region.[22]

The climate varies from wet tropical in the northern part with about 4,000 mm annual rainfall to dryer subtropical climate in the southern part with less than 2,000 mm rainfall per year.[23] Average temperatures range between 21 and 27°C and average humidity between 75 and

80%.[21] During the wet (and warmer) season from November to April an average of four to six tropical cyclones of hurricane strength can be expected.[24]

1.2 HISTORY

At least 40,000 years ago Australoid people began moving towards Australia and the Solomon Islands. A subsequent wave of people from Southeast Asia finally crossed the huge (for people only using outrigger canoes) distance from the Solomon Islands to the Vanuatu and settled the archipelago about 3,000 B.C.E.. The oldest archaeological evidence in Vanuatu, Lapita pottery from the island Malo, is dating back to 2,000 B.C.E.. Prehistoric life was marked by inter-tribal warfare and strong spiritual beliefs. All natural and human-induced bad luck or calamities were attributed to sorcery and lavish festivals which even claimed human sacrifice were staged to appease the gods. In April 1606 with the Portuguese explorer Pedro Fernández de Qu(e)irós the first European set foot on the islands. He discovered Mera Lava (San Marcos) of Banks group (Fig. 3), followed by Maewo (Margaritana), Merig Island (Vergel), Mota (Las Lagrimas de San Pedro), Vanua Lava (Portales de Belen) and Gaua (Virgen Maria) of Banks group, Aoba (Cardona), Pentecost (La Clementina), Malekula (Malicolo) and Ambrym. In 3 May 1606 he anchored in Espirito Santo, believing to have found *Terra Australis*.[25]

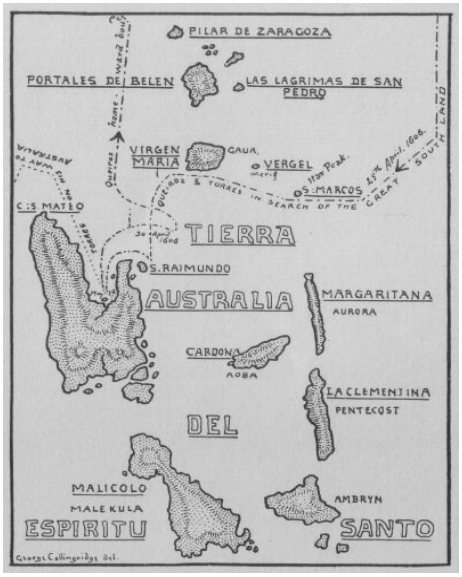

Fig. 3 Map of Quiros' journey

Europeans did not return until 1768, when Louis Antoine de Bougainville sailed between Espiritu Santo and Malekula on his frigate *La Boudeuse* and so disproved Qu(e)irós' theory of *Terra Australis*. He rediscovered the islands of Aoba, Pentecost, and Maewo and named them "Les Grandes Cyclades".[26]

On his second Voyage, on 17 July 1774, Captain James Cook visited several islands and named them the New Hebrides[27], a term lasting till independence in 1980.

In 1839 Europeans began settling the islands bringing various disasters on the inhabitants: whalers, sandalwood-, and sea slug-traders unscrupulously exploited the resources at the cost of the indigenous population, missionaries foisted their beliefs upon the people, penalising indigenous customs and traditions, and in addition their infection-ridden vessels brought diseases the people of the Pacific had little resistance to: influenza, measles, venereal diseases to name just a few examples, even the common cold wiped out whole populations. But by far the greatest misery inflicted on the islanders was “blackbirding” - the South Seas' version of slavery that continued into the early years of the 20th century where thousands of Ni-Vanuatu (meaning “of Vanuatu”) were persuaded or downright kidnapped to work on the sugarcane and cotton plantations of Queensland (Australia) and Fiji, and many never returned.

In 1887 the two declared enemies England and France settled uneasily next to each other in the New Hebrides and - forced to cooperate in a far-flung outpost of the European empire - they formed probably the weirdest colonial administration the world has ever seen crowned with the Anglo-French Condominium in 1906 as a response to German expansionism in the Pacific region.[28]

In 1942 in WWII US troops were stationed in Efate and Espiritu Santo, which became crucial bases in the Pacific War. The country was awash with American know-how and dollars, and many Ni-Vanuatu received respect and earned real wages for the first time in their lives. More importantly, the islanders were astounded at the apparent equality with which black and white military personnel were treated, and this played no small part in their agitation for independence. At the end of the war, in 1945, the Americans left as swiftly as they had arrived.

Now, land ownership became Vanuatu’s central political concern. After several partly violent conflicts full sovereignty was finally granted by both European nations on 30 July 1980 and Vanuatu became a republic with the Commonwealth of Nations.[29]

1.3 POPULATION AND LANGUAGES

94% of the 211,971 (July 2007) Ni-Vanuatu are Melanesians; furthermore there are Europeans, Australians, New Zealanders, Vietnamese, Chinese, and people from other parts of the Pacific.

In addition to the three official languages in Vanuatu: English, French, and Bislama at least 80 indigenous ones are spoken, which makes it to linguistically (and resulting from this also culturally) the world’s most diverse nation in terms of the number of actively spoken indigenous languages per head of population, with an average of only about 2,500 speakers (minority languages) each.[30] All of these languages are members of the Oceanic subgroup of the Austronesian language family, which extends from Easter Island in the east, New

Zealand in the south, Hawaii in the north, and parts of Irian Jaya in the west, including Newaweteme, the language spoken in Lungharighi, Loh, Torres Islands and Rallglëin, the language spoken in Southwest Ambrym, two of the research areas with Newaweteme being an extreme example of a minority language with only about 75 speakers. The whole population of Loh representing about 150 people is almost equally distributed to two villages speaking two different languages. Rather distinct from the languages of the rest of the country and suggested to be more closely related linguistically to those of neighbouring New Caledonia are the southern languages spoken in Erromango and Tanna including Indass Khermo, the language of Aneityum (the third research area). There are also three languages in Vanuatu that are of Polynesian origin (Mele-Fila, the language of the village Mele on Efate, Emae, the language of the island Emae, which belongs to the Shepherd's group and West-Futunan or Futuna –Aniwa, the language of Futuna and Aniwa).[31]

According to Crowley, Bislama is English based Creole which contains many French and Melanesian loan words due to Vanuatu's history: it has evolved as a result of multilingual contact in camps of recruited labourers in the islands of Southern Vanuatu around the mid-1800s, when sea slugs and sandalwood were processed for sale by a work force recruited from different speech communities. In this situation an English-lexifier pidgin rapidly emerged and became the *lingua franca* of these camps. It was named *Biche-de-mer*-English after the French word for sea slug, rapidly abbreviated to simply *Bichelamar* (or Beach-la-Mar to English-speakers), eventually yielding modern Bislama. During the blackbirding-period Bislama rapidly became the *lingua franca* of overseas plantations in Queensland (Australia) and Fiji, too. When returning to Vanuatu, people began to move as plantation labourers within Vanuatu for the first time, resulting in the continuation of the spread of this language as a plantation *lingua franca* to many parts of the country where it had previously been unknown or little known.[32]

1.4 TERRESTRIAL FLORA AND ITS USES

THE PACIFIC REGION

By geographers, four major regions have been delimited in the Pacific Ocean; these are Melanesia, Micronesia, Polynesia, and New Zealand. (Fig. 4) Vanuatu is part of the Melanesian region, located immediately east of the floristically rich Indo-Malaysian region and essentially continuous with it, but also containing elements of the Pacific flora. The relatively large land areas and physiographic and geological diversity led to large and diverse floras, relative to those of the other three Pacific regions.

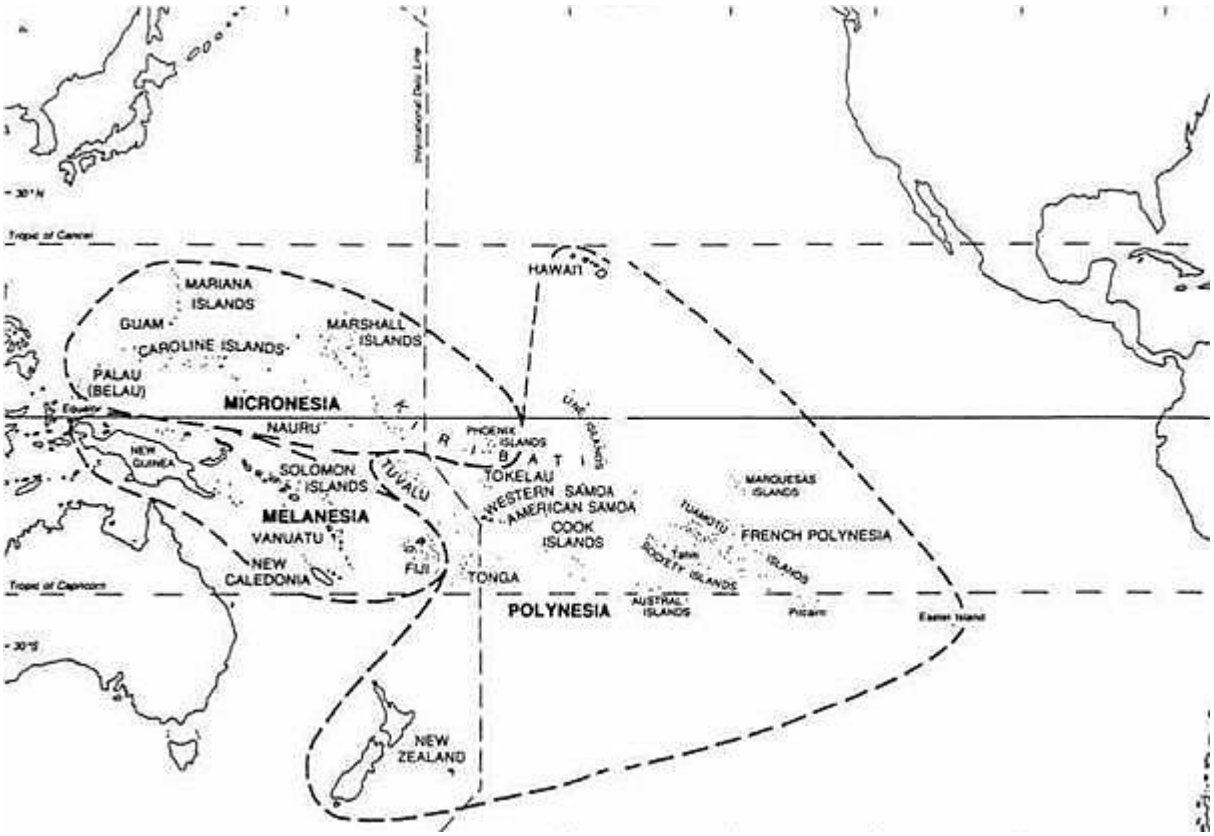

Fig. 4 Map of the Pacific region

The Melanesian region can be further divided into Eastern and Western Melanesia. The western part comprises Papua New Guinea (PNG), the Bismarck Archipelago, and the Solomon Islands; the eastern includes the Santa Cruz Islands, Vanuatu, Fiji, and New Caledonia.[24] Mallick says that compared to the other Eastern Melanesian islands Vanuatu is geologically young: 90% of its present land surface originates from late Pliocene-Pleistocene volcanism and the growth of Pleistocene coral reef platforms combined with uplifting, about 1.8 million years ago, thus only 10% of the landmass was formed between 10 and 38 million years ago.[22] So Vanuatu as the youngest of the four island groups supports the most recent vegetation as well as a poor biodiversity compared to its neighbours (but not in comparison with the other major Pacific regions), resulting not only from its geological youth but also from

the islands' size, their relative isolation from large expands of land, and frequent damages inflicted by cyclonic, seismic, and volcanic activity.[24]. Nevertheless, a certain number of endemics at species level have evolved but not all have been identified and catalogued yet[33] and more prospecting is likely to be required, because unfortunately up to date no review article dealing with Vanuatu's flora exists and so only controversial statements concerning biodiversity are on hand. Personally counting Vanuatu's species yielded 1,124 species by examining even the tiniest bit of literature on this subject (Mourgues, 2004[21] speaks of around 1,000 and Chew, 1975[33] of ca. 870) including 172 endemics, with a level of endemics of 15.3% (Mourgues assumes 150 and a level of 15%). Approximately 700 species of bryophytes and about 250 pteridophytes are also found[21]. As for plant identification in the field, only one field guide to common trees[34] is obtainable, based on other studies,[35, 36] but it only covers about 100 species and only trees, however the included list of vernacular plant names is pretty helpful. Therefore an own field guide was developed by collecting vernacular names, phytogeographic distributions, and uses of the 1,124 species in the list (literature used see LIST OF ETHNOBOTANICAL AND TAXONOMIC SURVEYS IN VANUATU), including photos of most species. By means of this guide plants were identified in the field and – back in the capital city Port Vila – verified in the herbarium.

FOREST TYPES AND DESCRIPTION OF THE RESEARCH AREAS

So far there have been no comprehensive descriptions created for the vegetation of Vanuatu as a whole, maybe related to a change in floristic patterns from north to south, but the studies available for Vanuatu (from [33, 36-56]) most of them an outcome of the Condominium Era from 1906 - 1980, when many French and English researchers visited the islands, were analysed by Mueller-Dombois and Fosberg (1998) resulting in six vegetation types:

Lowland rain forest

This forest type provides the natural vegetation of all south-eastern windward sides inland of the coastal zone up to about 500 to 600 m. It can be further divided into six variations, but to go into this in detail would take us too far afield and will not be discussed in this study.

Montane cloud forest and related vegetation

Practically only excluding the Torres Islands, montane forest is found everywhere in Vanuatu, beginning at approximately 500 m (300 m on smaller islands). Mueller-Dombois and Fosberg wrote that it is characterized by stunted trees with gnarled crowns and by trunks and branches covered with bryophytes and filmy ferns, which paints a vivid portrait of this kind of forest. Treeless low-scrub and herbaceous patches make up part of the summit vegetation.

Seasonal forest, scrub, and grassland

This type is found on the Northwest side of most islands. Three variations in vegetation pattern can be recognised: First of all the semideciduous transition forest, whose soil, often

strongly enriched with organic matter, forms a favourite habitat for indigenous tree gardens. The second variation, the so called *gaiac* (*Acacia spirobis*) forest, mainly consists of low to medium sized trees with wide branching crowns. The last variation, the *Leucaena* thickets, savannas, and grassland are found in the drier strongly wind- and rain-sheltered habitats on the western and north-western sides of the islands.

Vegetation of new volcanic surfaces

Vanuatu's volcanoes seem to be colonised first by lichens and herbaceous ferns, followed by tree ferns, pandanas, and palms associated with tall grasses and shrubby trees of the families Cunoniaceae and Moraceae.

Coastal vegetation, including mangroves

The beach vegetation is composed of a frontal herb zone, followed by a shrub zone, and littoral forest. However, in most coastal areas it has been replaced by human habitation and coconut plantations. Mangroves are even more rarely found, only on some sheltered coasts there are small areas left.

Secondary and cultivated woody vegetation

Secondary vegetation develops in response to shifting cultivation and disturbances by cyclones (characterized by a predominance of fast-growing, heliophytic colonisers) or indigenous uses of the forests in form of tree gardens and bush fallow. The cultivated woody vegetation mostly refers to coconut plantations.

Loh, Torres Islands, the first research area, located in Vanuatu's wet and hot north, is a raised limestone island with a maximum height of 139 m (Mt. Luwovunea), with most of its interior surfaces formed about 1.8 million years ago, while its coastal areas developed during Holocene. The inner part is predominantly covered with rain forest, the outer with littoral forest and thickets. Plants were collected in all of these ecosystems.

Ambrym, the second research area, situated in the middle of the archipelago, has two active volcanoes, Mt. Marum (1,270 m) and Mt. Benbow (1,159 m), surrounded by a large area denuded of vegetation. Downslope, extending to about 200 m altitude and nearly surrounding the island is a sparse cover dominated by ferns, frequently disturbed by ash fallout. The next lower elevational zone, extending to about 100 m altitude is covered with open, arborescent scrub, mixed with tree and herbaceous ferns, followed by a dense forest scrub, disrupted by coconut plantations, mainly in the South. The research took place in all of the described ecosystems, except from – of course - the ash covered and vegetation-free zone surrounding the volcanoes.

The third and last research area, Aneityum or Anatom, is the southernmost island of the archipelago and has a subtropical climate resembling that of New Caledonia. Its degraded and deforested mountainous interior is dominated by three mountains, two of them extinct volcanoes, Mt Inrerow Atahein (835 m) and Mt Tahentchai (794 m). The highly eroded old

volcanic soils of the interior which support only impoverished vegetation have been interpreted to be the result of a large population of up to 12,000 people that inhabited the island prior to the severe post-proselytization depopulation that resulted in a low of 550 people in these days. The mountainous region, extending to 300 m altitude is covered by cloud forest with tree crowns often colonised by epiphytic orchids and ferns: Pandanaceous climbers are also locally common. A subtype of the lowland rain forest, the so called *Agathis-Calophyllum,* or Kauri-forest is unique in the southern islands Erromango and Aneityum. Its altitudinal range extends from 100 to 500 m, often mixing with montane forest in the upper parts. It has to a large extent been disturbed and exploited by human activity. Downslope *gaiac* forest, occasionally containing sandalwood (*Santalum austro-caledonicum*), another victim of extensive forest exploitation, is followed by thickets of *Hibiscus tiliaceus* and coastal vegetation. In addition to coconut plantations lining the coasts pine (*Pinus caribaea*) plantations, initially planted to assist erosion control, but are now being managed by the community for timber production are also found here.[24] The research took place in all mentioned areas.

PLANTS IN TRADITIONAL LIFE

Some literature illustrating life in Vanuatu's countryside is already available. The studies "Magic gardens in Tanna"[57], "Agriculture in Vanuatu"[20], "Knowledge for survival: traditional tree farming in Vanuatu"[58], "Plantes magiques, plantes protectrices: quelques techniques d'horticulture traditionelle à Vanuatu",[59] and "Jardins d'Océanie"[60] describe traditional agricultural plant uses in Vanuatu, whereas "Ethnobotanique à Vanuatu et substances naturelles nématicides" copes with plants used in traditional agriculture to protect crops from parasitic infestation.[61]

In rural communities starchy root- or fruit vegetables like *maniok* (*Manihot esculenta*), *yam* (*Dioscorea sp.*), *kumala* (*Ipomoea batatas*), *taro* (*Colocasia esculenta*), or *bredfrut* (*Artocarpus altilis*) predominantly or exclusively form the traditional diet. An example is *nelot* (Fig. 5) prepared from *Artocarpus altilis*.

Fig. 5 Diana preparing *nelot* (Loh)

It is supplemented with various nuts like *navale* (*Barringtonia edulis*), *nangai* (*Canarium vulgare*), or *natapoa* (*Terminalia catappa*), several vegetables like *aelan kabis* (*Abelmoschus manihot),* or *bolkabis* (*Brassica oleracea*) and fruits e.g. *popo* (*Carica papaya*), *nagavika* (*Syzygium malaccense*), a number of *Annona* species and a variety of *Citrus* fruits. Very seldom food of animal origin, e.g. chicken, beef, pork, flying fox, or coconut crab, except from fish is part of the menu (Fig. 6, Fig. 7). The composition varies highly between the islands because of differences in habitats and remoteness. Islands close to Efate and Santo and of tourist interest generally have well-stocked stores, remote places like e.g. Loh are strongly dependent on island resources, as there is at the utmost one maintenance ship per year (when staying in Loh this ship had not come for more than a year and there was only one spool of scotch tape left in the shop, which by the way became very handy in the end when using it to tinker bags for the plant transport, which had been intended to buy on site).

Fig. 6 *Krab kokonas* (coconut crab) a delicacy (Loh)

Fig. 7 William with *longmaot* (Loh)

Some species or places have special importance in *Kastom* (pidjin word used to refer to traditional culture, including religion, economics, art, and magic in the Pacific islands, originating from the English custom), which is still very strong in Vanuatu.[62] Tree ferns (Cyatheaceae spp.) are used for carving *nimangaki* (grade taking)-figures (Fig. 8.), some sorts of timber are used for carving of the so called *tamtams* (slit-gongs) used e.g. as a medium in the delivery of messages, leaves of *Cycas sp.* are used to signify taboos and are also represented on Vanuatu's flag and *Piper methysticum* (Kava) is the most important Kastom plant as it is used in a *nakamal* (central meeting place in the village) (Fig. 9.) in various situations of traditional life, in other words it is the most fancied drug in this spot.

Fig. 8 *Nimangaki* figures, Kew Gardens, London

Fig. 9 *Nakamal* in Lélé, Ambrym

1.5 TRADITIONAL MEDICINE AND ITS PLANTS

Traditional medicine in Vanuatu has already been studied to a certain extent: The medicinal systems of Espiritu Santo[63], Malekula[64], Tongoa,[65] and Erromango[66] have previously been investigated, but no plant collections took place in this context. A review article about the

work of ORSTOM ("L'institut français de recherché scientifique pour le développement"),[67] talking of a preliminary screening of about 300 plants native in Vanuatu for presence or absence of certain medically interesting chemical drugs (a list of the screened plants is not available) of which 30 have been subject of biological screenings: these studies cope with antiprotozoal[68] and antimycobacterial[69] effects of plants traditionally used in New Caledonia and Vanuatu. In "Maternity and medicinal plants in Vanuatu I. The cycle of reproduction"[70] 13 different islands of all climate regions including Aneityum, (which has also been investigated in this thesis) were examined exclusively dealing with plants utilised in a clearly defined therapeutic context (plants used by women during pregnancy and delivery and for birth control), and "Maternity and medicinal plants in Vanuatu II. Pharmacological screening of five selected plants"[71] describes a screening of five plants collected in this context. One study, "Les usages médicinaux de quelques plantes communes de la flore des îles Banks (Vanuatu)[72] gives an overview about plants traditionally used in the Banks Islands.

So, why is there still need for further studies in this region? First of all, because of strong cultural differences between the islands, as mentioned previously in this study, different kinds of medicinal systems can be expected. Furthermore the floral composition varies from island to island, on the one hand a result of the comparatively great inter-island distances, on the other hand originating from soil and climate differences found in the archipelago as previously mentioned in this text. So people are maybe forced to use different kinds of plants because of the variety of floras and maybe also because the illnesses diverge, e.g. dermatophytic complaints are due to be more frequent in the hotter and more humid northern part. Moreover there could be a difference between places that are close to the more developed islands Efate and Espiritu Santo or with a touristy infrastructure (e.g. Aneityum) and those which are very remote and where connections are often unsteady and expensive and the people were not already influenced by tourism, leading to a loss of their traditional habits and knowledge: on one side people are thereby capable of earning (higher) wages in the cities or in the tourism industry, which could (but unfortunately not always does) result in a better education and therefore better conservation of traditional wisdom. On the other side they gain a better accessibility of Western doctors, hospitals, and drugs, which may lead to the adaptation of the as "new and better" considered Western style, resulting in the loss of traditional medicine, regrettably observed in Aneityum. Another reason for why Vanuatu is still an interesting place for an ethnobotanical/ethnopharmaceutical study is that the islands carefully chosen for this survey have never (Ambrym and Torres Islands) or only poorly (Aneityum) been investigated before. At last former studies either simply concentrated on collection of medicinal data without a subsequent screening or they only dealt with medicinal plant uses in a very narrow therapeutic context, e.g. the studies of Bourdy and Walter,[70, 71]

concentrating on plants used in gynaecology. A wide screening including various biological assays has never been performed before.

2. *BACCAUREA STYLARIS* MUELL. ARG. (PHYLLANTHACEAE)

2.1 THE PHYLLANTHACEAE

The Phyllanthaceae, a diverse cosmopolitan family with greatest diversity in the tropics is the largest segregate from Euphorbiaceae *sensu lato* (largely congruent with Euphorbiaceae-Phyllanthoideae in previous classifications) and comprises about 60 genera and approx. 2,000 species.[73, 74] The circumscription of Phyllanthaceae was modified from Webster's Euphorbiaceae-Phyllanthoideae to include *Croizatia* (from Euphorbiaceae-Oldfieldoideae), *Dicoelia* (from Euphorbiaceae-Acalyphoideae), and *Tacarcuna* (previously *incertae sedis* in Euphorbiaceae). The genera *Drypetes* and *Putranjiva* are excluded as Putranjivaceae, *Centroplacus* as Centroplacaceae, and *Phyllanoa* as Violaceae.[75]

2.2 TAXONOMIC POSITION OF *B. STYLARIS* MUELL. ARG.

The Phyllanthaceae fall into two major clades (Phyllanthoideae and Antidesmatoideae) now recognized at subfamilial level and characterized by inflorescence and leaf anatomical features.[76] The subfamily Phyllanthoideae *sensu stricto* covers four tribes: Poranthereae, Bridelieae, Wielandieae, and Phyllanthoideae. They lack tanniniferous cells in leaf epidermis, usually have contracted inflorescence axes, and predominantly explosively dehiscent fruits. The subfamily Antidesmatoideae includes six tribes: Antidesmateae, Scepeae, Jablonskieae, Spondiantheae, Uapaceae, and Bischofieae. They are characterised by tanniniferous cells in the leaf epidermis, usually elongated inflorescence axes, and predominantly indehiscent or tardily dehiscent fruits; almost all taxa are dioecious.

The tribe Antidesmateae e.g. holds the genera *Antidesma*, *Martretia*, *Thecacoris,* and *Apodiscus* and Scepeae consists of *Aporosa* and *Baccaurea*. The smaller tribes only contain one genus: Spondiantheae (*Spondianthus*), Uapaceae (*Uapaca*), and Bischofieae (*Bischofia*), except from Jablonskoieae, which includes *Jablonskia* and *Celianella.*

Division	Angiospermae
Subdivision	Eudicots
Clade	Eurosids I (Fabids)
Order	Malpighiales
Family	Phyllanthaceae
Subfamily	Antidesmatoideae
Tribe	Scepeae
Genus	*Baccaurea* LOUR.[77]

2.3 MORPHOLOGY OF *B. STYLARIS* MUELL. ARG.:

Baccaurea stylaris MUELL.ARG. (Phyllanthaceae) is an evergreen shrub or tree 2–20 m high with usually weak *Terminalia* branching pattern growing in Vanuatu, Fiji, and the Solomon Islands. Cut bark strongly smells of pepper. The discolorous leaves are simple with entire margins, rounded base, and retuse apex (Fig. 10). The petioles are slightly pulvinate and winged. The inflorescences are reduced thyrses with white actinomorphic flowers, which are pleasantly scented. The fruits are globose to ovoid, 1- (or 2-) seeded, fleshy capsules.

Fig. 10 *Baccaurea stylaris* MUELL. ARG. (whole plant, cut bark, leaves)

2.4 ECONOMIC USES OF *B. STYLARIS* MUELL. ARG. AND OTHER MEMBERS OF THE PHYLLANTHACEAE

Some taxa are regionally cultivated as ornamentals or for their fleshy edible fruits, *B. dulcis* (JACK) J.VOIGT, *B. motleyana* (MUELL. ARG.) MUELL. ARG., or *B. ramiflora* LOUR., the (Indo) Malesian species *Antidesma bunius* (L.) SPRENGEL, the South American *Phyllanthus acidus* (L.) SKEELS (one of the richest sources of natural Vitamin C), the African *Uapaca guineensis* MUELL. ARG., and *Uapaca kirkiana* MUELL. ARG. to mention just a few.[78]. Some provide also timber, weaving material, dyes, and fish poison or insecticides, or they show medicinal promise, e.g. the already mentioned Malesian *B. motleyana* (MUELL.ARG.) MUELL. ARG., whose squeezed inner bark is applied to sore eyes in Thailand, *B. courtallensis* (WIGHT) MUELL. ARG., which is used as an antipyretic by Kani tribes in South India[79], *B. ramiflora* LOUR., utilised in Chinese Dai medicine as an antiphlogistic and anodyne against rheumatoid arthritis, cellulites, abscesses, and to treat injuries[80] and also used as medicine by hill-tribes in Northern Thailand. An ethanolic extract of the leaves evidently shows antioxidant activities.[81] The leaves of the Malesian *B. lanceolata* (MIQ.) MUELL. ARG. are pounded in bamboo, mixed with water, and drunk as a remedy against stomach-ache in Thailand. Some *Antidesma spp*. and *Phyllanthus spp* are also used in Thai medicine: the

leaves of the in Indomalesia and Australia distributed *Antidesma montanum* BL. var. *montanum* are applied to ulcers and lumber pains, and the roots are also externally used to treat stomach-ache, whereas the fruits or tea made from the leaves are drunk as a tonic after childbirth. The juice from fruits of the Malesian *Antidesma orthogyne* (HOOK.F.) AIRY SHAW are utilised as an antiseptic and the chewed roots of *Antidesma tomentosum* BL. var. *tomentosum* are used to treat internal pain by external application of the mush. A decoction of the whole plant of the pantropical *Phyllanthus amarus* SCHUM. & THONN., whose ethanolic extract also shows antiviral activity against hepatitis B[82] can be used to treat stomach complaints or is freshly applied as a diaphoretic just as the Malesian species *Phyllanthus pulcher* WALL. EX MUELL. ARG. and *Phyllanthus urinaria* L. (http://www.nationaalherbarium.nl, Flora of Thailand, National Herbarium Nederland, Leiden, NL).

2.5 ETHNOBOTANY OF *B. STYLARIS* MUELL. ARG.

In the indigenous language of Aneityum, Indass Khermo, the plant is called *niht*[ʃ]*schaub* [nɪθ'tʃaub]. A handful of leaves and/ or inner bark respectively are boiled in water and the whole body is bathed in the chilled decoction once or twice a day. The medicine is used to treat asthma or cough.

This plant seems to be unique to the people of Aneityum, since no other ethnomedicinal uses of this species were found during systematic biographic research elsewhere, both in Vanuatu and elsewhere in the world.

2.6 PHYTOCHEMISTRY AND PHARMACOLOGY OF *BACCAUREA* LOUR. AND OTHER PHYLLANTHACEAE

As mentioned previously in this text, the family Phyllanthaceae is further divided into two subfamilies: Phyllanthoideae *sensu stricto*, covering the four tribes: Bridelieae, Phyllanthoideae, Poranthereae, and Wielandieae, and the subfamily Antidesmatoideae which includes the six tribes Scepeae, Antidesmateae, Bischofieae, Uapaceae, Jablonskieae, and Spondiantheae.

For the genus *Baccaurea* LOUR., belonging to the tribe Scepeae, so far only one study [81] exists, in which ten compounds, comprising among others a prenylated flavonol, a flavonoid and a lignan, isolated from the leaves of *Baccauera ramiflora* LOUR. were screened for their antioxidant activities. For another member of the tribe Scepeae, *Aporosa lindleyana* BAILL., the antioxidant activity of a root extract, maybe due to the presence of glycosides, saponins, tannins, and phenols[83] and hypoglycaemic effects[84] has been described.

Members of the tribe Antidesmateae demonstrate e.g. antimicrobial[85] and antiplasmodial[86] activities. Some interesting compounds have been reported in this tribe, too, e.g. alkaloids, a

lupeolactone, and triterpenoids[87]. In the Bischofieae the presence of for example alkaloids, flavonoids, saponins, sterols, and triterpenoids showing anti-microbial activities[88] and a strong activity as DNA topoisomerase II inhibitors, originating from the presence of the lupan-type triterpene betulinic acid and its derivatives[89] have been demonstrated. Some members of the tribe Uapaceae display antiprotozoal activity[90, 91] partly due to their content of betulinic acid[92] and antimicrobial effects[93]. Representatives of the genera Jablonskieae and Spondiantheae have not been studied so far.

Compared to Antidesmatoideae, the members of the second subfamily Phyllanthoideae *sensu stricto* have intensely been investigated concerning their bioactive secondary metabolites. In Bridelieae phenolic compounds with radical scavenging and xanthine oxidase inhibitory activity[94], quinic acid derivatives, flavonoids and flavanols with antibacterial activity[95], or complement-inhibiting substances[96], beta-lactamase[97] inhibitors, triterpenoids with significant inhibitory activity against snake venom phosphodiesterase-I, [98] and tetraterpenglycosides[99] have been identified, to mention just a few. A great variety of species belonging to the Phyllanthoideae has also been phytochemically investigated, leading to many compounds, including alkaloids, coumarins, monoterpenoids as well as highly condensed sterols, flavonoids, lactones, lignans, and others [100]. Members of this tribe have also intensely been investigated for further pharmacological activities and so analgesic, anti-allergic, antiinflammatory, antineoplastic, antiviral, and anti-lipoxygenase activities could be shown.[100] In addition moderate antifungal and antiplasmodial effects were described.[101] From members of the Poranthereae alkaloids[102] and flavonoids[103] have already been isolated and antibacterial, antifungal,[104] and lipoxygenase-inhibition activities[105] have been reported and finally even in the small tribe Wielandieae, alkaloids have already been described.[106]

EXPERIMENTAL PART

1. ETHNOBOTANY

Ethnobotany, a sub-field of ethnological as well as botanical sciences investigates the relationships between ethnic groups and their herbal environment, including plants used as food, medicine, and raw materials for construction and other applications.[107] The term was coined by the botanist J. W. Harshberger during a lecture in Philadelphia in 1895 and defined as the study of “plants used by primitive and aboriginal people”.[108] Ethnomedicine in turn a sub-field of ethnobotany studies the pharmacopoeia of an ethnic group which is orally transmitted from generation to generation. Ethnopharmacology eventually investigates pharmacological mechanisms of plants used in traditional medicine by indigenous groups.[107]
There are three major objectives in the investigation of ethnopharmacopoeias:
(1) The botanical and pharmacological purpose, trying to find new plants and potent chemical compounds respectively, together with sanitary and economic interests (empirical use of plants over generations by indigenous people facilitates the selection of particularly useful species and exclusion of toxic or ineffective ones).[7]
(2) The ethnobotanical and ethnomedicinal objective, with the aim to understand cultural concepts and believes as well as classification of plants and illnesses.
(3) The intention to preserve traditional knowledge and healing concepts as well as respect and protection of indigenous cultures and conservation of natural resources as legally stipulated in 1992 in the Convention on Biological Diversity (Rio “Earth Summit”). While forests all over the world continue to fall – the Amazon alone lost 200,000 miles since 1970 - too often undiscovered maybe pharmaceutically useful species simply disappear from the world, their secrets dying with them. An almost loss occurred recently with Calanolide A from *Calophyllum lanigerum* var. *austrocoriaceum* (Guttiferae), first collected in 1987 on a NCI-sponsored expedition in Sarawak, Malaysia, Borneo, reported by Rhett Butler from mongabay.com in 2005. Once determined, that the compound showed significant activity against HIV, researchers returned to the place of collection to get more plant material. The tree was gone and its disappearance led to a wild search by botanists for further specimen finally fruitful in Singapore Botanical Garden which contains a collection of several plants once gathered by the British. Calanolide A was successfully synthesised by Sarawak MediChem Pharmaceuticals but it is not approved by the U.S. Food and Drug Administration.
However, when biological material is chosen to be screened for active compounds it is crucial both for the development of flora rich areas and the pharmaceutical industry to protect and promote the rational exploitation of the resources. If possible cultivated plants should be preferred, because they guarantee the production of chemical homogenous material and allow the preservation of threatened species. As an example for both, the importance of

natural products for the investigation new pharmacologically active agents and the necessity to find alternative ways for their production can serve the diterpenoid paclitaxel (Taxol®), isolated from *Taxus brevifolia* (Taxaceae), one of the most important chemotherapeutic agents currently in use. At the beginning obtaining the material was very complicated, because in order to produce 2.5 kg of Paclitaxel, 27,000 tons of bark were required, viz. 12,000 trees had to be cut. Due this threat of extinction, alternative ways to obtain paclitaxel were developed, including partial synthesis from precursors found in the European yew *Taxus baccata*.[109]

1.1 LEGAL COVER OF THE SURVEY

The commitment of the researcher to the indigenous healer should always be remembered in every stage of the study. It is essential to win the trust of healers and chiefs, which can be a long way. Hence, before conducting an ethnobotanical research it is very important to obtain agreements among all parties, addressing prior informed consent, confidentiality, ownership of intellectual properties, and tangible biological materials, collecting area scope, conservation of medicinal plants as well as their habitats, responsibilities for parties, benefit sharing (in this case a popular scientific book of all plants collected in the three main languages of Vanuatu, English, French, and Bislama, had to be made), compensation due parties at all stages of the research, development and commercialisation and supplier of materials.[110] In the present survey negotiations had to be conducted and contracts had to be made with the Vanuatu National Cultural Council (Vanuatu Cultural Centre) and the Vanuatu government, represented by the Environment Unit, part of the Ministry of Lands, Survey, Environment, Energy, Minerals, and Water as well as the Ministry of Health.

1.2 COLLECTION OF DATA

During five months between May and November 2006 an ethnobotanical survey was conducted on three different islands of Vanuatu: Loh in Torres Islands, Ambrym, and Aneityum.

The specialists in traditional medicine were first asked about their healing experiences and about themselves. Next, during an excursion to the surroundings, the healer chose the plants he knew and was willing to show. On-site the specialist was interviewed about use(s), preparation, application(s), plant name(s), as well as his healing concepts (Fig. 42, p. 173). Representative pictures of the plant were taken and herbarium specimens were prepared. In addition information about illnesses and their causes were collected (Fig. 43, p. 174).

The interviews were conducted in Bislama, in a few cases a fieldworker was consulted, to translate from vernacular language. Data were collected in an oral interview, using the questionnaires mentioned above as a matrix for the interviewer.

1.3 PREPARATION OF HERBARIUM SPECIMENS

The voucher specimens were directly dried in the field using a conventional plant press. A number tag was added to each specimen and it was placed on an open folder (wrapping-paper or newspaper) and sandwiched between pieces of newspaper and corrugated paper. The straps were fastened tightly and the press was hung up in the house to allow a steady flow of warm air and to avoid ants. The papers were changed regularly to keep the moisture content as low as possible (to avoid mould and decay) and to check for insect attack.

Fig. 11 Plant press

1.4 IDENTIFICATION OF THE SPECIMENS

Voucher specimen had to be identified directly in the field. The correct classification, where a self-made field guide (see 1.5 Traditional medicine and its plants) was used, was essential, as it had to be decided on-site, which plant to collect for the screening regimen, as a second visit on the islands was not possible. Back in the capital city, the plants were verified at the National Herbarium in Port Vila, Vanuatu and back in Europe in the Royal Botanic Gardens, Kew, London, Great Britain and are deposited at the University of Regensburg.

1.5 COLLECTION OF PLANT MATERIAL

Eighteen plants with immunomodulatory properties were chosen for the screening procedure and between 500 and 1,000 g dry weight were collected:

Acalypha grandis BENTH. (leaves), *Aidia racemosa* (CAV.) D.D. TIRVENG. (leaves), *Allophylus timoriensis* DC. BL. (leaves), *Dysoxylum arborescens* (BL.) MIQ. (leaves), *Euodia latifolia* DC. (leaves), *Pipturus argenteus* WEDD. (inner bark), *Syzygium malaccense* (L.) MERR. & L.M. PERRY (leaves), and *Tabernaemontana pandacaqui* LAM. I (leaves) were collected and dried in Lungharigi, Loh, Torres Islands, Vanuatu between June and July 2006. The plant material was smoke dried at about 40°C using a self-made dryer built of stems of coconut wood which are very hard and heat resisting, a grid of lengthwise splitted bamboo stalks covered with bamboo mats.

Zingiber zerumbet (L.) SM. (rhizome), *Dracontomelon vitiense* ENGL. (inner bark), *Gyrocarpus americanus* JACQ. (leaves), *Intsia bijuga* (COLEBR.) O. KTZE. (leaves), *Macaranga dioica* MUELL. ARG. (inner bark and leaves), *Macaranga tanarius* (L.) MUELL. ARG. (inner bark and leaves), *Macropiper latifolium* (L.F.) (stems), and *Tabernaemontana pandacaqui* LAM. II (leaves) were collected and dried in Lélé, Ambrym, Vanuatu between July and August 2006. Here the plant material was slowly heat dried at about 40°C using a copra dryer.

Baccaurea stylaris MUELL. ARG. (inner bark and leaves), *Bidens pilosa* L. (whole plant), and *Grewia inmac* GUILL. (leaves) were collected and smoke dried in Anelcauhat, Aneityum, Vanuatu in August 2006 using the same method as in Loh.

Fig. 12 Drying in Loh, Ambrym, and Aneityum (from left to right)

1.6 QUANTITATIVE ETHNOBOTANY

A database of ethnobotanical information collected during the six months of fieldwork was generated, consisting of 420 use reports on 130 species of 54 plant families, contributed by 27 informants of different age, gender, occupation, education, and class to ensure that the data collected were not biased in favour of any social group. They included 16 men and 11 women, aged between 25 and 79 years. Four people were interviewed at least twice. Information on the medicinal system and ethnological background were obtained by interviewing high-ranking community members, the priests, doctors, the community leaders, and the fieldworkers.

In order to analyse the relative frequency of certain diseases and the cultural importance of a species the reports were divided into 17 categories of use. The reports were grouped according to their medicinal affiliation or sociocultural relevance, whereas a species can be listed in more than one category.

2. BIOLOGICAL ASSAYS

Biological targets in the screening of crude extracts or pure compounds for bioactivity can be classified into five major groups: (1) lower organisms, such as microorganisms, insects, crustaceans, and molluscs, (2) cultivated cells of human or animal origin, (3) isolated organs of vertebrates (e.g. guinea pig ileum or rat tail artery), (4) whole animals, and (5) isolated subcellular systems, such as enzymes, receptors, and organelles. Most of the biological assays require specialised facilities and know how, so only in a few cases it makes sense to built up such an assay intramural within a phytochemical laboratory, and therefore collaborations with other groups are useful, even became necessary.[1]

In this study the regimen consisted of four major parts: (1) a screening for cytotoxicity has been carried out in this lab, (2) assays for antibacterial, antifungal, and antiprotozoal activities were carried out in the Laboratory for Microbiology, Parasitology and Hygiene (LMPH), Antwerp, Belgium, (3) assays in the development of drugs effective against *Alzheimer's* disease (AChE and BChE-inhibitors, and NMDA-antagonists) were performed in Department of Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy, University of Jena, Germany or Department of Pharmaceutical Biology, Institute of Pharmacy, University of Jena, Germany, respectively, and (4) assays targeting at anti-inflammatory processes were carried out at Division of Cell- and Neurobiology, Institute of Anatomy, University of Zurich, Switzerland.

2.1 CYTOTOXICITY ASSAY

In this project a screening regimen on the basis of the disease oriented so called NCI60 (panel of 60 human tumour cell lines, organized into subpanels representing leukaemia, melanoma, and cancers of the breast, central nervous system, colon, kidney, lung, ovary, and prostate) was developed. In the early years the NCI had screened compounds in a murine model, but as the seemingly positive molecules were showing a relative lack of activity against common human adult solid tumours this system was replaced by the NCI60. This *in vitro* "disease-oriented", drug-discovery screen was developed between 1986 and 1990, ran as a primary drug screen between 1990 and 2000 and since 2000 it operates as a screening service to the research community. The primary intention was to identify compounds with growth-inhibitory or toxic effect on particular tumour types but the patterns of relative drug sensitivity and resistance generated with standard anticancer drugs were soon showing mechanisms of drug action giving the opportunity for molecular-targeted anticancer drug discovery.[111] This screen already yielded in many plant-derived anticancer drugs, e.g. camptothecin from *Camptotheca acuminata* (Nyssaceae).[112-114]

In the present study a subpanel of the NCI60 consisting of eight cell-lines was used because of two reasons: (1) profiles of cell line sensitivity can give information of selective activity on particular tumour types - meaning that a cell line can be inhibited to a given extent at a lower drug concentration than required to exert the same effect on other cell lines [111] - which may provide information about molecular mechanisms of growth inhibition and cell killing[115] as the cell lines included into the NCI60 screen are (2) better characterised pharmacologically and at the molecular level than any other set of cell lines. Their cytogenetical characterisation by chromosome banding in 1970 by Walter Nelson-Rees and colleagues has for instance unearthed the true origin of the KB cell line, thought to be derived from an epidermoid carcinoma of the oral cavity[111] and many other relatively widely used tumour cell models of

various tumours to be in fact derivatives of the well established HeLa cervical carcinoma cell line.

The assessment of *in vitro* cytotoxicity was determined using the MTT assay, a quantitative colorimetric method to determine cell proliferation, viability, and cytotoxicity. It utilises the yellow tetrazolium salt 3-(4,5–Dimethyl–2-thiazolyl)-2,5–diphenyl-2H-tetrazolium bromide) which is predominantly metabolised by mitochondrial succinic dehydrogenase activity of proliferating cells to form insoluble purple formazan crystals, but many non-mitochondrial dehydrogenases and flavin oxidases also seem to be able to reduce MTT.[116-118] The crystals are then solubilised by the addition of a detergent and the colour can be quantified by spectrophotometric means, whereas the amount of colour produced is directly proportional to the number of viable cells.[119] Secondary plant metabolites like phytoestrogens and antioxidants were also shown to interfere with the assay by extracellular reduction of the MTT.[120]

Leukaemia was not included into the screening, because the MTT assay is difficult to apply to suspension cell lines and neither HL-60 nor Jurkat cells could be established for an alternative assay, using WST-1 instead of MTT-reagent.

CELL LINES

786-0	human renal cell adenocarcinoma
A549	human epithelial cell lung carcinoma
HT-29	human colorectal adenocarcinoma
MCF7	human breast adenocarcinoma (from metastatic site pleural effusion)
OVCAR-3:NIH	human ovarian adenocarcinoma
PC-3	human prostate carcinoma cells (from metastastatic site bone)
SK-MEL-28	human malignant melanoma cells
SNB-19	human glioblastoma cells

All cell lines were obtained from the Cell Lines Service (CLS) (Eppelheim, Germany; http://www.cell-lines-service.de), except from SNB-19 cell line, which was obtained from Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) (Braunschweig, Germany; http://www.dsmz.de).

CELL LINE MAINTENANCE

The cells were splitted weekly. The culture medium was removed and the cells were rinsed with 2.5 mL PBS to remove all traces of serum that contains trypsin inhibitor. The monolayer was coated with 1.5 mL Trypsin-EDTA (0.025%/ 0.03%) and the flasks were placed at 37°C for up to 10 min. until the cell layer was dispersed. 5 mL of the appropriate complete growth medium was added, the cells were separated into single-cell suspensions by gentle pipetting and an aliquot of $1x10^6$ cells (cell number was determined in a haemocytometer via the well

known Trypan Blue dye exclusion method) was transferred to a new culture flask containing 24 mL of fresh medium.

786-0	RPMI 1640 supplemented with 10% FBS, 1 mM sodium pyruvate, 10 mM HEPES buffer, 100 U/mL penicillin, and 50 U/mL streptomycin
A549	Ham's F12K supplemented with 10% FBS, 2 mM L-glutamine, 100 U/mL penicillin, and 100 µg/mL streptomycin
HT-29	RPMI 1640, supplemented with 10% FBS, 50 U/mL penicillin, and 50 U/mL streptomycin
MCF7	DMEM, supplemented with 10% FBS, 2 mM L-glutamine, 1% non-essential amino acids, 100 U/mL penicillin, and 100 µg/mL streptomycin
OVCAR-3:NIH	RPMI 1640 supplemented with 20% FBS, 2 mM L-glutamine, 1 mM sodium pyruvate, 10 mM HEPES, 1.5 g/L sodium bicarbonate, 4.5 g/L glucose, 0.01 mg/mL bovine insulin, 100 U/mL penicillin, and 100 µg/mL streptomycin
PC-3	Ham's F12K supplemented with 10% FBS, 2 mM L-glutamine, 100 U/mL penicillin, and 100 µg/mL streptomycin
SK-MEL-28	DMEM, supplemented with 10% FBS, 2 mM L-glutamine, 1% non-essential amino acids, 100 U/mL penicillin, and 10 µg/mL streptomycin
SNB-19	DMEM, supplemented with 10% FBS, 100 U/mL penicillin, and 100 µg/mL streptomycin

MEDIA, SUPPLEMENTS, BUFFERS, AND ENZYMES

Dulbecco's modified Eagle's medium	Biochrom AG, Berlin, D
Ham's F12K	Biochrom AG, Berlin, D
RPMI 1640	Biochrom AG, Berlin, D
Foetal bovine serum (FBS)	Biochrom AG, Berlin, D
D-(+) -glucose, anhydrous	Fluka, Buchs, CH
L-glutamine	Biochrom AG, Berlin, D
HEPES-buffer	Biochrom AG, Berlin, D
Insulin, bovine	Biochrom AG, Berlin, D
Non-essential amino acids (NEA)	Biochrom AG, Berlin, D
Penicillin	Biochrom AG, Berlin, D
Penicillin-streptomycin	Invitrogen, Karlsruhe, D
Sodium bicarbonate	Merck KG aA, Darmstadt, D
Sodium pyruvate	Biochrom AG, Berlin, D
Streptomycin	Biochrom AG, Berlin, D
PBS solution with Ca/Mg	Biochrom AG, Berlin, D
Titriplex III (EDTA)	Merck KG a. A., Darmstadt, D
Trypsin	Biochrom AG, Berlin, D

COLORIMETRIC MTT ASSAY

Cells were inoculated in a volume of 100 µL per well onto 96-well microtiter plates (Techno Plastic Products AG, Trasadingen, Switzerland) at densities between 2.6×10^3 and 47.5×10^3 cells per well (Tab. 1) to form a confluent cell layer, whereas the cell number was determined using the well known Trypan Blue exclusion method. The microtiter plates were preincubated for approximately 24 h at 37°C to allow stabilisation prior to drug addition.

For initial screening 50 µL of a solution of 150 µg/mL (0.1% DMSO) crude extract in cell culture medium (final DMSO content 0.033%) were added to each well and the plates were incubated in a humidified atmosphere (37°C, 5% CO_2). After 72 h stock MTT solution (dissolved in PBS at 4 mg/mL and filtered to sterilise and remove a small amount of insoluble residue) at a concentration of 15 µL per 150 µL medium was added and incubated for 4 h under the same conditions. The medium was evacuated and sodium dodecyl sulphate (SDS) (10% in Millipore H_2O) was added to all wells to lyse the cells. After 24 h at room temperature in the dark to ensure, that all formazan crystals have been dissolved, the plates were measured at 560 nm against a background control (150 µL SDS), using a microplate reader (Tecan Spectrafluor plus, Tecan Deutschland GmbH, Crailsheim, Germany). Every test was performed at least in triplicates and all experiments have been repeated three times (n=4).

The cell viability for each experiment was calculated as a ratio of treated cells ($y_T = (\bar{x}OD_T - \bar{x}OD_B)$ against an untreated control ($y_U = (\bar{x}OD_U - \bar{x}OD_B)$, yielding the viability in % after multiplication with the factor 100:

$$viability[\%] = \frac{y_T}{y_U} \times 100$$

Fig. 13 $y_T = (\bar{x}OD_T - \bar{x}OD_B)$: average optical density of treated cells minus average OD of blank-wells (medium without cells)

$y_U = (\bar{x}OD_U - \bar{x}OD_B)$: average OD of untreated cells minus average OD of blank-wells (untreated cells = aliquot of cells in medium plus 15 µL MTT, which was set to 100% viability).

Extracts showing a decrease of cell viability greater than 50% were further tested at a concentration of 25 µg/mL (0,02% DMSO; final DMSO content 0.017%) and for those showing a cell viability less than 50% under these conditions, IC_{50} values were determined with six three-fold dilutions, starting from a maximum concentration of 50 µg/mL. This step-by-step measuring procedure had to be applied to minimise costs and effort.

CELL INOCULATION DENSITIES

Cells were inoculated in a volume of 100 µL per well at twelve densities between 825 and 20.000 (SNB-19 between 2.000 and 47.500) cells per well. The cells were preincubated for 24 h to allow stabilisation and after this period 50 µL of medium were added and the assay was performed as described above. Every test was performed in quintuplicates and all experiments have been replicated twice (*n*=3). The results were compared to inoculation densities used in the NCI60 *in vitro* screen performed by the National Cancer Institute, Frederick, MD, USA (http://dtp.nci.nih.gov/docs/misc/common_files/cell_list.html) and values with strongest consensus were chosen, if meeting the criteria above.

Tab. 1 Human tumour cell lines and inoculation densities used in the *in vitro* drug screen (*n*=3)

Cell Line	cells/well	NCI60 panel
786-0	$20x10^3$	$10x10^3$
A549	$11.25x10^3$	$7.5x10^3$
HT-29	$2.6x10^3$	$5x10^3$
MCF7	$11.25x10^3$	$10x10^3$
OVCAR-3:NIH	$11.25x10^3$	$10x10^3$
PC-3	$15x10^3$	$7.5x10^3$
SK-MEL-28	$15x10^3$	$10x10^3$
SNB-19	$47.5x10^3$	$15x10^3$

CONTROLS

Negative control experiments were performed as described above with 0.033% DMSO, representing the final assay concentration.

The positive control experiments were conducted with podophyllotoxin or parthenolide, respectively and the IC_{50} values had to be established for each cell line prior implementation. Both substances were initially solubilised in DMSO and tested at nine ten-fold dilutions, starting from a maximum concentration of 100 µM and the assay was performed as described above, only using these except from the crude extract solutions. The IC_{50} values were determined for an incubation time of 48 h and 72 h respectively. The dose response curves for the incubation period of 48 h are not shown in the section "2.1 Cytotoxicity Assay, Establishment of a positive control", because an incubation period of 72 h was finally chosen for the assay as described above. Every test was performed in triplicates and all experiments have been replicated twice (*n*=3).

Tab. 2 Human tumour cell lines and concentrations of the positive controls used in the *in vitro* drug screen (*n*=3). Data expressed as mean ± SD.

Cell Line	Positive Control			
	c Podophyllotoxin ± SD [µM]		c Parthenolide ± SD [µM]	
	48 h	72 h	48 h	72 h
786-O	-	0.005 ± 0.0005	-	-
A549	0.074 ± 0.001	0.038 ± 0.005	-	-
HT-29	0.651 ± 0.025	0.624 ± 0.017	-	-
MCF7	1.021 ± 0.004	0.961 ± 0.041	-	-
OVCAR-3:NIH	1.187 ± 0.033	0.778 ± 0.021	-	-
PC-3	1.154 ± 0.033	0.455 ± 0.024	-	-
SK-MEL-28	-	-	0.518 ± 0.010	0.427 ± 0.035
SNB-19	-	-	4.111 ± 0.584	0.780 ± 0.063

INTERACTION OF EXTRACTS AND MTT IN CELL-FREE SYSTEM

The direct reduction of MTT by the plant extracts was tested to exclude false negative results. 100 µL PBS per well were put in first onto 96-well microtiter plates, 50 µL of a solution of 150 µg/mL crude extract in PBS and 15 µL stock MTT solution were added to each well and the plates were incubated in a humidified atmosphere (37°C, 5% CO_2) 4 h. 150µL SDS (10% in Millipore H_2O) were added to all wells to solve the formazan crystals and after 24 h at room temperature in the dark to ensure, that all formazan crystals were dissolved, the plates were measured at 560 nm against a background control (blank plus 150 µL SDS), using a microplate reader (Tecan Spectrafluor plus, Tecan Deutschland GmbH, Crailsheim, Germany). Every test was performed at least in triplicates and replicated twice (*n*=3).

DATA ANALYSIS

The results were expressed as mean ± SD (processed with *Graph Pad*). To compare more than two groups, data were analysed by two way ANOVA, followed by Dunnet's multiple comparison test, using *Graph Pad*; *p<0.05* was considered to be significant, *p<0.01* as very significant and *p<0.001* as extremely significant).

REAGENTS

Dimethyl sulfoxide (DMSO)	Merck KG aA, Darmstadt, D
Sodium dodecyl sulphate (SDS)	Sigma-Aldrich, Steinheim, D
MTT (3-(4, 5-Dimethyl-2-thiazolyl)-2, 5-diphenyl-2H-tetrazolium bromide	Fluka, Buchs, CH
Parthenolide	Calbiochem, San Diego, USA
PBS solution with Ca/Mg	Biochrom AG, Berlin, D
Podophyllotoxin	Sigma-Aldrich, Steinheim, D
Trypan Blue	Sigma-Aldrich, Steinheim,

2.2 ANTIBACTERIAL AND ANTIFUNGAL ASSAYS

Infectious diseases caused by bacteria, viruses, and fungi are still a major threat to public health, with an impact particularly large in developing countries due to poor access of drugs and the emergence of widespread drug resistance.[121] Current research on natural molecules and products with antimicrobial activity primarily focuses on microorganisms, but plants are also of interest due to two reasons: they are easy to source and as they are often part of ethnopharmacopoeias all over the world, a pre-selection of plants due to their traditional use may enhance the success in new drug-finding efforts. Even if no plant derived compound has been found which can compete with clinically used antibiotics yet, the search of novel lead structures remains a task to be pursued.[1]

Due to an increasing incidence of opportunistic mycoses associated with AIDS or immunosuppressive drugs, the search for antifungal drugs has been revived in the last years, as there are currently only a few antifungal agents with very limited efficacy indicated for the treatment of systemic mycoses.[1]

In the present study the antiprotozoal, antifungal, and antibacterial assays have been performed together at the Laboratory of Microbiology, Parasitology and Hygiene (LMPH), Antwerp University, Belgium, because their use of an integrated *in vitro* screening, including a cytotoxicity evaluation on the host cell lines and different microbial screens, allows the exclusion of false-positives as a result of aspecific cell toxicity.[122]

ANTIBACTERIAL ASSAYS

The Gram-positive *Staph. aureus* and Gram-negative *E. coli* served as model organisms in the evaluation of potentially antibacterial properties of the plant extracts tested in this study. *Staph. aureus* can cause a range of illnesses from minor skin infections, such as boils, carbuncles, or abscesses to life-threatening diseases, like pneumonia, meningitis, osteomyelitis, endocarditis, Toxic Shock Syndrome, and septicaemia. The development of "multi-resistant" strains, namely MRSA (methicillin-resistant *Staph. aureus*) is especially troublesome in hospital-associated (nosocomial) infections, as patients with open wounds, invasive devices, and weakened immune systems are especially prone to infections.[123]

Most *Escherichia coli* strains - commonly part of the normal gut flora - are harmless, but some can cause serious food poisoning, urinary tract infections, neonatal meningitis, peritonitis, mastitis, septicaemia, and Gram-negative pneumonia or are also responsible for the severe Haemolytic-Uraemic Syndrome.[123]

The resazurin assay, the method of choice in this study, a simple, sensitive, rapid, robust, and reliable method is widely used to determine the minimum inhibitory concentration (MIC) values of natural products, including crude extracts against various bacteria and fungi. Resazurin, an oxidation–reduction indicator used for the evaluation of cell growth, is a blue non-fluorescent and non-toxic dye becoming pink coloured and fluorescent when reduced to resorufin by oxidoreductases within viable cells.[124]

Staph. aureus (ATCC6538) and *E. coli* (ATCC8739) were maintained in TSB (Tryptone Soy Broth) and on TSA (Tryptone Soy Agar) and all cultures and assays were conducted under a humidified atmosphere (37°C, 4% CO_2, 3% O_2, and 93% N_2). Assays were performed in sterile 96-well microtiter plates, each well containing 10 µL of the watery extract dilution (DMSO final content <1%) together with 190 µL of bacteria inoculum ($5x10^3$ CFU/mL). Bacterial growth was compared to untreated-control wells (100% cell growth) and medium-control wells (0% cell growth). After an incubation of 17 h (or longer – depending on the organism), bacterial viability was assessed fluorimetrically (λ_{ex} 550 nm, λ_{em} 590 nm) 0.5 h after addition of 20 µL resazurin per well. The results were expressed as % reduction in bacterial growth/viability compared to control wells and an IC_{50} was determined. The extracts were tested at five concentrations (64; 16; 4; 1 and 0.25 µg/mL) and an extract was classified as inactive with an IC_{50} > 15 µg/mL. Between 5 and 15 µg/mL it was regarded as moderately active. An IC_{50} < 5 µg/mL was classified as highly active. Standard bacterial reference compounds included ampicillin (*Staph. aureus*) and doxycyclin (*E. coli*).

ANTIFUNGAL ASSAYS

The dermatophytic fungus *Trichophyton rubrum* is the most common cause of athlete's foot, ringworm, and jock itch (*Tinea cruris*). *Microsporum canis*, another dermatophytic fungus is

usually found in cats, but it is also sometimes transmitted to humans and if so it is very contagious and causes a severe form of hair-loss. *Candida albicans*, often associated with opportunistic oral or genital infections in humans, can also be the causal agent for severe fungaemias (systemic fungal infections), particularly common in immunocompromised patients. Infections with *Aspergillus fumigatus* are also common in these individuals, sometimes eliciting severe illnesses: acute invasive aspergillosis in the lung or disseminated invasive aspergillosis widespread in the body.[123]

The antifungal assays were performed the same way as the antibacterial assays, only using Sabouraud agar or broth instead of TSB or TSA. Models utilised in the antifungal screen were *Trichophyton rubrum* strain 68183 and *Microsporum canis* as representatives of the dermatophytes, the opportunistic yeast *Candida albicans*, and the opportunistic filamentous fungus *Aspergillus fumigatus* strain 42928. Standard reference compounds included econazole (*T. rubrum*), terbinafine (*M. canis* and *A. fumigatus*), or flucytosine (*C. albicans*), respectively.

2.3 ANTIPROTOZOAL ASSAYS

Malaria is without doubt one of the major scourges of humanity, with about 1.5 to 2.7 million deaths per annum (most of them children) and chemotherapy is hindered by the increase in drug resistant strains, particularly of *Plasmodium falciparum*, which causes Malaria tropica, the most severe form (WHO, 1997). It is transmitted by female mosquitoes of the genus *Anopheles*. Among synthetic drugs quinine, the first effective drug against malaria is still in clinical use. Another plant derived drug, artemisinin, an unusual sesquiterpen endoperoxide has been isolated as the active principle from *Artemisia annua* “Qing hao” (Asteraceae), an herb used as a febrifuge and against malaria in China for almost two millennia. Together with its derivatives it was found to be effective against multi drug resistant strains of *Plasmodium falciparum* and created a breakthrough in preventing almost a million deaths from severe malaria per year.[4]

Leishmaniasis is a group of usually tropical diseases caused by representatives of the genus *Leishmania*, affecting about 12 million people each year.[125] As transmitters have been identified female flying insects of the genus *Phlebotomus* (Old World leishmaniasis) and *Lutzomya* (New World leishmaniasis).[126] The WHO has classified leishmaniasis in four clinical forms: visceral, muco-cutaneous, cutaneous diffuse or disseminated, and cutaneous. Although a number of drugs have been developed to date, only the recently launched miltefosine has demonstrated to be fully effective against *Leishmania* parasites.[127]

Sleeping sickness or African Trypanosomiasis is a parasitic disease caused by subspecies of *Trypanosoma brucei* which are transmitted by the Tsetse fly (*Glossina sp*.). The disease is endemic in certain regions of Sub-Saharan Africa and it is estimated that 50,000 to 70,000

people are currently infected (WHO, 2006). The four drugs registered for the treatment of sleeping sickness are of synthetic origin.

Chagas disease or (South-) American Trypanosomiasis is caused by subspecies of *Trypanosoma cruzi* transmitted mostly by blood-sucking assassin bugs of the family Reduviidae, subfamily Triatominae. It is estimated, that 11-18 million people are infected in South America and 100,000 are at risk acquiring this disease.[128] Drugs of choice in its treatment are the very toxic azole or nitroderivatives such as benznidazole, which causes many side effects and in addition resistances have also already been observed. Studies on natural products have already taken place, so dermaseptins from the frog species *Phyllomedusa oreades* and *Phyllomedusa distincta*[129] have shown some effects as well as the sesquiterpene lactone dehydroleucodine isolated from an *Artemisia* species.[130]

CYTOTOXICITY

Although many other cell types can be used, MRC-5SV2 cells are utilised by the LMPH because of their receptiveness and sensitivity for many viruses and parasites and therefore possible standardisation across different bioassays. The cells were cultured in Earl's MEM supplemented with 5% heat-inactivated FCS, 20 mM L-glutamine, and 16.5 mM sodium bicarbonate. Assays were performed in 96-well microtiter plates, each well containing $1x10^4$ cells. Compounds were tested at five concentrations (64; 16; 4; 1 and 0.25 µg/mL) and after an incubation of 72 h in a humidified atmosphere (37°C, 5% CO_2) and addition of resazurin (see also "2.3 ANTIBACTERIAL AND ANTIFUNGAL ASSAYS"); cell viability was assessed fluorimetrically (λ_{ex} 550 nm, λ_{em} 590 nm). The results were expressed as % reduction in cell growth/viability compared to untreated control wells and IC_{50s} were determined. An extract was classified as inactive with an IC_{50} > 15 µg/mL. Between 5 and 15 µg/mL it was regarded as moderately active. An IC_{50} < 5 µg/mL was classified as highly active. Tamoxifen was included as reference drug.

IN VITRO ANTI-*PLASMODIUM FALCIPARUM* ACTIVITY

The chloroquine-sensitive 1/ GHA (*P.falGHA*) *Plasmodium falciparum* strain - derived from a Ghanese patient - was used: It was maintained in RPMI-1640 medium supplemented with 0.37 mM hypoxanthine, 25 mM HEPES-buffer, 25 mM sodium bicarbonate, and 10% human 0+ serum together with 2 - 4% washed human 0+ erythrocytes.[131] All cultures and assays were conducted under a humidified atmosphere (37°C, 4% CO_2, 3% O_2, and 93% N_2) with the assay being an adaptation of the procedure described by Desjardins et al., 1979.[132] Assays were performed in 96-well microtiter plates, each well containing 10 µL of the watery extract dilutions together with 190 µL of the malaria parasite inoculum (1% parasitaemia, 2% haematocrit). After an incubation of 72 h at 37°C, plates were frozen and stored at -20°C. After thawing, 20 µL of each well was transferred into another plate together with 100 µL

Malstat® reagent and 20 µL of a 1/1 mixture of PES (phenazine ethosulphate, 2 mg/mL) and NBT (Nitro Blue Tetrazolium Grade III, 0.1 mg/ml). The plates were kept in the dark for 2 h and change in colour was measured spectrophotometrically at 655 nm. The results were expressed as % reduction in parasitaemia compared to control wells. The extracts were tested at five concentrations (64; 16; 4; 1 and 0.25 µg/mL) and an extract was classified as inactive with an IC_{50} > 15 µg/mL. Between 5 and 15 µg/mL it was regarded as moderately active. An IC_{50} < 5 µg/mL was classified as highly active. Chloroquine was included as reference drug.

IN VITRO ANTI-*LEISHMANIA INFANTUM* ACTIVITY

In this study the visceral species *Leishmania infantum* was chosen, because visceral show a higher sensitivity to available reference drugs than cutaneous forms, validated models are available, and they represent a greater medicinal need.[122] The strain *Leishmania infantum* MHOM/MA (BE)/67 was maintained in the golden hamster and spleen amastigotes were collected for preparing infection inocula. Primary peritoneal mouse macrophages were used as host cells and collected 48 h after peritoneal stimulation with a 2% potato starch suspension. Assays were performed in 96-well microtiter plates, each well containing 10 µL of the extract dilutions together with 190 µL of macrophage/parasite inoculum ($3x10^5$ cells and $3x10^6$ parasites/well in RPMI-1640 + 5% heat-inactivated FCS). After an incubation of 120 h in a humidified atmosphere (37°C, 5% CO_2), parasite burdens (mean numbers of amastigotes/macrophage) were microscopically assessed after Giemsa staining. The results were expressed as % reduction in parasite burden compared to untreated control wells and IC_{50s} were calculated. The extracts were tested at five concentrations (64; 16; 4; 1 and 0.25 µg/mL) and an extract was classified as inactive with an IC_{50} > 15 µg/mL. Between 5 and 15 µg/mL it was regarded as moderately active. An IC_{50} < 5 µg/mL was classified as highly active. Miltefosine was included as reference drug.

IN VITRO ANTI-*TRYPANOSOMA BRUCEI BRUCEI* ACTIVITY

Because of its non-pathogenicity for humans, a drug sensitive strain of *Trypanosoma brucei brucei* is used in the primary screening performed in the LMPH. The strain *Trypanosoma brucei brucei* Squib 427 (suramin-sensitive) was maintained in HMI-9-medium supplemented with 10% heat-inactivated FCS. Assays were performed in 96-well microtiter plates, each well containing 10 µL of the extract dilution together with 190 µL of the parasite suspension ($7x10^4$ parasites/mL). After incubation in a humidified atmosphere (37°C, 5% CO_2) for 72 h, resazurin (see also “2.3 ANTIBACTERIAL AND ANTIFUNGAL ASSAYS”) was added and 24 h later under the same conditions the parasite growth was assessed fluorimetrically (λ_{ex} 550 nm, λ_{em} 590 nm). The results were expressed as % reduction in parasite growth/viability compared to control wells and IC_{50s} were calculated. The extracts were tested

at five concentrations (64; 16; 4; 1 and 0.25 µg/mL) and an extract was classified as inactive with an IC_{50} > 15 µg/mL. Between 5 and 15 µg/mL it was regarded as moderately active. An IC_{50} < 5 µg/mL was classified as highly active. Suramin was included as reference drug.

IN VITRO ANTI-*TRYPANOSOMA CRUZI* ACTIVITY

As a model for *Chagas* disease the biohazard class-3 pathogen *Trypanosoma cruzi* was used. The nifurtimox-sensitive *Trypanosoma cruzi*, Tulahuen CL2, β galactosidase strain was maintained on MRC-5SV2 cells in MEM medium, supplemented with 200 mM L-glutamine,16.5 mM sodium bicarbonate, and 5% heat-inactivated FCS. All cultures and assays were conducted under a humidified atmosphere (37°C, 5% CO_2). Assays were performed in 96-well microtiter plates, each well containing 10 µL of the watery extract dilutions together with 190 µL of MRC-5SV2 cell/parasite inoculum ($2x10^4$ cells/mL and $2x10^5$ parasites/mL). After an incubation of 168 h parasite growth was compared to untreated-infected controls (100% growth) and non-infected controls (0% growth). Parasite burdens were assessed after adding of the substrate: 50 µL/well of a stock solution containing 15.2 mg CPRG (chlorophenolred *ß*-D-galactopyranoside) and 250 µL Nonidet in 100 ml PBS. The change in colour was measured spectrophotometrically at 540 nm after an incubation of 4 h at 37°C. The results were expressed as % reduction in parasite burdens compared to control wells and IC_{50s} were calculated. The extracts were tested at five concentrations (64; 16; 4; 1 and 0.25 µg/mL) and an extract was classified as inactive with an IC_{50} > 15 µg/mL. Between 5 and 15 µg/ml it was regarded as moderately active. An IC_{50} < 5 µg/mL was classified as highly active. Benznidazol was included as reference drug.

2.4 INFLICTIONS OF THE CENTRAL NERVOUS SYSTEM (CNS) - ASSAYS

There still remains an urgent need for drugs effective in diseases caused by malfunctions of the central nervous system (CNS), e.g. pain disorders such as migraine, sleeping disorders, epilepsy, dementia like *Alzheimer's* disease (AD), *Parkinson's* disease, and *Huntington's* chorea, and affective disorders like bipolar, schizophrenia, depression, and anxiety. Natural products have already shown CNS activities, e.g. caffeine, codeine, or nicotine and it is likely that there are further such drugs still to be found in nature.[4]

AD is a degenerative and terminal disease whose cause and progression are only poorly understood, but research indicates that it is associated with plaques and tangles in the brain. Three major competing hypotheses exist to explain the cause of the disease, the cholinergic, the amyloid, and the *tau* hypothesis.

ACETYLCHOLINESTERASE- AND BUTYRYLCHOLINESTERASE-INHIBITORS

The oldest hypothesis is the “cholinergic hypothesis”, stating that AD begins as a deficiency in the production of acetylcholine (ACh), a vital neurotransmitter.[133] Usually acetylcholine is synthesized by the enzyme choline acetyltransferase (ChAT) from choline and acetyl-CoA. The discovery of a correlation between the loss of ChAT and a decline in mental status scores[134] lead to the cholinergic hypothesis of cognitive impairment in AD. Cholinesterases are a ubiquitous class of serine hydrolases and apart from their classical role in cholinergic transmission they are involved in cell proliferation, differentiation, responses to various insults including stress, and amyloid formation.[135] Two forms occur in vertebrates, the acetylcholinesterase (AChE) and the butyrylcholinesterase (BChE). AChE catalyzes the cleavage of ACh in the synaptic cleft after depolarization and whereupon acetylcholinesterase-inhibitors are frequently used in the pharmacotherapy of AD, the less specific BChE has only recently got into focus of research, because BChE concentration stays the same or is even up-regulated while AChE concentration is dramatically down-regulated in brains of patients suffering from AD.[136] Some natural or naturally-derived structurally different AChE-inhibitors are already in use, e.g. the Amaryllidaceae-alkaloid galantamine (isolated from the Caucasian snowdrop *Galanthus woronowii*), the physostigmine-derivative rivastigmine, the piperidin-congener donepezil-HCl, desoxyvasicine, an alkaloid isolated from *Peganum harmala* (Nitrariaceae), and dehydroevodiamine, an alkaloid from *Euodia rutaecarpa* (Rutaceae)[137] which are not able to stop AD, but may slow its progression and hippocampal atrophy and may have at least disease-modifying effects.[138]

More recent hypotheses focus upon the effects of the misfolded and aggregated peptides amyloid *beta* (A*β*) and *tau*. Soluble and harmless A*β* monomers can undergo a dramatic conformational change forming *beta*-sheet rich tertiary structures that aggregate to neurotoxic amyloid fibrils, which deposit outside neurons as so called senile or neuritic plaques, a process promoted by AChE[139] and BChE.[140]

In AD patients hyper-phosphorylated microtubule associated and stabilizing *tau* proteins accumulate as paired helical filaments and aggregate into neurofibrillary tangles, associated with amyloid plaques.[141]

To date the approved therapeutical options to AD are extremely limited to only four AChE inhibitors, namely galantamine, rivastigmine, donepezil-HCl, and tacrine, whereas the last one seems to have hepatotoxic properties, and the NMDA receptor antagonist memantine, so research in this area is highly eligible.

<u>Ellman Test</u>

This assay has been performed in the Department of Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy, University of Jena, Germany.

The Ellman Test is a photometric method to determine cholinesterase-activity of tissue extracts, homogenates, cell suspensions, etc., whereas the enzymatic activity correlates with the formation of a yellow coloured product, based on the following formula:[142]

$$acetylthiocholine \xrightarrow{cholinesterase} thiocholine + acetate$$
$$thiocholine + dithiobisnitrobenzoate \rightarrow yellow\ colour$$

100 µL extract (final concentration 160 µg/mL), 3 mL phosphate buffer pH 8, 100 µL 5,5'-dithiobis-2-nitrobenzoate, and 100 µL AChE (or BChE respectively) were mixed in a cuvette and the self-absorption of the extract (blank) was measured at 412 nm. 20 µL acetyl-thiochinolineiodide (or butyryl-thiochinolineiodide) were added, the probe was measured at 412 nm, and after subtraction of the blank the actual inhibition-value was obtained. Cloudy and yellow-coloured probes were excluded from the test. Inhibition-values greater than 70% were considered as positive. Each test has been performed in triplicates, but was not replicated yet.

NMDA RECEPTOR ANTAGONISTS

The NMDA (*N*-methyl *D*-aspartate) receptor is an ionotropic receptor for glutamate. Its activation causes the opening of an ion channel, resulting in Na^+- and Ca^{2+}- influx and K^+-efflux. The Ca^{2+}-influx is thought to play a role in synaptic plasticity, a cellular mechanism for memory and learning.

NMDA receptor antagonists are used as anaesthetics, e.g. ketamine and also often as recreational drugs, e.g. ibogaine because of their hallucinogenic properties. Since NMDA receptors play an important role in excitotoxicity, a pathological process in which nerve cells are damaged or killed by glutamate and similar substances, their antagonists are promising agents in the treatment of traumatic brain injury, stroke, or neurogenerative diseases, such as AD, *Parkinson's* disease, or *Huntington's* chorea.

NMDA-Assay

This assay has been performed in the Department of Pharmaceutical Biology, Institute of Pharmacy, University of Jena, Germany.

The utilised murine L12-G10 cells were obtained by stable transfection of murine fibroblast L(tk-) cells with the subunits NR1-1a and NR2a of the human NMDA-receptor (generously provided by Prof. D. Steinhilber, University of Frankfurt am Main, Germany), in which the receptor expression is regulated by addition of dexamethasone, mediated by a glucocorticoid-responsive element. The cells were cultivated in Earl's MEM supplemented with 10% heat-inactivated FCS, 0.5 mM sodium pyruvate, 1% penicillin and streptomycin, 80 µg/mL G418 (geneticin), and 100 µM ketamine. The assay was performed according to Steinmetz et al. (2002)[143] (slightly modified) in 96-well microtiter plates, each well containing $1x10^4$ cells in 200 µL cultivation medium. The cells were preincubated for 30 h in a humidified

atmosphere (37°C, 5% CO_2); the medium was removed and substituted with fresh medium (plus 4 µM dexamethasone). After an incubation time of 18 h under the same conditions the cells were washed twice with MEM (without Phenol red) containing 1% bovine serum albumin (BSA) and once with MEM (with Phenol red) to remove the ketamine. 200 µL of an extract-dilution at a concentration of 50 µg/mL in MEM without Phenol red were added to each well (DMSO final content <0.1%) and after a pre-incubation of 30 min. under the same conditions as above for 30 min., a mixture of glycine and L-glutamate (10 µM) was added and the cells were incubated for 4 h. Excitotoxicity was determined by detection of LDH (lactate dehydrogenase) release into culture supernatants using the *Cytotoxicity Detection Kit*® (Roche Diagnostics, Mannheim, D) 100 µL of the supernatant were mixed with 100 µL reaction reagent (containing iodonitrotetrazoliumchloride (INT)) and after an incubation of 35 min. in the dark, allowing the formation of a red coloured formazan product, metabolised by LDH from INT, the plates were measured at 492 nm (HTS 7000 plate reader, Perkin Elmer). Every test was performed at least in hexaplicates and all experiments have been repeated only once yet (*n*=2). Memantine [4.4 µM] and ketamine [6.4 µM] were included as reference drugs.

The calculation of the excitotoxicity was carried out using the following formula:

$$excitotoxicity[\%] = \frac{Aextract - Aneg.ctrl.}{Apos.ctrl. - Aneg.ctrl} x100$$

$Aneg.ctrl.$ Absorption of the negative control, containing 100 µM ketamine in Earl's MEM without Phenol red; excitotoxicity = 0%

$Apos.ctrl.$ Absorption of the positive control, containing Earl's MEM without Phenol red; excitotoxicity = 100%

$Aextract$: Absorption of the extract-dilution (50 µg/mL extract in Earl's MEM without Phenol red)

3. EXTRACTION

The heat-dried plant material used in the biological assays (30 g) was ground to powder (RETSCH ZM1, Retsch GmbH, Haan, Germany) with a particle size of 0.5 mm, mixed with 10 g of sea sand and first extracted with dichloromethane (DCM) (all solvents used were pure grade or purified by distillation prior to use) at 50°C in four cycles of five minutes each, using an "Accelerated Solvent Extractor" (ASE 100, Dionex GmbH, Idstein, Germany). The remaining plant material was then extracted with ethyl acetate (EtOAc) and finally with methanol (MeOH) under the same conditions (Fig. 14). The crude extracts were stored at -80°C.

For the phytochemical investigation of *Baccaurea stylaris* MUELL. ARG. (voucher no. 1786-6C), 750 g of the heat-dried drug material were processed and extracted as above, yielding 90.9 g crude extract from the extraction with DCM, 4.99 g from that with EtOAc, and further 79.32 g with MeOH/H_2O (8:2).

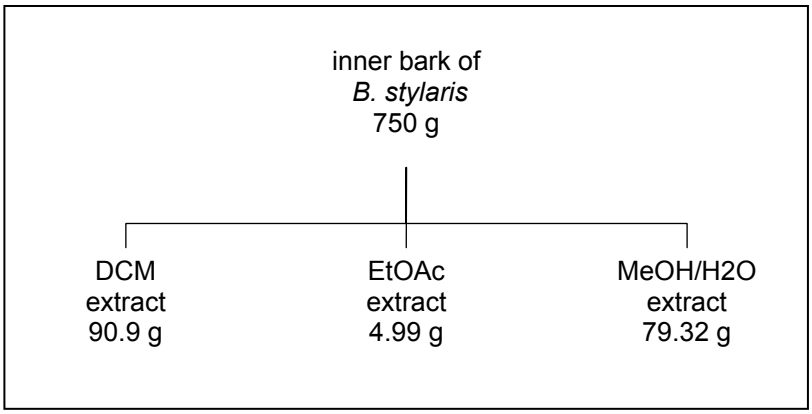

Fig. 14 Extraction scheme

4. ISOLATION

The separation of substances from a crude extract or from a fraction often is a long and expensive process. Like the proverbial needle in a haystack a lot of hay has to be removed to leave only the needle, without knowing what the needle looks like or where it is in the haystack.[144] The nature of the separation problem varies considerably and most separation procedures require several steps.

Thin layer chromatography (TLC) is a classic and simple planar chromatography method in which the mobile phase migrates through a stationary phase with a flat geometry by capillary action. Only a suitable vessel and a coated plate are required to carry out separation or qualitative and semiquantitative analyses. The broad choice of layers – modified or unmodified – developing solvents as well as detection reagents, lead to unsurpassed specificity in TLC and - being an off-line method - the various steps of procedure can also be carried out independently.[145]

In the present study NP (normal phase: silica gel) TLC was used in routine laboratory work for identifying and monitoring the behaviour of components during purification and at the final purification step, and it was also used to select and optimize the mobile phase for column chromatography conditions. It was performed on precoated silica gel 60 F_{254} plates (Merck KG a. A., Darmstadt, D), while detection was achieved at 254 nm by (Camag UV Cabinet, Berlin, D) and by spraying with anisaldehyde-sulphuric acid followed by heating.

Although a variety of modern techniques are also available, conventional gravity-driven open column chromatography is still widely used in natural product research, since silica gel chromatography provides a mild and efficient technique for preliminary fractionation of crude extracts or fractions and may also yield pure compounds.[146]

Vacuum-liquid chromatography (VLC) is a very convenient and simple open column method mostly used for crude fractionation of plant extracts. The reduced pressure utilised in this technique leads to an increase of the flow rate of the mobile phase through a short bed of stationary phase.[146] The VLC column is a glass funnel, which is dry packed with TLC grade sorbents. Uniform and tight packing is achieved by initially tapping onto the funnel and by application of a vacuum from below it. The sample is applied to the top and eluted with appropriate solvent mixtures, starting with solvent of low polarity while working with NP. Advantages of the VLC include the simplicity of equipment, low costs, low solvent consumption as well as the speed of separation.[146]

In the present work VLC was used as an initial separation procedure for the crude extracts. High performance liquid chromatography (HPLC) has developed in the recent years into one of the leading chromatographic techniques in natural product research, in both analytical and preparative scale. The combination of rapid analysis, high resolution, and separation power as well as elimination of a prior derivatization step, gives HPLC a marked advantage over other methods of separation.[147] The use of microparticulate supports (7-18 µm) and high flow rates at pressures up to 300 – 400 bar, permits very high separation efficiency. However, detection is still one of the weakest points of practical HPLC, although a definite progress has been made in the design of sensitive and specific detectors in the recent years. [148] The complexity, high capital-, and maintenance costs are other disadvantages of this method. HPLC (Varian Pro Star, Darmstadt, Germany) was applied as final purification step.

FRACTIONATION PROTOCOL

Fractionation and isolation (Fig. 15) were carried out from the DCM-extract of *Baccaurea stylaris* MUELL. ARG. by various chromatographic methods as described previously.

10 g of the extract were crudely fractionated via VLC using a column of 4.5 cm diameter and 29 cm of the stationary phase in height (consisting of 250 g silica gel Geduran SI60 (Merck, Darmstadt, D) with a particle size of 0.063 – 0.2 mm), while the extract was eluted two times with 5,400 mL solvent each and with a step gradient (100%, 75/25%, 50/50%, 25/75%,

100%) of petrol ether (PE) with increasing concentrations of EtOAc and EtOAc and increasing concentrations of MeOH to give seven fractions (V1 – V7).

0.35 g of the fraction V2 (eluted with PE/EtOAc 7.5:2.5) were processed by open column chromatography using a column of 2.5 cm diameter and 43.5 cm length of the stationary phase (silica gel; 70 g) with 1,515 mL PE/ EtOAc (10:1) as elution agent yielding in six fractions (I1 – I6).

Fraction I4 (eluted between 555 and 690 mL) was further processed by HPLC using a RP_{18}-Eurospher 100 column of 1.6 cm in diameter and 22 cm length; particle size C18 - 7 µm) using ACN/H_2O (9:1) giving six fractions (I4G1 – 6), including 20 mg of the pure compound I4G5 (eluted between 7 and 22 min. with a flow rate of 4.6 mL/min.).

Fraction I5 (eluted between 690 and 825 mL) was further processed by HPLC as described above yielding seven fractions (I5G1 – 7), including 12.1 mg of the pure compound I5G5 (eluted between 9.5 and 13 min. with a flow rate of 4.6 mL/min.).

0.88 g of the fraction V3 (eluted with PE/EtOAc 5:5) were processed by open column chromatography using a column of 4.5 cm diameter and 50 cm length of the stationary phase (silica gel; 300 g) with PE/ EtOAc (8:2) as elution agent yielding in 13 fractions (G1 - 13), with G7 (40 mg; eluted between 3,480 and 3,945 mL) already pure.

0.2 g of the fraction G6 (eluted between 2,760 and 3,480 mL) were further processed by open column chromatography using a column of 3.5 cm diameter and 20.5 cm length of the stationary phase (silica gel; 60 g) with PE/ EtOAc (7.5:2.5) as elution agent yielding in seven fractions (D5G1 - 7) and giving 20.6 mg of the pure compound D5G2 (eluted between 465 and 705 mL).

0.23 g of the fraction G9 (eluted between 4,440 and 6,375 mL) were further processed by open column chromatography using a column of 2.0 cm diameter and 46 cm length of the stationary phase (silica gel; 70 g) with PE/ EtOAc (7.5:2.5) as elution agent yielding in five fractions (D6G1 - 5).

25 mg of fraction D6G2 (eluted with 1,140 and 1,560 mL) were further processed by HPLC as described above yielding three fractions (D6.1G1 – 3) and giving 15 mg of the pure compound D6.1G2 (eluted between 6.2 and 8 min. with a flow rate of 4.6 mL/min.).

0.2 g of the fraction V4 (eluted with PE/EtOAc 2.5:7.5) were further processed by open column chromatography using a column of 3.5 cm diameter and 19.8 cm length of the stationary phase (silica gel; 60 g) with PE/ EtOAc (1:1) as elution agent yielding in six fractions (E1 - 6). Fraction E6 (eluted between 1,965 and 2,115 mL) was further processed by HPLC as described above yielding three fractions (E6G1 – 3), including 10 mg of the pure compound E6G3 (eluted between 5.4 and 25 min. with a flow rate of 4.6 mL/min.).

0.35 g of the fraction V5 (eluted with EtOAc 100%) were further processed by open column chromatography using a column of 3.5 cm diameter and 27.8 cm length of the stationary

phase (silica gel; 75 g) with PE/ EtOAc (2:1) as elution agent yielding in ten fractions (H1 - 10). Fraction H9 (eluted between 3,045 and 3,345 mL) was further processed by HPLC as described above yielding two fractions (H9G1 – 2), including 7 mg of the pure compound H9G1 (eluted between 0 and 5.6 min. with a flow rate of 4.6 mL/min.).

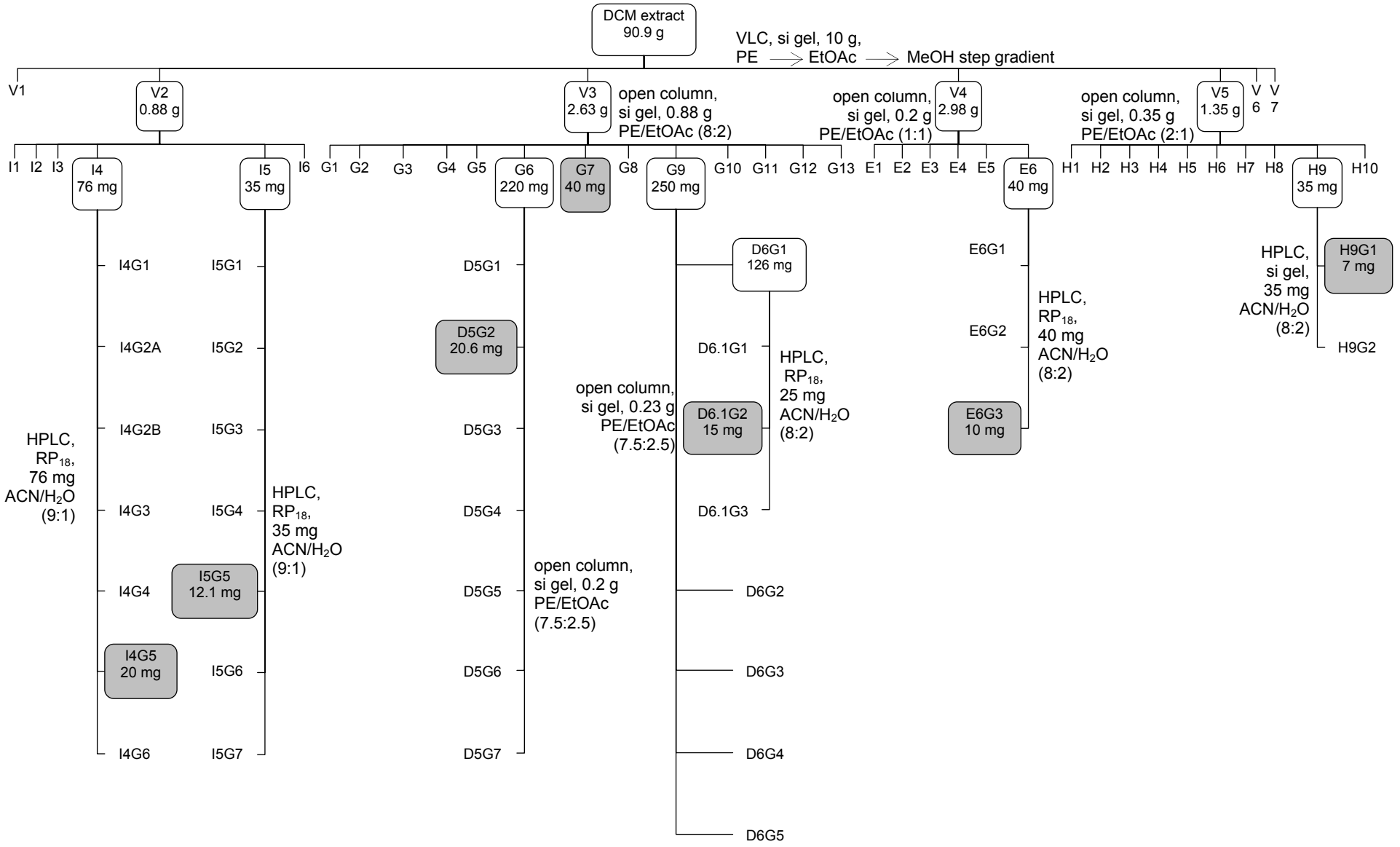

Fig. 15 Isolation scheme of the DCM-extract of *B. stylaris*

5. STRUCTURE ELUCIDATION

The process of structure elucidation is like a puzzle being pieced together to yield a chemical structure. It involves the accumulation of data obtained from numerous sources, each giving some structural information. Nowadays a wide range of spectroscopic, spectrometric, and physical methods are available and the methods used in this study will be briefly in the following.

5.1 SPECTROSCOPIC METHODS

UV/ VIS SPECTROSCOPY

Organic molecules are able to absorb ultraviolet (UV) or visible (VIS) light, whereas different molecules absorb radiation of different wavelengths. UV/VIS spectroscopy deals with this interaction of electromagnetic radiation with the molecules in a wavelength range between 200 and 800 nm (UV: 200-380 nm; VIS: 380-800 nm). The frequency of the absorbed radiation correlates with the structure of the molecule and therefore absorption spectra, in which the amount of absorbed light for each wavelength is shown, show a pattern of maxima characteristic for the chemical structure of the molecule.
UV spectra were recorded on a Cary 50 Scan (Varian, Darmstadt, Germany), all compounds in $CHCl_3$, purity > 99.9%.

NMR-SPECTROSCOPY

Atomic nuclei such as ^{1}H or ^{13}C can be visualised like tops, turning on their own axis (this feature is called “spin”, but this doesn’t mean that they actually turn on their own axis but describes a quantum mechanical property).[149] Due to this fact and that nuclei are charged they behave like tiny bar magnets and when placed in a magnetic field, two things happen: they adopt one of two possible orientations, aligned with the external magnetic field or opposite to it and exhibit a characteristic rotational motion, known as “precession”. Its resonant frequency, the so called Larmor frequency, differs characteristically for each type of nucleus. All nuclei that contain a non-zero spin quantum number can be used for NMR spectroscopy, e.g. ^{1}H, ^{2}D, ^{13}C, ^{15}N, ^{17}O, or ^{19}F. Four isotopes appear to have the greatest potential for structure determination of natural organic molecules: ^{1}H, ^{13}C, ^{15}N, and ^{17}O.[150]
In NMR spectroscopy the behaviour of certain nuclei in a magnetic field is observed. A method for obtaining an NMR spectrum is the pulse-Fourier-transformation technique. It involves irradiation of the sample with a single radiofrequency pulse of only a few microseconds duration and if the resonant frequency is chosen, all nuclei are excited and emit signals known as free induction decays (FID). Fourier transformation of this decay yields the NMR-spectrum.[151]

Of all modern methods used for structure elucidation, NMR spectroscopy provides the most complete information, either with or without prior structural knowledge. Not only number and type of nuclei present, but also their individual environment in a molecule can be determined. Disadvantages of this method are on the one hand high acquisition costs of the instrument and the deuterated solvents and on the other hand the difficulty of a valid interpretation, particularly of two-dimensional spectra, which usually requires considerably more than minimal experience.[151]

One dimensional NMR techniques (1D-NMR)

Most NMR studies begin with recording of 1D-NMR spectra, most notably ^{1}H- and ^{13}C measurements.

In the ^{1}H NMR nuclei in a molecule are also influenced by their surrounding electrons. These produce a weak magnetic field which slightly shields the nucleus from the applied magnetic field. This causes differences in the Larmor-frequencies of the nuclei due to the chemical environment, an effect called chemical shift. Thus, ^{1}H NMR supplies a convenient method for the determination of the chemical shift for each resonance as well as the relative number of protons responsible for each resonance calculated from their integrated intensities. If multiplicity and coupling pattern of each signal are also interpretable, the number and the stereochemical orientation of adjacent protons can be proposed as well.[149]

The ^{13}C NMR provides important chemical information since it directly arises from the nuclei forming the framework of an organic molecule. It also gives information on non-protonated carbon atoms such as carbonyl groups, which are not detectable in the ^{1}H NMR. In the ^{1}H decoupled ^{13}C spectrum - the most frequent type - all ^{13}C signals appear as single lines. Altogether ^{13}C-spectra provide important structural information such as the number of carbon atoms present in a molecule, their substitution, as well as presence and sometimes also position of sugar moieties. A disadvantage is the larger sample amount compared with ^{1}H spectra.[151]

All ^{1}H and ^{13}C NMR experiments were recorded on a Bruker Avance 300 (operating at 300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C) at 296.1 K. The spectra were recorded in $CDCl_3$ (Deutero GmbH, purity 99.8%, Kastellaun, Germany) and referenced against residual non deuterated solvent.

Two dimensional NMR techniques (2D-NMR)

The interpretation of a 1D spectrum for complex molecules is not possible due to signal overlapping, but if a new dimension is brought in, these overlaps can be solved. The resulting spectra show the frequency on both axes, while the signal intensities correspond to the third dimension. Thus the spectra are represented as contour plot, just as mountains on an ordinary map. The spectra are obtained by recording a series of 1D spectra differing only by a time increment.[149] 2D NMR techniques can be divided into two groups, homonuclear,

and heteronuclear methods, the homonuclear correlating couplings within the same type of atoms (COSY, NOESY) and the heteronuclear correlating ^{1}H coupling with ^{13}C atoms. (HMBC, HSQC).

The correlation spectroscopy (COSY) correlates protons through homonuclear coupling and is thus the primary 2D technique utilised for structure elucidation. In a COSY spectrum only signals of protons which are coupled over only two or three bonds are visible. For aliphatic compounds this technique is very useful, but for highly substituted aromatic compounds heteronuclear experiments also have to be performed.[152]

The nuclear Overhauser effect allows to determine the local neighbourhood of the nuclei within a molecule and to infer information about their distances. In the nuclear Overhauser enhancement spectroscopy (NOESY) information of all nuclei in a molecule is given in a single experiment, helping to identify protons close enough to interact, yielding the relative stereochemistry of the molecule.[149]

Heteronuclear shift correlation NMR-spectroscopy is a 2D technique utilised to determine, which ^{1}H of a molecule is bonded to which ^{13}C atom (or another nucleus) in the molecule. The heteronuclear multiple bond correlation (HMBC) experiment performs the H-C correlation via ^{13}C chemical shift evolution of double quantum coherence. It is extremely useful in determination of connectivity between ^{1}H and ^{13}C atoms separated by two or three bonds via their coupling constants. They provide the means to span heteroatoms and quaternary carbons, thus giving useful structural information.[152]

The heteronuclear single quantum coherence (HSQC) experiment yields the same information as the HMBC, but only signals of directly bond atoms are shown and it is therefore sometimes superior in the case of crowded ^{13}C spectra.[149]

The ^{1}H and ^{13}C NMR, COSY, NOESY, HSQC, and HMBC experiments were recorded on a Bruker Avance 400 (operating at 400.X MHz for ^{1}H and 100.X MHz for ^{13}C) at 296.1 K. The spectra were recorded in $CDCl_3$ (Deutero GmbH, purity 99.8%, Kastellaun, Germany) and referenced against residual non deuterated solvent.

5.2 MASS SPECTROMETRY

Mass spectrometry (MS) is a method in which an organic compound is degraded into fragments and the fragmentation pattern is recorded according to the mass. The sample vapour diffuses into a vacuum system of a mass spectrometer, where it is ionized to cause fragmentation of the chemical bonds. The resulting positively or negatively charged ions are accelerated in a magnetic field which disperses the fragments and permits the measurement of the relative abundance of ions with a given mass-to-charge ratio. Presented in a diagram as ion constituents versus mass it yields the mass spectral graph, consisting of a series of lines representing varying intensities at different mass units.[153] This technique only requires a

microgram of the substance to provide an accurate molecular weight and it also yields a complex fragmentation pattern, often characteristic for a particular compound.[154]

Electron Impact (EI) is the original mass spectrometry (MS) ionization method and is still probably the most widely used of all ionization methods. In the EI process, the sample of interest is bombarded with a stream of high energy electrons, in which an electron is removed from the molecule forming a positively charged ion. This electron removal leaves an unpaired electron in the molecule, making it to a highly reactive radical cation (molecular ion). The ionizing electrons carry an excess of energy, part of which is transferred to the newly produced ion as internal energy. This energy may cause the molecular ion to fragment into neutral pieces and smaller fragment ions.

The fragmentation of molecular ions into an assortment of fragment ions is a mixed blessing. The nature of the fragments often provides a clue to the molecular structure, but if the molecular ion has a lifetime of less than a few microseconds it may decompose entirely and the most vital piece of data, the molecular mass is lost. In such cases softer ionization techniques should be preferred.[155]

HR- and LREIMS (70 eV) was measured on a MAT 710A.

5.3 PHYSICAL METHODS

MELTING POINT

The melting point is a characteristic physical constant of amorphous or crystalline compounds that does not provide structural information but is a measure for their purity. In a dirty compound or a mixture of compounds it is always lower than in the pure analogue.

The melting points in this study were determined on a Melting Point B-545 apparatus (Buechi Labortechnik GmbH, Essen, Germany) (uncorrected).

RESULTS

1. ETHNOBOTANY

In Vanuatu most people do not assume Western *hospitel meresin* (hospital medicine) or *meresin blong waetman* (white man's medicine) and traditional *lif meresin* (leaf medicine) or *Kastom meresin* (*Kastom* medicine) as contradictory systems, but regard them as complementary elements creating one comprehensive medicinal system. In Aneityum this medical pluralism slightly lost balance towards Western medicine because of a good disposability of Western medicinal care all over the island for about 60 years by now, leading to a loss of former traditional knowledge and lack of interest in its preservation. Besides the two major hospitals in Port Vila (Efate) and Luganville (Espiritu Santo) and two smaller ones in Malekula and Tanna, there are health centres, dispensaries, and small "aid posts" dispersed over the islands. Hospitals, health centres, and dispensaries are run by the government and differ only in the number of employees. Aid posts are community owned health stations with volunteer workers trained by the Ministry of Health, providing first aid and health education service.[63] Building and volunteer workers are provided by the community, but medicines and medical equipment are supplied by the Ministry of Health.[65]

In previous ethnobotanical studies in Vanuatu it was assumed, that indeed the general population is knowledgeable about local plants and everyone seems to know at least a few recipes, but that some individuals, especially experienced in plants and treating sicknesses are known in their communities as true therapists and some of them with an extra knowledge of the supernatural powers, are the so called *klevas*.[67, 70, 71] This system could be proven in Aneityum and partly in Ambrym, but in Loh, Torres Islands every family had its special recipes for a variety of illnesses and preferably the elders of the own family of the same gender were consulted in case of a sickness. Indeed some elders were more experienced and knowledgeable, but no strict differentiation between ordinary and special healers was made. In Ambrym every member of a village was a specialist for a specific kind of illness and the adequate specialist was consulted by the patient no matter which family he belonged to. The knowledge on plants and traditional medicine is usually inherited from generation to generation. In Loh it is given from mother to daughter and father to son in a strict consexual manner and is most likely conserved in one family. In Ambrym and Aneityum this system has been eased. If a consexual heir is not at hand, these rules can be changed, and knowledge can be passed on inter-sexually from father to daughter or mother to son or even to third parties. In Ambrym also the transmission of knowledge of plant medicine with a "proven effect" to all community-members regardless of which family is common. Some especially gifted people in Ambrym, an island with strong magical beliefs, claimed to obtain their knowledge directly from spirits. Nowadays the traditional medicine is also partly influenced by

Christianity, which is very strong in Vanuatu. Not only maleficent magic implemented by an enemy, conjured magic "backfiring" to the initiator by careless use, or breaking an important taboo, but also sinful behaviour are regarded as possible sources of illnesses and former Christian rituals like exorcism mixed with herbal medicine and magic could be observed in treating a person with a diabetic foot in Ambrym. God is also sometimes named as creator of the "natural apothecary", e.g. in an interview in Loh a healer told me, that every plant on the island has properties as a medicinal plant, that even plants against AIDS and cancer could be found there due to the reason that god does not create an illness without setting an antipole and this special knowledge can be obtained in a dialogue with god.

1.1 SELECTION OF THE STUDY AREAS

One of the first priorities was to select the study sites. Due to the huge linguistic diversity (see 1.3 Population and Languages), Vanuatu cannot be considered as a consistent cultural area, a region where the inhabitants share the same culture, defined by ideas, behaviour, techniques, and social organisation[156]. In addition, by reason of the comparatively large distances between the single islands, inter-cultural exchange was only possible in a small degree. Furthermore due to diverse ecosystems as a result of dissimilar climate zones and soils (see 1.1 Geography, Geology, and Climate) a diverse island biodiversity can be at least expected for distant islands. Traced back to these facts, different medicinal systems should have developed on each island and sometimes even more than one. Therefore, islands in three climate zones and with different ethnological background were chosen which also had never or only poorly been studied before: in Loh and Southwest Ambrym ethnobotanical studies had never been performed before and in Aneityum only an investigation concentrating on plants used in gynaecology had taken place.[70, 71] The culture and mentality of the inhabitants of Loh is said to be related to that in the Solomon Islands and even though more Melanesian than Polynesian, the culture is located in a borderland sharing many values and practices that are idiosyncratic to both of these Oceanic regions.[157] The climate is tropical and the soil of coral origin. Ambrym, located in the middle of Vanuatu with a climate settled between tropical and subtropical, is a mountainous volcanic Island with pure Melanesian background and strong beliefs in magic. Aneityum in the far South is a mountainous island with a floral composition and subtropical climate resembling New Caledonia's and a pure Polynesian ethnological background.

1.2 ETHNOTAXONOMY

Taxonomy is regarded as one of the oldest fields of biological science, dating back at least to the time of Aristotle (381-323 $_{B.C.E.}$) who under the patronage of Alexander the Great undertook a large-scale classification, arranging biological organisms into a hierarchical

pattern, whereas the term “taxonomy” was coined not before 1813 by the Swiss botanist Augustin de Candolle. The tendency of organising the biological world is not peculiar to the Western world, but common to all cultures studied so far[158]. These folk taxonomies have attracted the attention of ethnotaxonomists over the last 50 years. Discrepancies between Linnean and folk taxonomy are widespread[159] and could be observed in this study, too. In the research areas visited medicinal as well as non-medicinal plants were classified by the healers exclusively by their leaves; flowers were never taken into account and it was even assumed, that some plants did not bear flowers at all. This situation sometimes posed a problem when identifying plants lacking flowers and the informant could give no information on their appearance. Another pitfall in plant taxonomy in the field is the use of vernacular names. Firstly it is essential to get a wordlist (see WORD LISTS) of the plant parts if the local language is not spoken, because local names of flower, fruit, or leaf or general categories as tree or shrub can be confused with the vernacular plant names. Secondly species can be under- or over-differentiated, a term used by anthropologists, viz. a single Linnean species can be split into two or more distinct species in the folk taxonomy system indicating different morphotypes, or *vice versa*. Scientific species of particular cultural significance are often over-differentiated. Under-differentiation may occur in cases where several taxa are used for the same purpose, e.g. as fuel wood[158]. Neither over- nor under-differentiation, but only one-to-one correspondence was observed in Vanuatu.

1.3 DISEASES AND THEIR CURES

The same problems have to be faced in the attempt to translate folk to Western medicinal terminology. Vanuatu’s ethnomedicine differs significantly from Western medicine in its descriptions of disease aetiology; so for some diseases the Western counterpart is not found, a dilemma often observed in traditional medicinal systems.

A good example for this is the definition of cancer, a term adapted to the folk medicine, but used in another context: In the Western medicine cancer is not just one disease, but a class of diseases with three main characteristics: uncontrolled cell-growth, invasion (intrusion on and destruction of adjacent tissues) and in case of malignant tumours metastasis, the ability of these cells to migrate from the original site and spread other locations in the body via blood or lymph, characteristics that can not be observed without specialised scientific equipment. In Vanuatu the term “cancer” was used for severe illnesses with a slow healing process, which may indeed correspond with the Western cancer in some cases but should be viewed sceptically. The term was sometimes further specified in “cancer inside the body” and “skin cancer”. “Cancer inside the body” was described as a sickness with a burning pain behind the sternum, occurring after consumption of fatty food and therefore most likely to be heart-burn. “Skin cancer” on the other hand was described as a big, slowly healing sore;

maybe indeed corresponding with skin-cancer in some cases, but infected wounds or carbuncles are most likely to be assumed because of its comparative fast and easy curability.

Another example for the adaptation of a Western term is “HIV”. To date only one case of HIV-infection or AIDS respectively has been confirmed in 1997, leading to a huge educational campaign[63] dealing with risks and prevention of this disease. However, some informants were sure to have cured themselves from “HIV” several times, so this term must be used for another disease, which unfortunately could not be specified.

Other illnesses mentioned in the interviews and not easily fitting into a Western illness category were *blad i soa, jes i soa, pispis waet, and soa leva:*

Blad i soa (painful blood) is described as a severe illness with painful blood, maybe leukaemia or sepsis, whereas sepsis is more likely, because it is treatable with the leaves of *Solenostemon scutellarioides* L. (Lamiaceae), which have already shown antibacterial effects in biological tests.[160]

Jes i soa (sore chest) is illustrated as a disease with pain and squeezing pressure behind the sternum, probably matching with angina pectoris in the Western terminology.

Pispis waet (white coloured urine) is portrayed as a severe and usually deadly disease, characterised by foamy (white coloured) urine probably showing albuminuria, a symptom of nephropathy (see also “Diseases of the kidney”).

Soa leva (painful liver) is pictured as an illness with pain in the upper part of the abdomen. A painful liver can be caused by several illnesses and it was not possible to translate this illness into a Western term.

Not only terms but also Western medicine has been adapted and included in the traditional system. Panadol® (trade name of Paracetamol in Australia) is carelessly consumed on a daily basis in some islands. Plants are also subsequently included into the ethnopharmacopoeia. A case in Tongoa (Vanuatu) was described in 1999.[65] During a severe dengue fever outbreak in 1989/1990 not only many Tongoans but also inhabitants of other islands in Vanuatu realised the existence of a sickness not even curable with Western medicine. The possibility of utilising plant medicine was discussed in a newspaper article published in *Vanuatu Weekly*. The Solanaceae *Physalis angulata* L., a traditional medicine for dengue fever in the Fijian pharmacopoeia, was described including a photo, vernacular and scientific names, characteristic features, and procedures of processing it for medicine by a Fijian botanist staying in Port Vila. In the same article a rather sceptical comment on the plant from the medical director of the main hospital in Port Vila who did not recommend the use of this plant since there was no scientific proof of its efficacy against the dengue virus was included. The sceptical comment was ignored by many islanders and the information on the wondrous herb, discovered by a *saentist* (scientist) rapidly spread to islands with good

access to newspapers, radio, and other mass media. The islanders diagnosed with dengue fever in health stations were treated with febrifuges and painkillers and additionally used the plant medicine if the symptoms remained. As soon as they had recovered, the plant was already an essential part of the Tongoan ethnopharmacopoeia and in this study it was also observed to be used in Ambrym for the same purpose and in the same mode of preparation and application (see “Multisystem Diseases”).

Traditional medicine in the research areas is based on techniques including the use of plants, massage, magical spells, and ceremonies. In the following the most common techniques are briefly summarised:

Cold digestion

The plant part of choice, sometimes previously ground or macerated (crushed, chopped, rubbed between the hands, etc. to gain access to the cell structure) is squeezed in cold fresh- or saltwater, coconut water, or coconut milk and then filtered through a cloth.

Infusion

Boiling water is poured over the plant part used (occasionally previously ground or macerated), it is allowed to steep for a time and then filtered through a cloth.

Decoction

The plain or previously macerated or ground plant part of choice is boiled for a time and afterwards filtered through a cloth.

Inhalation

A decoction or (mostly) ingestion is prepared as described above and the steam is inhaled.

Bath and Wash

A cold digestion, infusion, or decoction is used to bathe the whole body or only a body part or it is chilled and used as a mouth- or head-wash.

Fumigation

The plant part is burnt in a fire to either fumigate the sick part of the body or to dispel evil spirits or poison (in food).

Massage

The sore body part is massaged with a maceration, infusion, or decoction of the plant used.

Cataplasm

The plant part used, mainly the leaf, maybe previously crushed, rubbed between the hands, or softened by heat over a fire is applied to the sore and sometimes fastened with a rope.

Kastom ceremony

In some cases the medicinal treatment is linked with a special ceremony or spells. Especially sicknesses caused by spirits or of unknown origin like pain disorders are treated this way and particularly male healers tended to combine plant medicine with several complicated rituals and spells.

1.4 RESULTS ETHNOBOTANY

In previous ethnobotanical publications it was postulated, that the culturally important plants which are used for the same category of illnesses by a large number of healers are also the most effective ones in terms of bioactivity, while plants cited only once are considered to be less important in the indigenous community as well as in terms of bearing potentially bioactive compounds. To evaluate the variability of the use of medicinal plants and to determine whether plants from certain groups are of particular interest in the search of bioactive compounds, the so called informant consensus factor F_{IC} can be calculated using the following formula.[161]

$$F_{IC} = \frac{(n_{UR} - n_{Species})}{(n_{UR} - 1)}$$

n_{UR} = number of use reports (UR) in each category

$n_{Species}$ = number of species used

This allows the comparison of the total case number (number of use reports) for each ailment with the number of separate remedies for this disease. The F_{IC} ranks between 0 and 1, whereas a high value indicates that relatively few species are used by many healers and a low one indicates that the healers disagree on the species used for the treatment of the certain disease, due to two reasons: Plant selection thus may be more random as no plant is very effective or little intra-cultural exchange of medicinal plant knowledge is taking place. Using the F_{IC} to compare the ethnobotanical data in a cross-cultural basis and to determine whether plants from certain groups are of particular interest in the search for bioactive compounds was not reasonable in the present study due to the following reasons:

As mentioned previously, the permission to collect ethnobotanical information was limited by the Cultural Centre to only well known and widely used plant species and preparations, because traditional knowledge in Vanuatu is subject to restrictions by reason of the *Kastom*-system. As a result of these restrictions or taboos a profound insight in the pharmacopoeia of the three ethnic groups could not be gained in this study.

As also indicated before, this study focused on remedies in a very narrow therapeutical context to improve the chance of getting good interview results, because healers are often reluctant to give information on their secrets due to the reason that knowledge of plant medicines is a secret family bound property, which is usually inherited even between closely related family members of the same gender, only. As a researcher in Vanuatu a fieldworker of the Cultural Centre, who is part of the visited community, is appointed to supervise the research in order to on the one hand protect the indigenous people, assuring that the *Kastom* laws are observed and that the researcher stands to the contract with the Cultural Centre and on the other hand to introduce the researcher to the chiefs, assisting in promoting the study to the community and acting as an interpreter if necessary. For female researchers

extra safety precautions are taken, since several women complained about sexual assaults. They are more or less adopted by the family of a female fieldworker, sharing bed and board and therefore being under the family's protection. This is on the one hand beneficial, because it gives a very good opportunity to gain insight into the family life and as being a family member, the new relatives are less reluctant in passing their knowledge to the researcher. On the other hand this situation also has disadvantageous effects. Members of other families are getting more reserved, even if they are willing to share their secrets with the researcher; they fear that the researcher's family could get hold of them. This was particularly distinct when interviewing male healers in the field, where in most cases a child of the fieldworker's family accompanied us due to the already mentioned extra safety precautions, although I must say, that I never had an unpleasant experience of that kind while staying in the research areas. Furthermore the strong patriarchal system in Vanuatu presented an obstacle while collecting ethnobotanical data as a woman. Sometimes male informants were much more communicative and it was possible to have very informative and cordial conversations when no other male community members were around, but some men, e.g. the priest in Loh were very supportive and showed much interest in the study and helped to persuade the more reluctant community members by discussing advantages and disadvantages of this study in a meeting with the researcher and the chiefs to find a consent of mutual benefit. In Aneityum, though the impact of the fieldworker constrained the project: by reason that the female fieldworker appointed by the Cultural Centre showed no interest to supervise the project and did not seem able to understand it either, the male fieldworker of the island was ordered to take charge instead. He made contacts and in preliminary talks with the interview partners in the vernacular language Indass Khermo he informed them about plants and remedies already mentioned in previous interviews advising them not to mention these plants again, because he could not understand, that the number of use reports on a single plant is also important in an ethnobotanical study. Due to the fact that the fieldworker commands respect in a community and due to his presence during the whole interview and participation on the conversation it was not possible to correct this mistake in some cases and people were also very reluctant in giving secret information when another community member was around.

At last the relatively short time of only about one month in each research area did not allow making contact and inspiring confidence with every community member, so that only a short glimpse on the existing medicinal system could be obtained. It would have been better to visit the islands a second or third time to emphasise the interest of the researcher in traditional life and medicine and to stabilise the contacts with the indigenous people. This would certainly have resulted in more data.

But however, a database of ethnobotanical information collected during the fieldwork was generated, consisting of 420 use reports on 130 species of 54 plant families, contributed by 27 informants, including 16 men and 11 women, aged between 25 and 79 years with four people interviewed at least twice.

The use reports (UR) were then divided into 17 categories of use (Tab. 3), grouped according to their medicinal affiliation and/or sociocultural relevance. The ranking results agree with a report of Vanuatu's Ministry of Health in the main lines, in which respiratory and skin diseases are the leading cause of morbidity in adults and diarrhoea plays an important role in the morbidity of children under four years (FAO, 2003). Vanuatu's traditional medicine is called *lif meresin* (leaf medicine) – reflecting the fact, that leaves are part of the majority of traditional remedies (Tab. 3).

Tab. 3 Quantitative ethnobotanical analysis of the 17 use groups

entity	[1]n_{UR}	UR [%]	[2]$n_{Species}$	Species [%]	leaf [%]	root/ rhizome [%]	bark/ wood [%]	flower/ fruit [%]
skin	75	17.9	45	34.6	74.7	6.7	16.0	2.7
gastrointestinal system	33	7.9	26	20.0	84.9	-	3.0	12.1
respiratory system	31	7.4	22	16.9	67.7	3.2	29.0	-
urogenital system	25	6.0	24	18.5	72.0	-	20.0	8.0
multi-system diseases	25	6.0	18	13.9	56.0	24.0	16.0	4.0
immune system	18	4.3	11	8.5	50.0	11.1	16.7	22.2
cardiovascular and haematopoietic system	13	3.1	6	4.6	92.3	-	7.7	-
nervous system/ pain disorders	10	2.4	9	6.9	50.0	-	50.0	-
skeleto-muscular system	9	2.1	6	4.6	66.7	-	33.3	-
dental system	9	2.1	9	6.9	33.3	11.1	44.4	11.1
ears	7	1.7	6	4.6	100.0	-	-	-
eyes	7	1.7	7	5.4	42.9	-	14.3	42.9
kidney	3	0.7	3	2.3	33.3	33.3	33.3	-
others:	182	43.3	45	34.6	23.6	6.6	26.9	42.9
food & stimulants	93	22.1	21	16.2	9.7	12.9	-	77.4
house & garden	65	15.5	15	11.5	23.1	-	72.3	4.6
Kastom	23	5.5	18	13.9	73.9	-	13.0	13.0
body care	2	0.5	2	1.5	-	-	-	100.0

[1] total 426 use reports, [2]total 130 species; UR [%] = Percentage of UR contributed to the total amount of UR for an entity; Species [%] = Percentage of Species contributed to the total amount of Species reported for an entity; leaf [%] = Percentage of leaf medicines contributed to the total amount of plant parts used reported for an entity (same for root/ rhizome, bark/ wood and flower/ fruit)

In the following the categories will be described regarding ethnobotanical importance, the illnesses their causes and their treatments and the most important plants will be described in detail including a literature survey.

DISEASES OF THE SKIN

About one third (34.6%) of all species are used to treat skin infections and nearly one fifth (17.9%) of all use reports falls into this group (Tab. 3). The ethnobotanical importance of dermatological disorders has already been shown for other indigenous groups, e.g. in Leonti et al.[162] for the Popoluca in Mexico. Parasites, reduced access to antibiotics, poverty,

malnutrition, and a hot and humid climate contribute to a high incidence of soft tissue infections in the tropics. Wounds caused by accidents while working in the garden or cutting wood and infections of the skin, e.g. boils (furuncles), carbuncles, and abscesses commonly caused by *Streptococcus pyogenes* and other *β*-haemolytic streptococci or by *Staph. aureus*[163] are particularly important (Tab. 4). Infestations with Scabies (*Sarcoptes scabiei*), transmitted by close personal contact and due to low quality of water are especially common in children. Scratching often results in second bacterial infection and pustule formation.[163]

Tab. 4 Quantitative analysis of skin ailments

skin ailment	[1]n_{UR}	UR [%]
wounds	29	38.7
boils/ carbuncles/ abscesses	13	17.3
scabies	10	13.3
bleeding	8	10.7
[2]skin cancer (severe wounds)	4	5.3
burns/ sunburns	3	4.0
centipede bites	3	4.0
insect bites	3	4.0
stings of a stonefish	2	2.7
hair loss	1	1.3
lice	1	1.3
neurodermatitis/ infantile eczema	1	1.3
splinter	1	1.3
sting of *Dendrocnide moroides*	1	1.3
warts	1	1.3

[1]total 75 use reports for skin ailments; UR [%] = Percentage of UR contributed to the total amount of UR reported for skin ailments; [2] see "Diseases and their cures"

Dermatological complaints are most commonly treated topically with fresh sap squeezed from the plant part used (in most cases leaves, see Tab. 3) or cataplasms, but sometimes the plant parts are also boiled in water and the inflicted area is bathed in the chilled infusion.

The most important plant in this category is *Mikania micrantha* KUNTH. (Asteraceae), followed by *Macaranga dioica* MUELL. ARG. and *Macaranga tanarius* (L.) MUELL. ARG. (both Euphorbiaceae), and further *Tabernaemontana pandacaqui* LAM. (Apocynaceae), *Gyrocarpus americanus* JACQ. (Hernandiaceae/Gyrocarpaceae), *Macropiper latifolium* (L.F.) (Piperaceae), *Aidia racemosa* (CAV.) D.D. TIRVENG (Rubiaceae), and *Pipturus argenteus* WEDD. (Urticaceae). *Epipremnum variegatum* (L.) ENGL. (Araceae), *Scaevola taccada* ROXB. (Goodeniaceae), and *Capsicum frutescens* L. (Solanaceae) play an important role in other categories and are therefore also briefly described in this section.

Most frequently the fresh leaf sap of *Mikania micrantha* KUNTH. (Asteraceae) is used to treat various kinds of skin ailments (Tab. 5). It is also used in other places in Vanuatu, in the Banks Islands the sap is applied to cuts to stop bleeding as observed in Torres, Loh, Lungharigi, and North Ambrym (Tab. 5) and taken internally against fever (Tab. 22). The "American rope", originally from tropical America, is an invasive species introduced by the

Americans during WWII to camouflage airfields. Disturbed habitats are rapidly overrun, as the English name mile-a-minute indicates. This vine is one of two major species threatening natural regeneration in logged or disturbed areas in Vanuatu and many programs have been established to eradicate this pest, in some islands there is even an obligation to inform the authorities if this plant is spotted. But however, it has been widely adapted as a medicinal plant, on the one hand certainly because of its wide distribution and good accessibility; but on the other hand, antibacterial activity of its methanolic and/or watery extracts against *Escherichia coli*, *Bacillus subtilis*, *Staph. aureus*, *Proteus vulgaris,* and *Enterobacter aerogenes*[164, 165] has already been proven in biological tests, and sesquiterpene lactones with activity against *Staph. aureus* and *Candida albicans* have been isolated as well,[166-169] some also showing cytotoxic activity.[164] For further uses of this plant in Vanuatu's pharmacopoeia see "Diseases of the gastrointestinal system" p. 75, "Diseases of the respiratory system" p. 81, "Urogenital system" p. 84, "Multi-system diseases" p. 87, and "Diseases of the eye" p. 98.

Second most commonly utilised plants for the treatment of skin ailments are *Macaranga dioica* MUELL. ARG. and *Macaranga tanarius* (L.) MUELL. ARG., both Euphorbiaceae. The sap of the leaves or the inner bark is usually freshly applied to wounds, sunburn, and to stop bleeding or the leaves are used to cover wounds as cataplasms (Tab. 5). Besides its uses in Vanuatu's traditional medicine it plays a role in agriculture, too. In Maewo (Vanuatu) taro seeds are wrapped into its leaves to protect them against *Papuana huebneri*, a plant pathogenic beetle.[59] *M. dioica* has not been studied yet but for *M. tanarius* radical-scavenging activities due to megastigmane glycosides isolated from the leaves,[170] *in vitro* inhibition of DNA topoisomerase II, and cytotoxic activities (against the human lung cancer cell line A549) due to triterpenoids isolated from the bark[171] have been demonstrated only recently (when the plant had already been collected) and allelopathic and anti-inflammatory active flavonoid derivatives have been isolated from the leaves.[172-174] Other members of the genus have also revealed anti-inflammatory activities: *M. adenanthera* due to the coumarinolignoid cleomiscosin A and ellagic acid derivatives,[175] *M. conifera* and *M. triloba*[176] due to prenylated flavonoids.[177] Antifungal activity was demonstrated for *M. monandra* due to the presence of a clerodane-type diterpenoid. Stilbenes with cytotoxic activity against human ovarian cancer cell lines SK-OV-3 and SKVLB-1 were isolated from *M. mappa*[178] and *M. schweinfurthii*[179] and antiproliferative prenylated stilbenes and flavonoids with antiproliferative impact from *M. alnifolia*.[180] For further uses of *Macaranga dioica* MUELL. ARG. in Vanuatu's ethnopharmacopoeia see "Diseases of the nervous system" p. 94, and "Diseases of the cardiovascular and haematopoietic system" p. 93, and for *Macaranga tanarius* (L.) MUELL. ARG. see "Diseases of the respiratory system" p. 81, and "Diseases of the teeth" p. 97. Both plants were chosen for the screening regimen performed in this study, due their ethnomedicinal use, their phytochemical composition, and the mentioned biological

activities already proven for other members of the genus. Leaves and bark of *M. dioica* and the leaves of *M. tanarius* were collected.

Crushed *Tabernaemontana pandacaqui* LAM. (Apocynaceae) leaves are applied to wounds or “skin cancer” (see “1.3 Diseases and their cures) and the latex to centipede bites to relieve the pain (Tab. 5). In Banks Islands, Moto Lava *T. pandacaqui* is used to prepare a love potion,[72] in Erromango the bark is used to stimulate the growth of banana plants, and in Gaua the leaves as a fertiliser for yam plants.[59] Ethnobotanical use of *T. pandacaqui* has also been reported from Tonga, where an infusion of the leaves is made to treat mouth infections of infants, toothache, and infections of teeth or gums.[181] In the Philippines the latex is applied to wounds[182] and swellings,[183] a decoction of the leaves is taken against snakebites and dysentery,[184] and a decoction of bark and roots to cure disorders of the stomach and intestines, including gastro-enteritis.[182] The leaves, mixed with powdered rice husks and fried, are rubbed over the body of a person suffering a relapse from any kind of illness and the pounded leaves are heated and placed on the navel and the small of the back to combat sudden sickness causing severe stomach-ache and cramps.[185] In Columbia *T. amygdalaefolia* leaves[186] and latex[187] and in Tanzania the root bark of *T. elegans* are traditionally used to treat cancer.[188] In biological assays ethanolic extracts obtained from stem, leaf, and flower of *T. pandacaqui* have already shown cardiovascular effects,[189, 190] extracts from stem, leaf, flower, and root caused sedation, decreased respiration, and skeletal muscle tone, showed analgesic effects and (except from the leaf extract) caused vasodilatation of ear vasculature in rats.[191] The isolated Iboga-alkaloid congeners coronaridine[192] and voacangine provoked analgesic and hypothermic effects in mice[193] and a crude alkaloidal fraction from the stem possessed CNS depressant activity.[194] Due to the alkaloidal components[192, 195-197] significant anti-inflammatory, antipyretic, and antinociceptive activities were observed in mice.[198] Other species of the genus showed good anti-leishmanial (*T. sananho*, root)[199] or cytotoxic properties, *T. holstii* roots or *T. arborea* sap against the murine lymphoma cell line P-388, and *T. calcarea* against the human ovarian cancer cell line A2780. See ”Diseases of the respiratory system” p. 81 and “Diseases related to the urogenital system” p. 84 for further uses of this plant in the Vanuatu ethnopharmacopoeia. This plant has been chosen for the screening regimen mainly due to various biological activities already proven for other members of the genus and its membership to the Apocynaceae, a family rich in alkaloids. The leaves of this plant have been collected twice for the screening regimen, because one plant has been misidentified as a second species due to a lack of flowers and because no latex was present. A phylogenetic sequencing analysis, using the internal transcribed spacer 2 (ITS2) sequence-structure alignment, a sufficient condition to distinguish even closely related species [200] has been performed in the Institute of

Botany, Team C. Oberprieler, University of Regensburg, Germany resulting in >99% sequence similarity between the two probes (data not shown).

The sap of freshly squeezed leaves of *Gyrocarpus americanus* JACQ. (Hernandiaceae/Gyrocarpaceae) is applied to wounds (Tab. 5), the inner bark is added the fodder to tame pigs and the wood is often used for carving (*kenutri* in Bislama, meaning canoe tree) in Vanuatu's ethnopharmacopoeia (Tab. 22). Ethnobotanical uses of this plant are also illustrated for Fiji, where it is used to treat relapsed illness, swellings, stomach-ache, and intestinal filariasis and Tonga, where an infusion of the leaves is taken internally[201] or applied to the skin in case of skin inflammations and wounds.[181] An infusion of the bark is taken as a potion for the treatment of stomach-ache[181] or skin infections[201] and utilised against breast cancer.[202] Alkaloids and flavonoids have been isolated from the bark and leaves,[164, 203-205] whereas the alkaloid Gyrocarpine showed strong *in vitro* activity against the promastigote forms of *L. braziliensis*, *L. amazonensis,* and *L. donovani*.[206] Hypotensive[164] and curare-like effects[207] have also been demonstrated in previous studies. The leaves of this plant were collected for the screening regimen because of their wound-healing properties described in Vanuatu's and other ethnopharmacopoeia(s) and the alkaloid- and flavonoid content expected for a member of the Hernandiaceae family.

The Piperaceae *Macropiper latifolium* (L.F.), the *wael* (wild) *kava*, is a plant widely used in the ethnopharmacopoeia of Vanuatu. Its leaves are prepared as a cataplasm to draw out a splinter (Tab. 5) and it is also an important Kastom plant; its fruits are eaten to protect against black magic and its leaves are used in a ceremony in which a person is lifted from the ground without being touched (Tab. 22). For further uses of this plant see "Diseases related to the urogenital system" p. 84, "Multi-system diseases" p. 87, "Modulators of the immune system" p. 90, and "Diseases of the eye" p. 98. In Moto Lava , Banks Islands (Vanuatu) the flowers are ingested against stomach-ache and ulcers and the leaves are used to dispossess an ill person. Against cough the inner part of an internode of a young branch is scratched out, squeezed in water, and drunk and the leaves are used to protect against black magic (both in Mota, Banks Islands).[72] In Ambae taro shoots are wrapped into the leaves after planting to protect them against *Papuana huebneri*, a plant pathogenic beetle.[61] Outside Vanuatu it is also widely used. In the Cook Islands for herbal medicines of unknown effects[208] and a preparation made from the leaves is used against breast cancer.[209] The essential oil component *ß*-asarone has been isolated from the roots.[210] The stalks of *M. latifolium* have been collected for the screening regimen on the one hand because of its wide ethnobotanical uses and on the other hand because of its close relationship to *Piper methysticum* J.R. & G. FORST., the real Kava, a very popular stimulant.[211] The roots have been proven useful for the treatment of stress disorders,[212] as an analgesic, anti-convulsive, and centrally muscle relaxing drug due to kavalactones,[213] and have shown many other effects on the CNS. The

maybe incorrectly attributed hepatotoxic effects of this plant have led to a slump of the kava trade in the global market with huge economic consequences for the major exporting countries in the Pacific, Fiji, and Vanuatu.

A decoction of the Rubiaceae *Aidia racemosa* (CAV.) D.D. TIRVENG (synonym *Randia racemosa*) leaves is used to bathe skin areas inflicted with scabies. This species has not been studied yet, but some investigations of the genus *Randia* already took place. The fruit extract of *R. echinocarpa*, which is used to treat and prevent cancer in the Sinaloa-ethnopharmacopoeia in Mexico, has shown antioxidant effects in the *β*-carotene bleaching method as well as antimutagenic activities in the *Salmonella* micro-suspension assay.[214] In addition diuretic and urolithiatic effects in rats were described.[215] Crude extracts of *R. siamensis*, used in Thai folkloric medicine to induce abortion and control blood pressure, demonstrated antinociceptive[216] as well as cardiovascular effects.[217] Triterpene saponins isolated from the fruits of *R. dumetorum* displayed haemolytic, molluscidal, and immunostimulating activities as well as significantly enhanced the proliferation of human lymphocytes *in vitro*;[218] crude extracts from the seeds induced infertility[219] and were also shown to possess antimicrobial impact.[220] Besides the already mentioned triterpene saponins flavonoids have been isolated from the leaves of *R. formosa*[221] and iridoids from the stems of *R. spinosa*[222] and *R. ruiziana*.[223] The leaves of this plant have been collected for the screening regimen due to antimicrobial activities shown in other *Randia* species and because of its affiliation to the alkaloid-bearing family Rubiaceae.

The bark of *Pipturus argenteus* WEDD. (Urticaceae) is used as a cataplasm, forming a protective occlusive layer to treat boils (Tab. 5). The same application has been reported from the Cook Islands ethnopharmacopoeia.[208] The tiny and rather tasteless fruits are eaten by children and birds (Tab. 22). The application of the leaves to muscle pain and sprains is also practised in Vanuatu.[66] *P. argenteus* has not been studied yet, but antiviral, against Herpes Simplex Virus (HSV) 1 and 2 and Vesicular Stomatitis Virus (VSV), antimicrobial, against *Staph. aureus* and *S. pyogenes*, antifungal against *Microsporum canis*, *Trichophyton rubrum,* and *Epidermophyton floccosum*, and anti-complement activities were shown for *P. albidus*, a plant used in Polynesian traditional medicine in Hawaii for the treatment of infectious diseases[224] and three phenolic acids, (+)-catechins, chlorogenic acid, and rutin with antioxidant activity have been isolated from its leaves.[225] For further uses of this plant in Vanuatu's ethnopharmacopoeia see "Diseases of the gastrointestinal system" p. 75, "Diseases related to the urogenital system" p. 84, and "Modulators of the immune system" p. 90. The proven biological activities of *P. albidus* have initiated the collection of the bark of this plant for the screening regimen.

The juice squeezed from a stalk of *Epipremnum variegatum* (L.) ENGL. (Araceae) is applied to wounds to stop bleeding (Tab. 5). For detailed information on this plant see “Diseases related to the urogenital system p. 84”.

A decoction of the leaves of *Scaevola taccada* ROXB. (Goodeniaceae) is used to bathe the whole body in case of itchy rashes caused by scabies (Tab. 5). A detailed description is found under “Modulators of the immune system” p. 90.

A fresh fruit of *Capsicum frutescens* L. (Solanaceae) is applied to boils (Tab. 5). In Tonga, Samoa, Tahiti, and the Cook Islands the crushed leaves mixed with coconut oil are used to cover sores[226] and boils.[227] In Fiji the leaves are prepared to a remedy against boils, abscesses, and wounds.[201] More information on this plant is found under “Diseases of the skeleto-muscular system” p. 96.

Tab. 5 Plants used to treat diseases of the skin

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Achyranthes aspera L.	Amaranthaceae	1	APP	L	boils
Crinum xanthophyllum HANNIBAL, 1972	Amaryllidaceae	1	SWA	Lat (L)	warts
Annona muricata L.	Annonaceae	1	TLL	L	scabies
		1	SWA	L	scabies
Tabernaemontana pandacaqui LAM.	Apocynaceae	1	TLL	Lat (L)	centipede bites
		1	AA	L	wounds
		1		L	"skin cancer" (severe wounds?)
Epipremnum pinnatum (L.) ENGL.	Araceae	2	TLL/ TLT	St	stops bleeding
Cocos nucifera L.	Arecaceae	1	NA	oB	wounds
Ageratum conyzoides L.	Asteraceae	1	AA	L	wounds
Mikania micrantha KUNTH.	Asteraceae	1	SWA	sap (L)	boils
		2	TLL	L	scabies
		2		L	insect bites
		1	BML	L	wounds
		1		L	wounds
		1		L	wounds
		2	TLL/ NA	wP	stops bleeding
Vernonia cinera (L.) LESS.	Asteraceae	1	AA	L	boils
		1		L	wounds
Diplazium latifolium MOORE	Athyriaceae	1	SWA	Fr	wounds
Ipomoea indica (BURM.F.) MERR.	Convolvulaceae	1	AA	Lat (St)	stops bleeding
Ipomoea pes-caprae (L.) R. Br.	Convolvulaceae	1	TLL	L	boils
Stictocardia campanulata (HALLIER F.) MERR.	Convolvulaceae	1	NA	St	"skin cancer" (severe wounds?)
		1		St	wounds
Luffa sp.	Cucurbitaceae	1	NA	L	scabies
Cycas seemannii A.BRAUN	Cycadaceae	1	TLT	L	sting of stonefish
Cycas weinmannii	Cycadaceae	1	TLL	L	centipede bites
Dioscorea bulbifera L.	Dioscoreaceae	1	NA	L	wounds

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Excoecaria agallocha L.	Euphorbiaceae	1	AA	Lat (L)	wounds
Macaranga dioica MUELL. ARG.	Euphorbiaceae	1	AA	yL	wounds
		1	SWA	iB	wounds
		1		L	wounds
		1		L	wounds
Macaranga tanarius (L.) MUELL. ARG.	Euphorbiaceae	1	SWA/ NA	yL	sunburn
		2		yL	wounds
		1	SWA	yL	stops bleeding
scientific plant name not known 1 # 0276-2	Euphorbiaceae	1	TLL	L	boils
		1		L	sunburn
		1		L	various skin diseases
scientific plant name not known 2 # 1176-10	Euphorbiaceae	1	TLL	L	boils (painful)
Scaevola taccada ROXB.	Goodeniaceae	1	TLL	L	scabies
Gyrocarpus americanus JACQ.	Hernandiaceae/ Gyrocarpaceae	2	TLL	L	wounds
Hyptis pectinata (L.) POIT.	Lamiaceae	1	AA	L	circumcision wounds
Salvia sp.	Lamiaceae	1	TLL	wP	scabies
		1		wP	boils
		1		wP	wounds
Derris trifoliata LOUR.	Leguminosae – Papilionoideae	1	TLL	L	boils
		1		L	carbuncles
		1		L	abscesses
Mucuna gigantea (WILLD.) DC.	Leguminosae – Papilionoideae	1	SWA	sap (L)	sting of *Dendrocnide moroides*
Hibiscus tiliaceus L.	Malvaceae	1	SWA	Sh	stops bleeding
		1		Sh	wounds
Marattia smithii METT. EX KUHN	Marattiaceae	1	AA	Fr	neurodermatitis, infantile eczema
Artocarpus altilis (PARK.) FOSB.	Moraceae	1	AA	Lat (L)	wounds
Ficus sp.	Moraceae	1	NA	iB	burns
Pandanus tectorius PARK.	Pandanaceae	1	TLL	Rt	lice
Macropiper latifolium (L.F.)	Piperaceae	1	SWA	St	to draw a splinter
Digitaria radicosa PRESL	Poaceae	1	BML	sap (L)	wounds
Drynaria rigidula (SW.) BEDD.	Polypodiaceae	1	AA	Fr	hair loss
Aidia racemosa (CAV.) D.D. TIRVENG.	Rubiaceae	1	TLL	L	scabies
Citrus aurantifolia CHRISTM.	Rutaceae	1	TLL	Frt	scabies
Pometia pinnata J.R. FORST. & G. FORST.	Sapindaceae	1	TLL	iB	boils
Capsicum frutescens L.	Solanaceae	1	APP	Frt	boils
Tectaria latifolia (FORST.) COPEL.	Tectariaceae	1	SWA	Fr	wounds
Pipturus argenteus WEDD.	Urticaceae	1	BML	iB	boils
Lantana camara L.	Verbenaceae	1	AA	L	wounds
Stachytarpheta cayennensis (RICH.) VAHL	Verbenaceae	1	AA	L	wounds
Cayratia trifolia (L.) DOMIN.	Vitaceae	1	NA	sap (St)	"skin cancer" (severe wounds?)
		1		sap (St)	wounds

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; #: voucher number; AA: Aneityum, Anelcauhat, APP: Aneityum, Port Patrick, BML: Banks Islands, Moto Lava, NA: North Ambrym, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi, TLT: Torres, Loh, Telaklak; Fr: frond, Frt: fruit, L: leaf, Lat: latex, iB: inner bark, oB: outer bark, Rt: root, Sh: shoot, St: stem, wP: whole plant, yL: young leaf

DISEASES OF THE GASTROINTESTINAL SYSTEM

A fifth (20%) of all species is used to treat gastrointestinal disorders and after skin diseases the second most use reports fall in this category (Tab. 3). The ethnobotanical importance of

gastrointestinal disorders has already been shown for other indigenous groups, e.g. in Leonti et al.[162] for the Popoluca in Mexico. In Vanuatu diarrhoea, liver complaints, and indigestion, followed by mouth infections and constipation are the most common gastrointestinal complaints (Tab. 6). In most cases diarrhoea is caused by entero-viruses or entero-bacteria; if blood is involved and the patient complains of fever, more severe infections with *Shigella sp*., *Campylobacter sp.*, *Salmonella sp*., *Vibrio cholerae,* or *Yersinia sp*. are also possible. Liver complaints are mostly caused by hepatitis viruses, indigestion and constipation are mainly a result of an unbalanced diet usually very rich in carbohydrates as consumed in most islands, and mouth infections are predominantly caused by *Bacteroides sp*., *Fusobacterium sp*., and *Leptotricha sp.* and triggered by bad water quality and malnutrition.[163]

Tab. 6 Quantitative analysis of gastrointestinal disorders

gastrointestinal disorder	[1]n_{UR}	UR [%]
diarrhoea	6	18.18
hepatitis and other liver disorders	5	15.15
indigestion	5	15.15
mouth infections	4	12.12
constipation/ ileus	4	12.12
abdominal pain	2	6.06
gastritis/ stomach-ache/ ulcer	2	6.06
severe illness with bloody faeces	2	6.06
appendicitis	1	3.03
[2]cancer (heart burn?)	1	3.03
protein intoxication	1	3.03

[1]total 33 use reports for gastrointestinal disorders; UR [%] = Percentage of UR contributed to the total amount of UR reported for gastrointestinal disorders; [2] see “Diseases and their cures”

Gastrointestinal disorders are most commonly treated systemically with infusions or decoctions mainly of fruits or flowers, or they are ingested as a whole. Only mouth infections are treated topically (Tab. 7).

The most important plant in this category is *Crinum asiaticum* L. (Amaryllidaceae), followed by *Acalypha wilkesiana* MUELL. ARG. (Euphorbiaceae), *Hibiscus tiliaceus* L. (Malvaceae), *Psidium guajava* L. (Myrtaceae), and *Syzygium malaccense* (L.) MERR. & L.M. PERRY (Myrtaceae). Furthermore *Dracontomelon vitiense* ENGL. (Anacardiaceae), *Mikania micrantha* KUNTH. (Asteraceae), *Canarium vulgare* LEENH. (Burseraceae), *Carica papaya* L. (Caricaceae), *Morinda citrifolia* L. (Rubiaceae), and *Pipturus argenteus* WEDD. (Urticaceae) are briefly summarised due to their importance in other disease entities.

The leaves of *Crinum asiaticum* L. (Amaryllidaceae) are squeezed in water and the resulting solution is taken to treat indigestion or the latex is mixed with water and drunk as an emetic (Tab. 7). The use as an emetic (and poison antidote) is also described in the Micronesian ethnopharmacopoeia for the bulbs and the leaves, the leaves, however, are used to relieve backaches and to prepare a treatment for permanent retraction of the testes.[164] In Malekula (Vanuatu) the latex in water or coconut milk is also used as an emetic with a view to cure

ciguatera.[64] In Fiji the leaves are used for wound healing and to reduce swellings and a preparation of the bulbs is utilised to facilitate childbirth and for the treatment of postpartum haemorrhage.[164] In Samoa inflammations are treated with the leaves[228] and in New Caledonia emetic and laxative, as well as diaphoretic and diuretic remedies are prepared from this plant.[229] In Vanua Lava (Vanuatu) and Loh *C. asiaticum* is planted near trees to protect them against the plant pathogenic fungus *Phellinus noxius*[59] and in Gaua (Vanuatu) the fruits are added as a fertiliser when taro is planted.[59] In biological tests cytotoxic activities due to alkaloids[230, 231] as well as antibacterial activities have already been demonstrated.[232] For further uses of this plant in Vanuatu's ethnopharmacopoeia see "Diseases of the teeth" p. 97 and "Diseases of the ear" p. 97.

The fresh leaves of *Acalypha wilkesiana* MUELL. ARG. (Euphorbiaceae) are either chewed or the sap is applied topically to treat mouth infections (Tab. 7). This activity may be due to the richness of tannins in the leaves,[233] which have already shown antimicrobial activities,[234] e.g. against *Staph. aureus*[235] and even against a methicillin-resistant *Staph. aureus* (MRSA) strain.[236] Antifungal activities[234] have also been demonstrated, e.g. against *Trichophyton rubrum*, *T. mentagrophytes*, *Candida albicans*, and *Aspergillus flavus*[235] and against *Tinea pedis*, *Pityriasis versicolor*, and *Candida intetrigo*.[237] The leaves reveal modulation of multiple cytokines[238] and the seeds, an essential component of a complex plant mixture used empirically by traditional healers in Southwest Nigeria to treat breast tumours and inflammation, displayed cytotoxic and immunomodulatory properties in biological tests.[239] For further uses in the Vanuatu ethnopharmacopoeia see "Diseases of the eye" p. 98.

The mucilaginous shoots of *Hibiscus tiliaceus* L. (Malvaceae) are both freshly eaten to treat gastritis, stomach-ache, and ulcers or ground and chewed for constipation or ileus. The shoots are squeezed in water and the slimy mash is put onto wounds to stop bleeding and accelerate the healing process (Tab. 6). Its multicoloured wood is often used for house construction, as fuel wood, and for carving (Tab. 22). In Gaua and Malekula the sap squeezed from the bark is taken to facilitate childbirth and in Erromango the sap collected from a trunk is drunk for the same reason.[70] In Moto Lava and Mota in the Banks Islands the excorticated stem is used like a needle to penetrate wounds, with the leaves pus is removed from inflamed skin areas, and a cataplasm to relieve pain caused by stings or bites is also prepared from the leaves.[72] The bark of a subspecies in Aneityum is cooked and eaten.[34] *H. tiliaceus* is also widely used in ethnopharmacopoeias outside Vanuatu. In Tonga and Samoa[228] the slimy sap from the bark (in Samoa the root) is dripped onto eye ailments or an infusion of the bark is taken in case of stomach-ache,[181] in Tahiti the flowers are used to treat sores[240] and in the Cook Islands they are mashed and put onto boils, carbuncles, and cuts,[226] whereas fractures and sprains are soaked with the sap[226] and in Samoa the bark is part of a remedy for appendicitis.[228] In the past the inner bark fibres were fashioned into grass skirts –

now unfortunately replaced by gorgeous pink coloured plastic fibres imported from China and sold as traditional grass skirts to cruise ship tourists - and many other artefacts, the leaves were used to wrap food, as baby nappies, and as serving platters.[34] Substances with cytotoxic activity against P-388 cells and human colon carcinoma HT-29 cells have been isolated from the wood[241] and methanolic extracts of the leaves have shown strong tyrosinase inhibitory activity.[242] *In vivo* antioxidant and antimutagenic properties of methanolic flower extracts have also been demonstrated[243, 244] and triterpenes have recently been isolated from stem and bark.[245] For further uses see “Multi-system diseases” p. 87.

The leaves of *Psidium guajava* L. are freshly chewed against diarrhoea or the leaf sap, squeezed in water, is taken to treat a severe illness with bloody faeces (Tab. 7), maybe caused by *Shigella sp*., *Campylobacter sp.*, *Salmonella sp*., *Vibrio cholerae* (does not occur anymore in Vanuatu), or *Yersinia sp*. (in Fiji a decoction of the leaves is used to treat Cholera[246]). The fruits are edible (Tab. 22) and a good source of vitamins B and C. An infusion of the leaves is used in many parts of the Pacific to treat diarrhoea.[228, 247] In the Cook Islands it is utilised to treat abdominal pain[208] and in Tonga for stomach-ache.[227] In Fiji the juice pressed from the young leaves is ingested for dysentery and upset stomach, an infusion of the roots or leaves for diarrhoea and indigestion, the unripe fruits are eaten as a laxative[246] and in Kerala (South India) they are eaten to prevent gastrointestinal complaints due to antimicrobial activities.[248] In the Cook Islands the leaves, chewed with or without coconut oil, are applied to cuts and boils and an extract of the young leaves is given as a bath to women who have just given birth, in order to speed recovery and relieve pain.[208] Many studies on *P. guajava* have already been achieved and antimicrobial activities,[249] even against *Vibrio cholerae*[250] have been proven, maybe due to their high content in tannins[251] and many other secondary plant metabolites.[252-255]

In Vanuatu the leaves of *Syzygium malaccense* (L.) MERR. & L.M. PERRY, another Myrtaceae, are chewed to treat mouth-infections and abdominal pain (Tab. 7) (the same is known from Tonga and other parts of Polynesia,[181] where the bark is also used for the same application and - together with that of other tree species - it is boiled and taken as a potion against stomach-ache and abdominal ailments).[181] In previous studies ethnobotanical uses of the bark as a remedy for Ciguatera[256] and rheumatism[229] were also described. In the Cook Islands and Western Polynesia, a solution of the leaves or bark is used to treat thrush,[226] or the bark is utilised to prepare an emetic.[208] In New Caledonia a laxative is made from the bark.[56] In Samoa the leaf galls are used to treat inflammations.[228] The fruits are eaten in Vanuatu as well as in other parts of the Pacific. The wood is very hard and durable and often utilised for house ground posts and as fuel wood (Tab. 22). Extracts of *S. malaccense* have shown abilities as xanthine oxidase inhibitors (used in the treatment of gout) in an *in vitro* assay and were able to prevent cataractogenesis in diabetic rats.[257] They have also

demonstrated inhibitory effects on cyclooxigenase-1 (COX-1) and 2 (COX-2), due to flavanol derivatives present in the extracts.[258] Antiviral activities against VSV and HSV-1 and 2, antimicrobial activities against *Staph. aureus* and *Streptococcus pyogenes* as well as complement inhibition were shown.[224] Extracts of other species of the genus *Syzygium* (synonym *Eugenia*) have demonstrated antiviral[259] and antifungal properties on the dermatophytes *Trichophyton mentagrophytes*, *T. rubrum*, and *Microsporum gypseum*.[260] A triterpenoid, isolated from the stems of *Eugenia sandwicensis*, revealed potential as a cancer chemoprevention agent[261] and *E. caryophyllus* demonstrated antioxidant activity.[262] For further uses in Vanuatu's ethnopharmacopoeia see "Multi-system diseases" p. 87. The leaves of this plant have been collected for the screening regimen due to its use in Vanuatu's ethnopharmacopoeia and proven biological activities of other members of the genus.

The inner bark of *Dracontomelon vitiense* ENGL., wrapped in a leaf of any plant, toasted and squeezed in water is a remedy for a severe illness with bloody faeces (Tab. 7), maybe caused by *Shigella sp*., *Campylobacter sp.*, *Salmonella sp*., *Vibrio cholerae* (does not occur anymore in Vanuatu), or *Yersinia sp*.. The tasteless fruits of this plant are edible and very popular (Tab. 22). A cold digestion of the bark is applied to the woman's navel to facilitate childbirth in Malekula.[70] *D. vitiense* ENGL. has not been studied, but crude methanolic extracts of leaves, bark, or root of *Dracontomelon dao* have shown significant antibacterial activities, and the leaf extract has also shown antifungal effects.[263] The caries-free *Kammu* women in Vietnam and Laos use a stain composed of an extract of *D. dao* nuts and the wood of two other plants to blacken their teeth. An extract of *D. dao* nuts has shown significant growth inhibition of salivary *mutans streptococci in vitro* and therefore a caries preventing effect of this extract is assumed.[264] The antibacterial activity shown for *D. dao* and antimalarial activities shown for other members of the family[265] have initiated the collection of the bark for the screening regimen performed in this study.

The leaf juice of *Mikania micrantha* KUNTH. (Asteraceae) mixed with water is used as a treatment of diarrhoea. See "Diseases of the skin" p. 68 for detailed information on this plant.
The leaves of *Canarium vulgare* LEENH. (Burseraceae) are prepared to a remedy against diarrhoea (Tab. 7). For a detailed description of this plant see "Multi-system diseases" p. 87.

A decoction of the flowers of *Carica papaya* L. (Caricaceae) is drunk as a potion for hepatitis (Tab. 7). The seeds are eaten to treat infestations with intestinal worms, as also reported from Samoa, Tahiti, and the West Indies.[226] In Tonga they are eaten in case of diarrhoea.[227] In Fiji the ripe fruit pulp is taken for ingestion, diarrhoea, and dysentery and as an appetizer[246] and in India as a stomachic and carminative. The latex is utilised for bleeding haemorrhoids, ulcers, and dyspepsia.[246] In the Caribbean an emetic is made from the leaves[266]. In biological tests effects on the contraction of the jejunum were shown.[267] See "Multi-system Diseases" p. 87 for a detailed description of this plant.

The fruits of *Morinda citrifolia* L. (Rubiaceae) are freshly eaten to treat constipation. In Malekula the leaves are ground, smelled, and rubbed on the stomach to treat constipation.[64] In the Cook Islands the fruit is used as a remedy for diaphragmatic hernia and other abdominal swellings.[226] In Tonga an infusion of bark or leaves is taken as a potion for stomach-ache, and the juice from a squeezed fruit is applied to mouth infections.[227] These effects have been proven *in vivo* in rats.[268] See "Modulators of the immune system" p. 90 for a more detailed description of this plant.

An infusion of the leaves of *Pipturus argenteus* WEDD. (Urticaceae) is taken to treat hepatitis (Tab. 7). See "Diseases of the skin" p. 68 for further information on this plant.

Tab. 7 Plants used to treat diseases of the gastrointestinal system

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Cordyline fruticosa (L.) A. CHEV.	Agavaceae	1	AA	L	leprosy in the mouth
Crinum asiaticum L.	Amaryllidaceae	1	SWA/NA	L	indigestion
		2	SWA	Lat (L)	to cause emesis
Dracontomelon vitiense ENGL.	Anacardiaceae	1	NA	iB	severe illness with bloody faeces
Mikania micrantha KUNTH.	Asteraceae	1	SWA	L	diarrhoea
Canarium vulgare LEENH.	Burseraceae	1	AA	L	diarrhoea
Carica papaya L.	Caricaceae	1	SWA	Fl	hepatitis
Ipomoea indica (BURM.F.) MERR.	Convolvulaceae	1	SWA	Lat (St)	laxative
Operculina turphetum (L.) SILVA MANSO	Convolvulaceae	1	TLT	Sh	abdominal pain
Acalypha wilkesiana MUELL. ARG.	Euphorbiaceae	1	TLL	L	aphthous ulcers
		1	AA	L	aphthous ulcers
Euphorbia cyathophora L., MURR.	Euphorbiaceae	1	AA	Frt	diarrhoea
Garcinia sp.	Guttiferae	1	AA	L	liver pain
Salvia sp.	Lamiaceae	1	TLL	wP	indigestion
		1		wP	gastritis, stomach-ache, ulcers
Desmodium incanum (SW.) DC.	Leguminosae – Papilionoideae	1	AA	L	diarrhoea
Inocarpus fagifer PARK.	Leguminosae – Papilionoideae	1	TLL	Sd	protein intoxication after consumption of too much seafood (flatulence + pain)
Pueraria lobata (WILLD.) OHWI	Leguminosae – Papilionoideae	1	SWA	L	hepatitis
Vigna luteola (JACQ.) BENTH.	Leguminosae – Papilionoideae	1	SWA	L	hepatitis
Hibiscus tiliaceus L.	Malvaceae	1	BML	Sh	gastritis, stomach-ache, ulcers
		1	TLL	Sh	constipation/ ileus
Sida rhombifolia L.	Malvaceae	1	AA	L	diarrhoea
Psidium guajava L.	Myrtaceae	1	BML	L	diarrhoea
		1	NA	L	severe illness with bloody faeces
Syzygium malaccense (L.) MERR. & L.M. PERRY	Myrtaceae	1	TLL	L	mouth infections
		1	SWA	L	abdominal pain (to cause emesis)
Piper methysticum J. R. & G. FORST.	Piperaceae	1	SWA	L	appendicitis
Gardenia tannaensis GUILL.	Rubiaceae	1	TLT	L	constipation
Morinda citrifolia L.	Rubiaceae	1	AA	Frt	constipation

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Pipturus argenteus WEDD.	Urticaceae	1	SWA	L	hepatitis
Cayratia trifolia (L.) DOMIN.	Vitaceae	1	NA	L	„cancer“ (heart burn?)

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; AA: Aneityum, Anelcauhat, BML: Banks Islands, Moto Lava, NA: North Ambrym, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi, TLT: Torres, Loh, Telaklak; Fl: flower, Frt: fruit, iB: inner bark, L: leaf, Lat:: latex, Sd: seed, Sh: shoot, St: stem, wP: whole plant

DISEASES OF THE RESPIRATORY SYSTEM

Respiratory complaints rank directly behind gastrointestinal disorders in Vanuatu's traditional medicine (Tab. 3). Cough is the most important disorder in this entity (Tab. 8) and is mainly of viral origin; second infestations with *Haemophilus influenzae*, *Streptococcus pneumoniae*, or *Pneumococcus sp.* are possible and common.[63] Close personal contact and an unbalanced diet lacking vitamins leads to a high incidence of cough in the outer islands. If fever is involved, cough can also be a symptom of a more severe illness like bronchitis or tuberculosis.

Tab. 8 Quantitative analysis of respiratory complaints

respiratory disease	[1]n_{UR}	UR [%]
[2]cough	14	42.42
asthma	12	36.36
[3]chest pain (angina pectoris?)	2	6.06
bronchitis	1	3.03
cold	1	3.03
sore throat	1	3.03
tuberculosis	1	3.03

[1]total 31 use reports for respiratory disorders; UR [%] = Percentage of UR contributed to the total amount of UR reported for respiratory disorders; [2] "simple" cough, lacking fever , [3]see "Diseases and their cures"

Diseases of the respiratory system are most commonly treated systemically with cold digestions prepared mainly from the leaves (Tab. 3).

The most important plants in this category are *Erythrina variegata* L. (Leguminosae – Papilionoideae) and *Baccaurea stylaris* MUELL. ARG. (Phyllanthaceae), followed by *Mikania micrantha* KUNTH. (Asteraceae), *Bidens pilosa* L. (Asteraceae), and *Acalypha grandis* BENTH. (Euphorbiaceae), but *Intsia bijuga* (COLEBR.) O. KTZE. (Leguminosae – Caesalpinioideae), *Euodia latifolia* DC. (Rutaceae), *Tabernaemontana pandacaqui* LAM. (Apocynaceae), *Macaranga tanarius* (L.) MUELL. ARG. (Euphorbiaceae), and *Ficus septica* BURM.F. (Moraceae) are also briefly described, because of their importance in other disease entities.

A cold digestion of the leaves of *Erythrina variegata* L. (Leguminosae – Papilionoideae) is utilised to treat cough, a cold digestion of the inner bark for chest pain, maybe angina pectoris (for definition of "chest pain" see "1.3 Diseases and their cures") and a cold digestion of the bark (toasted beforehand) for asthma (Tab. 9), which is also used as a laxative[229] and a potion against ciguatera is produced by adding bark of *Pterocarpus indicus* WILLD..[269] In

Samoa a remedy for inflammation and with anti-viral properties is prepared from the bark[228] and in Tonga an infusion to treat stomach-ache is made from the bark of this plant and that of *Cananga odorata* (LAM.) HOOK.F. & THOMSON (Annonaceae).[181] Throughout Vanuatu, *E. variegata* is planted as an ornamental or as a living fence due to its showy red flowers and variegated leaves. In central Pentecost (Vanuatu) the onset of flowering at the end of the dry season is an indication sign for the planting season,[34] in the Cook Islands it marked the beginning of the whaling season in former times.[208] The light wood is utilised as fuel wood or for fishing floats.[240] *E. variegata* has already extensively been studied in the last years. Antibacterial,[270, 271] antiinflammatory,[228] cytotoxic,[272] and other biological properties[228] due to flavonoids[273, 274], alkaloids,[275-277] and other secondary plant metabolites have been determined.

A decoction of the leaves and/or inner bark of *Baccaurea stylaris* MUELL. ARG. is used to bathe the whole body when suffering from asthma or cough (Tab. 9). Not much is known about this genus so far; only one study has been carried out[81] in which ten compounds, comprising among others a prenylated flavonol, a flavonoid and a lignan, isolated from the leaves of *Baccauera ramiflora* LOUR. showed significant antioxidant activities. Other members of this genus are often planted for their edible fruits.[278] Bark and leaves of this plant have been collected for the screening regimen due to biological activities demonstrated for the tribe Antidesmateae (see “2.6 Phytochemistry and Pharmacology of *Baccaurea* LOUR. and other Phyllanthaceae”) and the lack of studies of the genus and the bark has also been chosen for the phytochemical purification procedure described later in this study.

The fresh leaf juice of *Mikania micrantha* KUNTH. (Asteraceae) mixed with water is taken as a remedy for cough or the leaves are boiled in water and the steam is inhaled to treat the symptoms of a cold (Tab. 9). See “Diseases of the skin” p. 68 for detailed information on this plant.

In Vanuatu a cold digestion of the shoots of *Bidens pilosa* L. (Asteraceae) is drunk as a remedy for cough (Tab. 9). In the Cook Islands the chewed or pounded leaves are put on cuts,[208] in Tonga they are utilised for the same purpose and are also applied to eye ailments, particularly those caused by evil spirits.[227] Many studies have been done before, dealing with its biological activities and spectrum of constituents, revealing antimalarial,[279] antibacterial,[280] cytotoxic,[281, 282] anti-inflammatory,[283-286] and other properties. This plant has been collected for the screening regimen by mistake, because it had been misidentified in the field.

The leaves of *Acalypha grandis* BENTH. (Euphorbiaceae) are freshly chewed to treat sore throat (Tab. 9). Decoctions of the leaves or flowers in saltwater can also be used as mouthwash or gargle to treat mouth infections or sore throat as done in Moto Lava.[72] In Erromango (Vanuatu) a remedy to induce temporary sterility is prepared from the leaves, mixed with fronds of a fern and the bark of another plant.[70] Until now no studies on *A. grandis*

have been achieved, but other members of the genus *Acalypha* have already shown several biological activities. For example *A. australis*,[287] *A. communis*,[288] *A. guatemalensis* ,[289, 290] *A. hederacea*,[291] *A. hispida*,[233] *A. siamensis*,[292] and *A. wilkesiana*[233-236] demonstrated antimicrobial, *A. australis*[287] antiviral, *A. fruticosa*,[293] and *A. wilkesiana*[237] antifungal, *A. guatemalensis*[294] antiprotozoal and *A. australis*[287] and *A. siamensis*[295] cytotoxic properties (see also *A. wilkesiana* in section “Diseases of the gastrointestinal system” p. 75). Further uses of *A. grandis* are described in the section “Diseases related to the urogenital system” p. 84. The leaves of this plant have been collected for the screening regimen due to the great variety of biological activities already demonstrated for other members of the genus in previous studies.

The inner bark of *Intsia bijuga* (COLEBR.) O. KTZE. (Leguminosae – Caesalpinioideae), squeezed in coconut water, is taken as a remedy for asthma (Tab. 9). The hard wood is used for carving (Tab. 22), ground posts, and house construction.[34] No studies have been carried out on this genus, but other members of the Leguminosae – Caesalpinioideae have already shown cytotoxic or antimicrobial activities, e.g. *Caesalpinia sappan* which exhibits both.[296-298] See also “Multi-system Diseases” p. 87 and “Modulators of the immune system” p. 90. The leaves of *I. bijuga* have been collected for the screening regimen due to cytotoxic activities already shown for other members of the family.

A remedy for cough is prepared from the leaves of *Euodia latifolia* DC. (Rutaceae) (Tab. 9). No studies have been performed on this species yet, but other members of the genus have already shown significant cytotoxic activities against various cancer cell lines,[299-301] and also anti-inflammatory,[302 303] antibacterial,[304-306] antifungal,[306] and antimalarial[307] activities due to a high content of alkaloids,[303, 304] flavonoids,[303] lignans,[303] and other secondary plant metabolites.[303] The leaves of this plant have been collected for the screening regimen due to their ethnomedicinal use, activities of other *Euodia sp.* in various biological tests, and phytochemical composition of the genus.

The latex escaping from a broken leaf of *Tabernaemontana pandacaqui* LAM. (Apocynaceae) is mixed with water and the solution is taken as a treatment for tuberculosis (Tab. 9). See “Diseases of the skin” p. 68 for detailed information on this plant.

The leaves of *Macaranga tanarius* (L.) MUELL. ARG. (Euphorbiaceae) are rubbed between the hands, squeezed in water and the solution is given to babies suffering from asthma (Tab. 9). See “Diseases of the skin” p. 68 for a more detailed description of this plant.

The leaves of *Ficus septica* BURM.F. (Moraceae) are squeezed in water and the milky solution is ingested to treat asthma (Tab. 9). See “Diseases of the nervous system” p. 94 for more information on this plant.

Tab. 9 Plants used to treat diseases of the respiratory system

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Achyranthes aspera L.	Amaranthaceae	1	AA	L	asthma
Crinum xanthophyllum HANNIBAL, 1972	Amaryllidaceae	1	AA	L	asthma
Kopsia flavida BL.	Apocynaceae	1	TLL	yL	cough
Tabernaemontana pandacaqui LAM.	Apocynaceae	1	SWA	Lat (L)	tuberculosis
Bidens pilosa L.	Asteraceae	1	AA	Sh	cough
Mikania micrantha KUNTH.	Asteraceae	1	AA	L	cold
		1		L	cough
Ipomoea indica (BURM.F.) MERR.	Convolvulaceae	1	TLL	wP	cough
Ipomoea littoralis (L.) BL.	Convolvulaceae	1	TLL	L	cough
		1		L	bronchitis
Zehneria sp.	Cucurbitaceae	1	SWA	L	cough
Acalypha grandis BENTH.	Euphorbiaceae	1	BML	L	sore throat
Chamaesyce hirta L.	Euphorbiaceae	1	AA	L	asthma
Macaranga tanarius (L.) MUELL. ARG.	Euphorbiaceae	1	TLL	L	asthma (babies)
Barringtonia edulis SEEM.	Lecythidaceae	1	SWA	iB	cough
Intsia bijuga (COLEBR.) O. KTZE.	Leguminosae - Caesalpinioideae	1	SWA	iB	asthma
Erythrina variegata L.	Leguminosae – Papilionoideae	1	SWA	L	cough
		1	TLL	iB	chest pain (angina pectoris?)
		2		iB	asthma
Pueraria lobata (WILLD.) OHWI	Leguminosae – Papilionoideae	1	TLL	L	asthma
Ficus septica BURM.F.	Moraceae	1	SWA	L	asthma
Baccaurea stylaris MUELL. ARG.	Phyllanthaceae	1	AA	L	asthma
		1		iB	asthma
		1		L	cough
		1		iB	cough
Piper methysticum J. R. & G. FORST.	Piperaceae	1	AA	L	cough
		1		Rt	cough
Oplismenus hirtellus (L.) P.BEAUV.	Poaceae	1	AA	Sh	cough
Euodia latifolia DC.	Rutaceae	1	TLL	L	cough
Pometia pinnata J.R. FORST. & G. FORST.	Sapindaceae	1	SWA	iB	asthma
Alpinia novae-pommeraniae K. SCHUM.	Zingiberaceae	1	SWA	St	chest pain (angina pectoris?)

[1]UR: number of use reports, [2] OPC: place of collection; [3] PPU: plant part used; AA: Aneityum, Anelcauhat, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi; iB: inner bark, L: leaf, Lat: latex, Rt: root, Sh: shoot, wP: whole plant, yL: young leaf

DISEASES RELATED TO THE UROGENITAL SYSTEM

Remedies to treat postpartum pain and to expulse the placenta are leading in this category, followed by potions that are said to be able to influence the sex of the embryo during pregnancy (this kind of medicine is considered as inefficient by the author, as it lacks a scientific basis, but is considered as very useful and effective in Vanuatu's ethnopharmacopoeia) medicine to treat all kinds of disorders concerning menstruation, and remedies to facilitate childbirth (Tab. 10).

Tab. 10 Quantitative analysis of diseases related to the urogenital system

Diseases related to the urogenital system	[1]n_{UR}	UR [%]
postpartum pain/ expulse placenta	8	25.81
influence sex of embryo during pregnancy	4	12.90
emmenagogue	3	9.68
facilitation of childbirth	3	9.68
abortive	2	6.45
urogenital tract infection	2	6.45
contraceptive	1	3.23
fertility drug	1	3.23
gonorrhoea	1	3.23

[1]total 25 use reports for diseases related to the urogenital system; UR [%] = Percentage of UR contributed to the total amount of UR reported for diseases related to the urogenital system

Diseases related to the urogenital system are most commonly treated systemically with cold digestions prepared primarily from the leaves (Tab. 3).

The most important plant in this category is *Epipremnum pinnatum* (L.) ENGL. (Araceae), followed by *Tabernaemontana pandacaqui* LAM. (Apocynaceae), *Acalypha grandis* BENTH. (Euphorbiaceae), *Erythrina variegata* L. (Leguminosae – Caesalpinioideae), *Macropiper latifolium* (L.F.), and *Pipturus argenteus* WEDD. (Urticaceae).

The leaf juice of *Epipremnum pinnatum* (L.) ENGL. (Araceae) - mixed with water - is taken in case of amenorrhoea and the leaves are chewed as an abortifacient (Tab. 11). In Gaua (Vanuatu) the root tips are eaten to facilitate childbirth,[70] in Singapore the leaves are used as a folk remedy to treat cancer.[308] Growth inhibition of breast cancer cells while treated with crude extract of *E. pinnatum* has been demonstrated.[309] For a more information on this plant see “Diseases of the skin” p. 68.

A fresh stalk of *Tabernaemontana pandacaqui* LAM. (Apocynaceae) is chewed to influence the sex of an embryo during pregnancy in favour of a girl (Tab. 11). In the Philippines the leaves are placed on the abdomen as a cataplasm to induce menstruation or to hasten parturition[310] and women have a bath of a decoction of the leaves after or a decoction of bark or roots as a drink during childbirth.[183] For a detailed description of this plant see “Diseases of the skin” p. 68.

The sap of the leaves of *Acalypha grandis* BENTH. (Euphorbiaceae) mixed with water is utilised as a remedy for gonorrhoea (Tab. 11). See “Diseases of the respiratory system” p. 81 for more information on this plant.

The young leaves of *Erythrina variegata* L. (Leguminosae – Caesalpinioideae) are freshly chewed to treat postpartum abdominal pain and to expulse the placenta (Tab. 11). For a detailed description of this plant see “Diseases of the respiratory system” p. 81.

The leaf galls of *Macropiper latifolium* (L.F.) are ingested to influence the sex of an embryo during pregnancy (Tab. 11). In Gaua (Vanuatu) the fresh leaves are eaten to expulse the placenta and the leaf galls to facilitate childbirth[70] or in Pentecost the leaves are combined

with the leaves of another (undetermined) species, squeezed in water, and the solution is taken to facilitate childbirth.[311] A detailed description of *M. latifolium* is found in "Diseases of the skin" p. 68.

The sap of *Pipturus argenteus* WEDD. (Urticaceae), squeezed from the inner bark and mixed with water, is drunk as an abortifacient (Tab. 11). The same is known from Epi (Vanuatu), where the inner bark, mixed with coconut, is ingested to induce sterility and as a contraceptive[70] and the sap or bark to facilitate childbirth.[312] For further information on this plant see "Diseases of the skin" p. 68.

Tab. 11 Plants used to treat disorders related to the urogenital system

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Achyranthes aspera L. (red variety)	Amaranthaceae	1	AA	L	increases fertility in woman
Cananga odorata (LAM.) HOOK.F. & THOMSON	Annonaceae	1	TLL	iB	postpartum abdominal pain (to expulse placenta)
Alstonia vitiensis SEEM.	Apocynaceae	1	AA	L	contraceptive
Tabernaemontana pandacaqui LAM.	Apocynaceae	1	AA	St	influences sex of embryo during pregnancy in favour of girl (magic)
Epipremnum pinnatum (L.) ENGL.	Araceae	1	SWA	L	amenorrhoea
		1	TLL	Sh	abortive
Polyscias cumingiana (C.PRESL) FERN.-VILL.	Araliaceae	1	SWA	L	influences sex of embryo during pregnancy in favour of girl (magic)
Polyscias scutellaria (BURM.F.) FOSB.	Araliaceae	1	SWA	L	influences sex of embryo during pregnancy in favour of girl (magic)
Hoya vanuatensis	Asclepiadaceae	1	SWA	L	facilitates childbirth
Ipomoea indica (BURM.F.) MERR.	Convolvulaceae	1	SWA	Fl	facilitates childbirth
Ipomoea pes-caprae (L.) R. BR.	Convolvulaceae	1	AA	St	severe abdominal pain during pregnancy caused by spirits
Stictocardia campanulata (HALLIER F.) MERR.	Convolvulaceae	1	NA	St	inflammation in the urogenital system
Zehneria sp.	Cucurbitaceae	1	SWA	L	facilitates childbirth
Acalypha grandis BENTH.	Euphorbiaceae	1	TLT	L	gonorrhoea
Salvia sp.	Lamiaceae	1	TLL	wP	menses pain
Cassytha filiformis L.	Lauraceae	1	TLL	wP	postpartum abdominal pain (to expulse placenta)
Entada pursaetha DC.	Leguminosae – Mimosoideae	1	AA	L	severe pain during pregnancy
Erythrina variegata L.	Leguminosae – Papilionoideae	1	TLL	yL	postpartum abdominal pain (to expulse placenta)
Ficus sp.	Moraceae	1	SWA	Lat (L)	postpartum abdominal pain (to expulse placenta)
Maesa ambrymensis GUILL.	Myrsinaceae	1	SWA	Frt	to initiate the menopause
Macropiper latifolium (L.F.)	Piperaceae	1	NA	LG	influences sex of embryo during pregnancy (girl or boy) (magic)
Pometia pinnata J.R. FORST. & G. FORST.	Sapindaceae	1	TLL	yL	bloody urine + pain
Pipturus argenteus WEDD.	Urticaceae	1	SWA	iB	abortive
not known 3 # 2286-1.4.1	plant family not known	1	AA	L	severe abdominal pain during pregnancy caused by spirits (magic)
not known 4 # 2286-1.4.2	plant family not known	1	AA	L	severe abdominal pain during pregnancy caused by spirits

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; #: voucher number; AA: Aneityum, Anelcauhat, NA: North Ambrym, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi, TLT: Torres, Loh, Telaklak; Fl: flower, Frt: fruit, iB: inner bark, L: leaf, Lat: latex, LG: leaf gall, Sh: shoot, St: stem, wP: whole plant, yL: young leaf

MULTI-SYSTEM DISEASES

Medicines to treat ciguatera, “cancer” (see “1.3 Diseases and their cures”), diabetes, dengue fever, malaria and AIDS (see “1.3 Diseases and their cures”) build the category “Multi-system diseases” (Tab. 12).

Most remedies are used to treat Ciguatera (Tab. 12), a foodborne disease transmitted by consumption of sea fish, contaminated with the heat-resistant ciguatoxin which is present in many microorganisms (particularly the micro-algae *Gambierdiscus toxicus*) living in tropical waters. It bioaccumulates in lower-level organisms, resulting in higher concentration of the toxin at the end of the food chain.[313] Hallmark symptoms of ciguatera include gastrointestinal and neurological effects, such as nausea, paresthesia, numbness, ataxia, and hallucinations.[313] Severe cases of ciguatera can also result in cold allodynia, which is a burning sensation on contact with cold.[314] There is no effective treatment or antidote for ciguatera poisoning yet.

In the last years an increasing prevalence of obesity, type II diabetes, and cardiovascular diseases has been assessed in Vanuatu. While the rural population follows a predominantly subsistence lifestyle, the urban population or the population with good transport connection to urban areas has adopted a more westernised lifestyle with decreasing consumption of traditional foods like root crops, such as yam and taro or starchy fruits such as plantain and breadfruit and increasing consumption of imports namely rice, fat/oils, canned meat/fish, refined sugar, bread, and ready meals. The rise in non-communicable diseases has been attributed, in part, to this transition away from traditional in favour of imported food.[315, 316]

Dengue fever is an illness caused by arboviruses transmitted by day-biting *Aedes aegypti* mosquitoes. An estimated 40–80 million people are infected each year with highest incidence in Southeast Asia. Dengue symptoms range from benign febrile illness to severe, life-threatening, haemorrhagic fever.[163] Only symptomatic treatment is possible yet due to lack of a suitable medicine.

Tab. 12 Quantitative analysis for multi-system diseases

Multi-system diseases	[1]n_{UR}	UR [%]
ciguatera	13	52.00
[2]cancer	5	20.00
diabetes	4	16.00
dengue fever	2	8.00
malaria	1	4.00
[2]AIDS	1	4.00

[1]total 25 use reports for multi-system diseases; UR [%] = Percentage of UR contributed to the total amount of UR reported for multi-system diseases; [2] see “Diseases and their cures”

Multi-system diseases are most commonly treated systemically with cold digestions prepared predominantly from the leaves (Tab. 3).

The leaf juice of *Canarium vulgare* LEENH. (Burseraceae) mixed with coconut water is taken in case of ciguatera (Tab. 13). In Malekula (Vanuatu) the juice pressed from leaves or bark is ingested to facilitate childbirth[70] and in ancient times the resin was used for light or as canoe caulk.[34] The tasty seeds are eaten in Vanuatu (Tab. 22) as well as in other parts of the Pacific. The nut oil is part of tanning lotions and other cosmetics.[278] In previous studies of other members of the genus *Canarium*, tannins with antioxidant activity,[317] flavonoids and triterpenoids with hepatoprotective effects[318-320] were isolated and crude extracts have shown anti-diabetic properties.[321] See "Diseases of the gastrointestinal system" p. 75 for further uses of this plant.

The flowers of *Carica papaya* L. (Caricaceae) are chewed to treat ciguatera; the roots are chewed with coconut milk in case of "AIDS" in the first stage (see also "Diseases and their cures") (Tab. 13), and the ripe fruits are edible and very popular (Tab. 22). A decoction of the flowers[269] or the leaves, which have shown cardiac actions and activities as laxative[229 56] are also utilised in the treatment of ciguatera in Vanuatu and New Caledonia. In Polynesia the unripe fruits are cooked and eaten and the cooking water is drunk for the same purpose.[322] A remedy to induce abortion is also reported from Vanuatu: the green fruits are swallowed with lime juice and four tablets of Nivaquine® (a malaria medication that should be avoided by pregnant women as it may cause abortion)[70] and in India the seeds are used as an emmenagogue and abortifacient.[246] In the Cook Islands the grated green fruit is mixed with coconut oil and rubbed onto boils and carbuncles, cuts and sores.[226] In Fiji the latex is applied to ringworm (*Tinea*, a superficial fungal infection of the skin) and in India the latex of an unripe fruit is used as a cosmetic for freckles or a medicine for ringworm and psoriasis and the ripe fruit is said to have diuretic properties [246]. In Tonga an infusion of the sap from a green fruit is taken for asthma and shortness of breath [227] and in Fiji the leaves are ground and taken with salt for coughs.[246] Many studies have been carried out on *C. papaya*, revealing e.g. antibacterial,[323-327] antioxidant,[328, 329] anti-diabetic,[330] diuretic,[330] liver-protective,[331] and abortifacient[323, 332-334] activities. For further uses of this plant see "Diseases of the gastrointestinal system" p. 75.

A cold digestion of the rhizome of *Zingiber zerumbet* (L.) SM. (Zingiberaceae) is taken in case of "cancer" (see also "1.3 Diseases and their cures") (Tab. 13). In Banks Islands, Moto Lava (Vanuatu) the leaf juice is applied to conjunctivitis.[72] In Fiji the juice squeezed from a rhizome is taken in case of ciguatera poisoning[201] and is also used for diabetes, coughs, and colds. In India the rhizome has multiple uses: as a stimulant and tonic, as a carminative for stomach troubles, dyspepsia, and flatulent colic, for fever or as a flavouring agent.[246] In Samoa it is used to treat inflammation,[228] in Tonga for peptic ulcers, stomach-ache, and mouth infections.[227] In the Cook Islands the copious fluid that accumulates in the bracts is said to elongate and soften the hair and a solution of the grated rhizome is applied to

haemorrhoids and prolapsed rectum.[208] Compounds isolated from the rhizomes such as flavonoids[335, 336] or the sesquiterpenoid zerumbone[337] have already shown cytotoxic activities against P-388 cells and the human promyelocytic leukaemia cell line HL-60,[338] human breast cancer MCF-7 cells,[335] and human liver cancer HepG2 cells.[339] Extracts also revealed cancer chemopreventive,[340-342] anti-allergic[343] as well as immunomodulatory[336, 342, 344-349] activities. Zerumbone and its derivatives have shown significant antibacterial activities,[350] and the extracts have demonstrated effects on *Giardia intestinalis*[351] and *Entamoeba histolytica* strain HTH-56:MUTM and strain HM1:IMSS.[352] The rhizomes of this plant have been collected for the screening regimen, because it has been misidentified as an *Alpinia* due to the lack of flowers. A phylogenetic sequencing analysis, utilising the internal transcribed spacer 2 (ITS2) sequence-structure alignment, a sufficient condition to distinguish even closely related species[200] has been performed in the Institute of Botany, Team C. Oberprieler, University of Regensburg, Germany resulting in 99% sequence similarity with *Z. zerumbet* (data not shown).

The leaf juice of *Mikania micrantha* KUNTH. (Asteraceae) in water is taken as a remedy for fever and dengue fever. For a more detailed description of this plant see “Diseases of the skin” p. 68.

The leaves or inner bark of *Intsia bijuga* (COLEBR.) O. KTZE. (Leguminosae – Caesalpinioideae) are squeezed in saltwater and the solution is ingested as a remedy for diabetes (Tab. 13). For more information on this plant see “Diseases of the respiratory system” p. 81.

A remedy for “cancer” (see “1.3 Diseases and their cures”) is prepared from inner bark or leaves of *Hibiscus tiliaceus* L. (Malvaceae). A detailed description of this plant is found under the section “Diseases of the gastrointestinal system” p. 75.

The juice squeezed from the inner bark of *Syzygium malaccense* (L.) MERR. & L.M. PERRY (Myrtaceae) mixed with water is taken as a remedy for ciguatera (Tab. 13). For more information on this plant see “Diseases of the gastrointestinal system” p. 75.

The roots of *Macropiper latifolium* (L.F.) (Piperaceae) - prepared like kava - are used as a remedy for ciguatera (Tab. 13). The use of this plant against ciguatera has previously been reported.[256] More information on *M. latifolium* is found under the section “Diseases of the skin” p. 68.

Tab. 13 Plants used to treat multi-system diseases

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Crinum xanthophyllum HANNIBAL, 1972	Amaryllidaceae	1	AA	sap (L)	ciguatera
Polyscias samoensis (A.GRAY) HARMS	Araliaceae	1	AA	L	ciguatera
Mikania micrantha KUNTH.	Asteraceae	1	SWA	L	dengue fever
Canarium vulgare LEENH.	Burseraceae	1	AA	L	ciguatera
		1	APP	L	ciguatera
Garuga floribunda DECNE.	Burseraceae	1	TLL	L	ciguatera
Carica papaya L.	Caricaceae	1	BML	Rt	"HIV" 1st stage
		1	AA	Fl	ciguatera
Stictocardia campanulata (HALLIER F.) MERR.	Convolvulaceae	1	SWA	L	pain of the spleen (malaria?)
Luffa cylindrica (LOUR.) ROEM.	Cucurbitaceae	1	SWA	L	"cancer"
Dracaena angustifolia ROXB.	Dracaenaceae	1	AA	L	ciguatera (to stimulate emesis)
Intsia bijuga (COLEBR.) O. KTZE.	Leguminosae – Caesalpinioideae	1	SWA	L	diabetes
		1		iB	diabetes
Hibiscus tiliaceus L.	Malvaceae	1	SWA	iB	"cancer"
		1		L	"cancer"
Syzygium malaccense (L.) MERR. & L.M. PERRY	Myrtaceae	1	AA	iB	ciguatera
Macropiper latifolium (L.F.)	Piperaceae	1	TLL	Rt	ciguatera
Saccharum robustum BRAND. & JESW. EX GRASSL F.	Poaceae	1	SWA	St	ciguatera
Physalis angulata L.	Solanaceae	1	SWA	L	dengue fever
Vittaria lineata (L.) JE. SMITH	Vittariaceae	1	AA	Fr	ciguatera
Alpinia sp.	Zingiberaceae	1	SWA	Rh	diabetes
Zingiber zerumbet (L.) SM.	Zingiberaceae	1	TLL	Rh	"cancer"
Hornstedtia sp.	Zingiberaceae	1	APP	Rh	diabetes
		1		Rh	"cancer"
not known 5 # 1886-5.2	plant family not known	1	AA	L	ciguatera
		1		L	ciguatera

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; #: voucher number; AA: Aneityum, Anelcauhat, APP: Aneityum, Port Patrick, BML: Banks Moto Lava, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi; Fl. flower, Fr: frond, iB: inner bark, L: leaf, Rh: rhizome, Rt: root, St: stem

MODULATORS OF THE IMMUNE SYSTEM

In this category tonics and panaceas are found. Information on the panaceas were given by only one healer from Ambrym who pretended to have cured himself several times from “cancer” and “AIDS” (see also “1.3 Diseases and their cures”) and who otherwise as well did not seem credible. Modulators of the immune system are mostly cold digestions prepared from the leaves (Tab. 3).

The most important plant used in Vanuatu as a modulator of the immune system is *Morinda citrifolia* L. (Rubiaceae), followed by the red variety of *Strobilanthes reptans* ENGL. (Acanthaceae), *Scaevola taccada* ROXB. (Goodeniaceae), *Intsia bijuga* (COLEBR.), and *Pipturus argenteus* WEDD. (Urticaceae). *Ficus septica* BURM. F. (Moraceae) and *Macropiper latifolium* (L.F.) (Piperaceae) are also briefly described, because of their importance in other disease entities.

The liquid that leaks from ripe fruits of *Morinda citrifolia* L. (Rubiaceae) is taken as a panacea and a decoction of the leaves as a tonic (Tab. 14), same as in India.[246] In Western countries an antioxidant remedy prepared from the fruits is already widely used due to its immunomodulatory activities and to aid digestion,[278] the effects being proven in biological test systems.[353-355] In Moto Lava, Banks Islands (Vanuatu), the leaves are rubbed between the hands and the smell is inhaled to protect from magic.[72] In Aneityum the leaves are used to stimulate the growth of sugarcane.[59] In Malekula the leaves are wrapped together with a string, the bundle is warmed over a fire and pressed onto an enlarged and sore spleen (maybe caused by malaria?) for 30 seconds to one minute.[64] A red or yellow dye is prepared from the root bark, the fruits are edible but have an unpleasant cheese-like smell, and the wood is occasionally used for house construction.[34] In Polynesia the juice squeezed from unripe and ripe fruits is mixed with coconut milk and taken as a remedy for ciguatera.[322] In the Cook Islands the leaves are applied to wounds,[208] the roots are used to treat external cancerous lesions,[209] an infusion of the fruits mixed with these of *Thespesia populnea* (L.) SOL. (Malvaceae) - occasionally combined with the leaves of *Cordia subcordata* LAM. (Boraginaceae) or the roots of *Piper methysticum* FORST. F. (Piperaceae) - is taken in case of painful urination, a solution of the grated root is put on the top of the head in treating stings of a stonefish, in Tahiti it is applied directly to the sting[226] and the leaves are put onto wounds.[208] In Fiji an infusion of powdered root- or stem bark is used to treat urinary tract infections and the warmed leaves covered with oil are utilised as a poultice for sprains and broken bones.[246] In Tonga an infusion of the leaves is taken internally to cure a variety of ailments caused by evil spirits. The leaves, heated over a fire, are applied to boils and in Samoa the flower is used for the same purpose.[227] In India an infusion of the leaves is taken for fever or put onto wounds and ulcers, unripe fruits mixed with salt are applied to gingivitis, and the leaf juice is rubbed on painful joints caused by gout.[246] In Hawaii a foetid insecticidal hair oil[278] and a treatment of breast cancer[308] are prepared from the fruits. Many studies on “noni” have already been performed;[356, 357] anthrachinones, lignans, flavonoids, and iridoids have been isolated,[358, 359] revealing e.g. anti-inflammatory and cancer-chemopreventive properties,[360-365] cytotoxic,[366-369], antibacterial,[370] and wound-healing,[371] anti-diabetes,[372] anxiolytic,[373] and analgesic[374] activities. See also “Diseases of the gastrointestinal system” p. 75 for further uses of this plant.

A cold digestion of the leaves of the red variety of *Strobilanthes reptans* ENGL. (Acanthaceae) is taken as a tonic (Tab. 14). In Pentecost the roots or leaves are eaten to facilitate childbirth[70] or the leaf juice is claimed to reverse sterility induced by *Asplenium nidus* L. (Aspleniaceae)[71]. This plant has not been studied yet, but other members of this genus have shown significant antiviral,[375-377] antimicrobial,[378] antioxidant,[379] antifungal,[380] antiinflammatory, and further biological activities[378, 381-383] due to triterpenoids, alkaloids, lignans, and other secondary plant metabolites.[379, 384-386] See also "Diseases of the cardiovascular and haematopoietic system" p. 93 for detailed information on this plant.

A decoction of the leaves or inner bark of *Scaevola taccada* ROXB. (Goodeniaceae) serves as a tonic (Tab. 14). The fruit - mixed with coconut milk - is used to treat ciguatera.[322] In Moto Lava, Banks Islands, the leaves are applied to swellings of the axillary or inguinal lymph nodes[72] and elsewhere in Vanuatu a remedy to induce sterility is prepared from the leaf buds.[70] In Aneityum the leaves are added as fertiliser when taro is planted.[61] In Samoa the bark is used for menstruation problems,[228] in several Polynesian archipelagos the leaves are constituents of herbal remedies, in Tokelau the pith of the stem is stung into leis, and in the Cook Islands in dancing skirts.[240] In Fiji, liquid from the leaves is used to treat weakness after childbirth which leads to pneumonia, the roots are used for stomach-ache, and a decoction of the bark and leaves as a tonic.[164] In Tonga, the sap squeezed from the bark is used in treating ringworm and the roots for beriberi, syphilis, and dysentery.[164] In the Solomon Islands, parts of the plant are utilised to treat cough, tuberculosis, and stings of the sting ray.[201] Many compounds have already been isolated from *S. taccada*[387, 388] and extracts have shown anti-inflammatory, antipyretic,[389] antibacterial,[390] and antiviral (HSV-1 and 2 and VSV)[224] effects. *S. balansae* extracts revealed activities against *Leishmania donovani* and *Trichomonas vaginalis*,[391] *S. spinescens* antiviral activity against human cytomegalovirus (HCMV).[392] Cytotoxic triterpenoids have also been isolated[393] and at last iridoids have been discovered in *S. racemigera* [394] and *S. montana*.[395] See also "Diseases of the skin" p. 68 for further uses of this plant.

The leaves or the inner bark of *Intsia bijuga* (COLEBR.) O. KTZE. (Leguminosae – Caesalpinioideae) are squeezed in saltwater and the solution is taken internally to defeat infections (Tab. 14). For more information on this plant see "Diseases of the respiratory system" p. 81.

The sap of *Pipturus argenteus* WEDD. (Urticaceae) collected from a cut root during nighttimes is ingested as a panacea and the sap squeezed from the shoots and mixed with water is given to children as a tonic (Tab. 14).

The dewdrops that have accumulated on a fruit of *Ficus septica* BURM. F. (Moraceae) during the night are collected as a tonic for children (Tab. 14). In "Diseases of the nervous system" p. 94 detailed information on this plant is found.

The juice of squeezed from a stalk of *Macropiper latifolium* (L.F.) (Piperaceae) mixed with water is drunk as a panacea (Tab. 14). More information on this plant is found in “Diseases of the skin” p. 68.

Tab. 14 Plants used as modulators of the immune system

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Strobilanthes reptans ENGL. red variety	Acanthaceae	2	TLL	L	tonic for children
Stictocardia campanulata (HALLIER F.) MERR.	Convolvulaceae	1	SWA	L	tonic for babies
Scaevola taccada ROXB.	Goodeniaceae	1	AA	L	tonic
		1		iB	tonic
Calophyllum inophyllum L.	Guttiferae	1	TLL	Frt	Tamanu oil (anti-inflammatory properties)
Intsia bijuga (COLEBR.) O. KTZE.	Leguminosae – Caesalpinioideae	1	SWA	L	to defeat infections
		1		iB	to defeat infections
Ficus septica BURM.F.	Moraceae	1	SWA	dd/rw (Frt)	tonic for children
Macropiper latifolium (L.F.)	Piperaceae	1	SWA	St	panacea
Morinda citrifolia L.	Rubiaceae	1	SWA	L	panacea
		1		Frt	panacea
		1		L	tonic
		1		Frt	tonic
Pipturus argenteus WEDD.	Urticaceae	1	SWA	sap (Rt)	panacea
		1		Sh	tonic for children
Hornstedtia lycostoma (LAUTERB. & K. SCH.) K. SCH.	Zingiberaceae	1	TLL	L	tonic
Hornstedtia sp.	Zingiberaceae	1	APP	Rh	tonic

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; AA: Aneityum, Anelcauhat, APP: Aneityum, Port Patrick, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi; dd/rw: dewdrops/ rainwater, Frt: fruit, iB: inner bark, L: leaf, Rh: rhizome, Rt: root, Sh: shoot, St: stem

DISEASES OF THE CARDIOVASCULAR AND HAEMATOPOIETIC SYSTEM

In this category mostly remedies for anaemia or with influence on the blood pressure are found. Hypertension is very frequent in Vanuatu, and it is estimated, that it is mostly originating from post-streptococcal glomerulonephritis, very often indicating threatening renal

failure.[63] They are almost always cold digestions of the leaves that are taken internally (Tab. 3). In this category exclusively red coloured plant parts or plant parts containing a red coloured sap were used, indicating plant selection based on the dictum *similia similibus curantur*. The most important plants in this category are *Graptophyllum pictum* (L.) GRIFF. (Acanthaceae), *Macaranga dioica* MUELL. ARG. (Euphorbiaceae), and *Solenostemon scutellarioides* L. (Lamiaceae), followed by the red variety of *Strobilanthes reptans* ENGL. (Acanthaceae).

The leaf sap of *Graptophyllum pictum* (L.) GRIFF. (Acanthaceae) - mixed with water - is drunk to treat hypotension or anaemia (Tab. 15). Planted near the house it is said to protect the residents from black magic (Tab. 22). Extracts of the red leaves, also used in the Indonesian folk medicine, have shown anti-inflammatory activities due to flavonoids.[396]

The leaf juice of *Solenostemon scutellarioides* L. mixed with water is drunk in case of anaemia, "leukaemia" (see "1.3 Diseases and their cures"), and sepsis (Tab. 15). See "Diseases of the skeleto-muscular system" p. 96 for a detailed description of this plant.

A remedy for hypertension is prepared from young red leaves of *Macaranga dioica* MUELL. ARG. (Euphorbiaceae) (Tab. 15). See "Diseases of the skin" p. 68 for a detailed description of this plant.

A cold digestion of the leaves of the red variety of *Strobilanthes reptans* ENGL. (Acanthaceae) is taken internally to treat anaemia (Tab. 15). For a detailed description of this plant see "Modulators of the immune system" p. 90.

Tab. 15 Plants used to treat diseases of the cardiovascular and haematopoietic system

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Graptophyllum pictum (L.) GRIFF.	Acanthaceae	2	SWA	L	hypotension
		1		sap (L)	anaemia
Strobilanthes reptans ENGL. red variety	Acanthaceae	2	NA	L	anaemia
Macaranga dioica MUELL. ARG.	Euphorbiaceae	2	SWA	yL	hypertension
		1	NA	yL	hypertension
Solenostemon scutellarioides L.	Lamiaceae	2	TLL	L	anaemia
		1		L	leukaemia and sepsis
Pterocarpus indicus WILLD.	Leguminosae – Papilionoideae	1	AA	iB	anaemia

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; AA: Aneityum, Anelcauhat, NA: North Ambrym, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi; iB: inner bark, L: leaf, yL: young leaf

DISEASES OF THE NERVOUS SYSTEM

Remedies to treat headache and other pain disorders are summarised in this category and the most important plants in this section are *Ficus septica* BURM. F. (Moraceae), *Macaranga dioica* MUELL. ARG. (Euphorbiaceae), and *Grewia inmac* GUILL. (Sparrmanniaceae).

The stalk of *Ficus septica* BURM. F. (Moraceae) can either be chewed or the healer chews the young leaves and spits them into the patients face to treat headache (Tab. 16). The leaves are prepared to a remedy for children's diseases caused by spirits (Tab. 22). In Malekula the fruits are eaten to expulse the placenta,[70] in Gaua to increase the fertility of the garden soil.[61] Alkaloids with cytotoxic activity against the human nasopharyngeal carcinoma cell line HONE-1 and the human stomach cancer cell line NUGC have been isolated from the stems.[397] See "Diseases of the respiratory system" p. 81, "Modulators of the immune system" p. 90, and "Diseases of the eye" p. 98 for further information on this plant.

The inner bark of *Macaranga dioica* MUELL. ARG. (Euphorbiaceae) is used in a special *Kastom* ceremony to relieve migraine headache (Tab. 16). A detailed description of this plant is found in the section "Diseases of the skin" p. 68.

A decoction of the leaves of *Grewia inmac* GUILL. (Sparrmanniaceae) is taken internally to treat pain. The plant is called "*aelan* Panadol®" (island paracetamol) due to its use as a painkiller (Tab. 16). Nothing is known about *G. inmac* yet, but other members of the genus have already shown activity in biological assays: *G. bilamellata* demonstrated cytotoxic and antimalarial – due to triterpenoids and lignans,[398] *G. bicolor*, *G. erythraea*, and *G. occidentalis* antibacterial,[399-401] *G. bicolor,*[400] *G. elyseoi,*[402 403] and *G. occidentalis* [404] oxytocic, and *G. asiatica* radioprotective[405] activities. Triterpenoids and alkaloids with oxytocic and antimicrobial properties have been isolated from *G. bicolor*[400, 406] and *G. tiliaefolia*[407] and flavonoids from *G. damine*[408] The leaves of this plant have been collected for the screening regimen due to activities of other members of the genus *Grewia* in various test systems and phytochemical composition.

Tab. 16 Plants used to treat diseases of the nervous system

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Crinum xanthophyllum HANNIBAL, 1972	Amaryllidaceae	1	TLL	St	headache
Codiaeum variegatum (L.) BL.	Euphorbiaceae	1	AA	L	migraine headache
Macaranga dioica MUELL. ARG.	Euphorbiaceae	1	AA	iB	migraine headache
Pterocarpus indicus WILLD.	Leguminosae – Papilionoideae	1	SWA	yL	pain
Artocarpus altilis (PARK.) FOSB.	Moraceae	1	AA	Sh	migraine headache
Ficus adenosperma MIQ.	Moraceae	1	AA	St	headache
Ficus septica BURM.F.	Moraceae	1	SWA	yL	headache
		1	AA	St	headache
Pandanus tectorius PARK.	Pandanaceae	1	TLL	L	headache
Grewia inmac GUILL.	Sparrmanniaceae	1	AA	L	pain "*aelan* panadol"

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used, [4] "aelan panadol" means island paracetamol; AA: Aneityum, Anelcauhat, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi; iB: inner bark, L: leaf, Sh: shoot, St: stem, yL: young leaf

DISEASES OF THE SKELETO-MUSCULAR SYSTEM

Diseases of the skeleto-muscular system include fractures, muscle- and back pain (which is not caused by kidney diseases), as well as disorders in the rheumatic sphere. The most important plants in this group are *Solenostemon scutellarioides* L. (Lamiaceae) and *Capsicum frutescens* L. (Solanaceae).

The leaves of *Solenostemon scutellarioides* L. (Lamiaceae) are utilised as a cataplasm for fractures (Tab. 17). *S. scutellarioides* is also planted as an ornamental (Tab. 22). In Pentecost (Vanuatu) the leaves - together with those of an undetermined species - are prepared to an abortifacient remedy, the sap is used as a contraceptive[409] and the whole plant or leaves respectively are prepared to an emmenagogue.[229, 410] In many parts of Vanuatu it is planted to protect trees from the plant pathogenic fungus *Phellinus noxius* and the plant pathogenic beetle *Papuana huebneri*.[61] Diterpenoids isolated from the leaves have shown antibacterial and antifungal effects.[160] For further information on this plant see “Diseases of the cardiovascular and haematopoietic system” p. 93.

The fresh leaves of *Capsicum frutescens* L. (Solanaceae) are rubbed onto painful muscles and rheumatism (Tab. 17). In Samoa the leaves are also used to treat maternity complications and the fruits are chewed to cure internal illnesses.[228] In New Caledonia a handful of the fruits are swallowed in case of ciguatera.[56] In Fiji remedies against tuberculosis, mild conjunctivitis, and jaundice and in Samoa a medicine for cough are prepared from *C. frutescens*.[201] This plant has also demonstrated several effects in biological tests: antibacterial,[411, 412] antifungal due to saponins,[413-415] or lectins,[416] anti-diabetic,[417-419] analgesic,[420-422] anti-inflammatory, and cytotoxic[421-423] effects. Capsaicin - the main compound - is able to neutralise the haemorrhagic effect of *Bothrox atrox* venom, a snake poison.[424] For further uses of this plant see “Diseases of the skin” p. 68.

Tab. 17 Plants used to treat diseases of the skeleto-muscular system

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Crinum xanthophyllum HANNIBAL, 1972	Amaryllidaceae	1	SWA	St	fractures
Cocos nucifera L.	Arecaceae	1	SWA	iB	back pain
Solenostemon scutellarioides L.	Lamiaceae	3	TLL	L	fractures
Freycinetia tannaensis MARTINELLI	Pandanaceae	1	AA	L	fractures
Capsicum frutescens L.	Solanaceae	1	AA	L	muscle pain
		1		L	rheumatism
Trema orientalis (L.) BL.	Ulmaceae	1	NA	iB	fractures

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; AA: Aneityum, Anelcauhat, NA: North Ambrym, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi; iB: inner bark, L: leaf, St: stem

DISEASES OF THE TEETH

Toothache is mostly treated with decoctions of the bark (Tab. 3) used as a mouthwash to relieve the pain. The most important plants in this section are *Crinum asiaticum* L. (Amaryllidaceae) and *Macaranga tanarius* (L.) MUELL. ARG (Euphorbiaceae).

A decoction of the bulbs of *Crinum asiaticum* L. (Amaryllidaceae) is used as a mouthwash for toothache (Tab. 18). A detailed description of this plant is found under "Diseases of the gastrointestinal system" p. 75.

A decoction of the inner bark of *Macaranga tanarius* (L.) MUELL. ARG (Euphorbiaceae) is utilised as a mouthwash for toothache (Tab. 18). For a detailed description of this plant see "Diseases of the skin" p. 68.

Tab. 18 Plants used to treat diseases of the teeth

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Crinum asiaticum L.	Amaryllidaceae	1	AA	Rt	toothache
Synedrella nodiflora (L.) GAERTN.	Asteraceae	1	AA	L	toothache
Terminalia catappa L.	Combretaceae	1	TLL	L	toothache
Macaranga tanarius (L.) MUELL. ARG.	Euphorbiaceae	1	AA	iB	toothache
Barringtonia asiatica (L.) KURZ	Lecythidaceae	1	AA	iB	toothache
Barringtonia edulis SEEM.	Lecythidaceae	1	SWA	iB	toothache
Pyrrosia confluens (R.BR.) CHING	Polypodiaceae	1	TLT	Fr	toothache
Micromelon minutum (FORST.F.) WIGHT & ARN.	Rutaceae	1	TLT	L	toothache
Alpinia novae-pommeraniae K. Schum.	Zingiberaceae	1	SWA	St	toothache

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; AA: Aneityum, Anelcauhat, SWA: Southwest Ambrym, TLL: Torres, Loh, Lungharigi, TLT: Torres, Loh, Telaklak; Fr: frond, iB: inner bark, Rt: root, L: leaf, St: stem

DISEASES OF THE EAR

Ear infections are mainly caused by *Staph. aureus*, *Streptococcus sp*. *Pneumococcus sp*., or *Haemophilus influenzae* and treated topically (Tab. 3). The most important plant in this section is *Cucurbita pepo* L. (Cucurbitaceae), but *Crinum asiaticum* L. (Amaryllidaceae) is also briefly described due to its importance in another category.

The leaf juice of *Cucurbita pepo* L. (Cucurbitaceae) is applied to the ear or a stalk is warmed over a fire and the healer spits into the infected ear using the stalk like a straw (Tab. 19). In the Cook Islands the leaves are occasionally used in herbal medicine.[208] In Germany the seeds are utilised as a treatment for irritable bladder and benign prostatic hyperplasia [425, 426, 427]. The seed oil showed antioxidant activities in biological tests[428, 429] and triterpenoids with cytotoxic activity against human cervix carcinoma HeLa cells have been isolated.[430]

The latex of *Crinum asiaticum* L. (Amaryllidaceae) leaves is applied topically to aching ears (Tab. 19). See "Diseases of the gastrointestinal system" p. 75 for further uses of this plant.

Tab. 19 Plants used to treat diseases of the ear

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Crinum asiaticum L.	Amaryllidaceae	1	SWA	Lat (L)	ear ailments
Crinum xanthophyllum HANNIBAL, 1972	Amaryllidaceae	1	TLL	L	ear ailments
Hippeastrum puniceum (LAM.) URBAN	Amaryllidaceae	1	TLL	L	ear ailments
Cucurbita pepo L.	Cucurbitaceae	1	BML	L	ear ailments
		1		St	ear ailments
Dioscorea bulbifera L.	Dioscoreaceae	1	TLT	St	ear ailments
Sansevieria trifasciata PRAIN	Dracaenaceae	1	AA	L	ear ailments

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; AA: Aneityum, Anelcauhat, BML: Banks Islands, Moto Lava:, SWA: Southwest Ambrym, TLL: Torres Islands, Loh, Lungharigi, TLT: Torres Loh, Telaklak; L: leaf; Lat: latex, St: stem

DISEASES OF THE EYE

Conjunctivitis, as presented in this study, is of bacterial origin, because it is described as an illness of the eye with a purulent discharge, typical for bacterial infections. It is treated topically. Plants used to treat conjunctivitis and briefly summarised here are *Mikania micrantha* KUNTH (Asteraceae), *Ficus septica* BURM. F. (Moraceae), *Macropiper latifolium* (L.F.) (Piperaceae), and *Acalypha wilkesiana* MUELL. ARG. (Euphorbiaceae).

Mikania micrantha KUNTH (Asteraceae) leaf juice is applied to the eye in case of conjunctivitis (Tab. 20). A detailed description of this plant is found under the section “Diseases of the skin” p. 68.

The dewdrops that have accumulated on a fruit of *Ficus septica* BURM. F. (Moraceae) during the night are applied to sore eyes (Tab. 20). In “Diseases of the nervous system” p. 94 a detailed description of this plant is found.

The juice squeezed from a stalk of *Macropiper latifolium* (L.F.) (Piperaceae) is applied to conjunctivitis. A detailed description of this plant is found in “Diseases of the skin” p. 68.

The juice pressed from the leaves of *Acalypha wilkesiana* MUELL. ARG. (Euphorbiaceae) is applied to sore eyes (Tab. 20). For more information on this plant see “Diseases of the gastrointestinal system” p. 75.

Tab. 20 Plants used to treat diseases of the eye

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Mikania micrantha KUNTH.	Asteraceae	1	SWA	L	conjunctivitis
Acalypha wilkesiana MUELL. ARG.	Euphorbiaceae	1	BML	L	conjunctivitis
Hibiscus rosa-sinensis L.	Malvaceae	1	TLL	Fl	conjunctivitis
Ficus aspera FORST.	Moraceae	1	AA	L	conjunctivitis
Ficus septica BURM.F.	Moraceae	1	SWA	dd/rw (Frt)	conjunctivitis
Macropiper latifolium (L.F.)	Piperaceae	1	SWA	St	conjunctivitis
Sphaerostephanos invisus (FORST. F.) HOLTTUM	Thelypteridaceae	1	BML	Fr	conjunctivitis

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used; AA: Aneityum, Anelcauhat, BML: Banks Islands, Moto Lava:, SWA: Southwest Ambrym, TLL: Torres Islands, Loh, Lungharigi; dd/rw: dewdrop/rainwater, Fl: flower, Fr: frond, Frt: fruit, L: leaf, St: stem

DISEASES OF THE KIDNEY

Diseases of the kidney comprise kidney pain (maybe caused by pyelitis or renal colic) and *pispis waet*, described as a severe and almost always deadly illness with foamy (white) urine, probably albuminuria, a symptom of post-streptococcal glomerulonephritis, a common sickness in Vanuatu (see also "Diseases of the cardiovascular and haematopoietic system" p. 93). Kidney problems are treated internally. In this section the information on *Dysoxylum arborescens* (BL.) MIQ. (Meliaceae), and *Allophylus timoriensis* DC. BL. (Sapindaceae) is summarised.

A remedy prepared from the inner bark of *Dysoxylum arborescens* (BL.) MIQ. (Meliaceae) is taken for kidney pain (Tab. 21) and the wood is used for construction.[34] Nothing is known about this species yet, but other members of this genus, also partly used in traditional medicine, have shown activities in biological tests. In Erromango (Vanuatu) *D. gaudichaudianum* leaf juice in water is taken to facilitate childbirth, in Efate a decoction of the leaves is drunk as an abortifacient,[70] and an emmenagogue is prepared from the bark in the Philippines.[310] A remedy prepared from the bark together with that of *D. bijugum*, and *Pandanus sp.* (Pandanaceae) and the twigs of *Terminalia catappa* (Combretaceae) is ingested to treat ciguatera,[256] but oxytocic activity could not yet be proven *in vitro*.[71] Triterpenoids from *D. gaudichaudianum* have demonstrated antiviral activity against respiratory syncytial virus (RSV).[431] In Espiritu Santo (Vanuatu) the bark of *D. aneityense* is burned in reach of the vagina to facilitate childbirth.[70] In Samoa a tonic is prepared from the bark of *D. maota.*[228] Alkaloids with contraceptive activity in rats[432] or anti-inflammatory and immunomodulatory activities[433] have been isolated from *D. binectariferum* and its crude extracts were significantly active against *Leishmania donovani in vitro* as well as *in vivo* (hamster), with lower effects of the pure alkaloids isolated from *D. binectariferum in vivo* (hamster).[434] Di- and triterpenoids have been isolated from *D. hainanense*,[435, 436] triterpenoids from *D. beddomei*[437] and *D. malabaricum,*[438] and diterpenoids and acetophenone from *D. lenticellare*.[439] Alkaloids isolated from *D. lenticellare* have shown cardioactivity *in vivo* in rats.[440] The triterpenoids from *D. malabaricum* and *D. beddomei* showed insecticidal activities against *Anopheles stephensi*, a malaria vector.[441] Cytotoxic effects have also been demonstrated: diterpenoids isolated from *D. kuskusense* were active against HL-60 cells, the human chronic myelogenous leukaemia (CML) cell line K-562, the human non-small cell lung carcinoma cell line NCI-H522,[442] and P-388 cells, the human colorectal adenocarcinoma cell line HT-29 and the human epithelial cell lung carcinoma cell line A549,[443] triterpenoids from *D. variabile* against the human HeLa contaminant KB cells,[444] di- and sesquiterpenoids from *D. cauliflorum* against the human non-small bronchiopulmonary carcinoma cell line NSCLC-N6[445] and crude extracts of *D. cumingianum* against the human renal cancer cell line UO-31, the human stomach cancer cell line NCI-H522,[446] and several leukaemia- and

melanoma cell lines.[447] The leaves of this plant have been collected for the screening regimen because of promising activities as cytotoxic agents proven for other members of the genus.

The leaves of *Allophylus timoriensis* DC. BL. (Sapindaceae) are prepared to a medicine to relieve kidney pain (Tab. 21). In Banks Islands, Moto Lava a tonic for children is prepared from the leaves[72] and elsewhere in Vanuatu the leaves are applied to swellings and inflammations[66]. No studies on this species have been performed yet, but other members of the genus have already shown activities in biological assays: *A. serratus* has shown anti-ulcerogenic activity in an *in vivo* rat ulcer model,[448] extracts of *A. cobbe*, in New Ireland used to stun fish,[278] demonstrated antifeedant activity against the larvae of the Mexican bean beetle, *Epilachna varivestis* MULS. (Coccinellidae),[449] and *A. comina* extracts anti-diabetic activities, maybe due to phenolic compounds, tannins, saponins, triterpenoids, and steroids isolated from this plant.[450] In addition flavones and sesquiterpenoids have been discovered in the fruits of *A. laevigatus*[451] and cyanolipids in the seeds of *A. natalensis* and *A. dregeanus*.[452] The leaves of this plant have been collected for the screening regimen due to its use in Vanuatu's ethnopharmacopoeia.

Tab. 21 Plants used to treat diseases of the kidney

scientific name	family	[1]UR	[2]POC	[3]PPU	use
Dysoxylum arborescens (BL.) MIQ.	Meliaceae	1	TLL	iB	kidney pain
Ficus adenosperma MIQ.	Moraceae	1	SWA	sap (Rt)	albuminuria
Allophylus timoriensis DC. BL.	Sapindaceae	1	TLL	L	kidney pain

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used, SWA: Southwest Ambrym, TLL: Torres Islands, Loh, Lungharigi; iB: inner bark, L: leaf, Rt: root

OTHER ETHNOBOTANICAL USES OF PLANTS IN VANUATU

In the following table non-medicinal uses of the plants are summarised, including uses in cosmetics, as food and stimulants, in house and garden, and for *Kastom* (mostly magical) purposes.

Tab. 22 Other ethnobotanical uses of plants in Vanuatu

scientific name	family	[1]UR	[2]POC	[3]PPU	use	sociocultural relevance
Cananga odorata (LAM.) HOOK.F. & THOMSON	Annonaceae	1	TLL	Fl	scents coconut oil	body care
Calophyllum inophyllum L.	Guttiferae	1	TLL	Fl	scents coconut oil	body care
Dracontomelon vitiense ENGL.	Anacardiaceae	1	NA	Frt	edible	food & stimulants
Annona muricata L.	Annonaceae	1	TLL	Frt	edible	food & stimulants
Polyscias cumingiana (C.PRESL) FERN.-VILL.	Araliaceae	1	SWA	L	edible	food & stimulants
Polyscias scutellaria (BURM.F.) FOSB.	Araliaceae	1	SWA	L	edible	food & stimulants

scientific name	family	[1]UR	[2]POC	[3]PPU	use	sociocultural relevance
Cocos nucifera L.	Arecaceae	6	TLL/TLT/SWA/NA/AA/APP	Sd	edible	food & stimulants
		6		Frt	edible	food & stimulants
Canarium vulgare LEENH.	Burseraceae	6	TLL/TLT/SWA/NA/AA/APP	Sd	edible	food & stimulants
Carica papaya L.	Caricaceae	1	BML	Frt	edible	food & stimulants
Terminalia catappa L.	Combretaceae	1	AA/ APP/ NA/ SWA/ TLL/ TLT	Sd	edible	food & stimulants
Cucurbita pepo L.	Cucurbitaceae	1	AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	edible	food & stimulants
Dioscorea bulbifera L.	Dioscoreaceae	1	NA	L	edible	food & stimulants
		6	AA/ APP/ NA/ SWA/ TLL/ TLT	Rh	edible	food & stimulants
Barringtonia edulis SEEM.	Lecythidaceae	1	SWA	Frt	edible	food & stimulants
Entada pursaetha DC.	Leguminosae - Mimosoideae	1	AA	Frt	edible	food & stimulants
Inocarpus fagifer PARK.	Leguminosae – Papilionoideae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	Sd	edible	food & stimulants
Vigna luteola (JACQ.) BENTH.	Leguminosae – Papilionoideae	1	SWA	Sd	edible	food & stimulants
Artocarpus altilis (PARK.) FOSB.	Moraceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	edible	food & stimulants
		6		Sd	edible	food & stimulants
Psidium guajava L.	Myrtaceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	edible	food & stimulants
Syzygium malaccense (L.) MERR. & L.M. PERRY	Myrtaceae	4	AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	edible	food & stimulants
Pandanus tectorius PARK.	Pandanaceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	edible	food & stimulants
		6		L	weaving	food & stimulants
Piper methysticum J. R. & G. FORST.	Piperaceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	Rt	folk drug	food & stimulants
Pometia pinnata J.R. FORST. & G. FORST.	Sapindaceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	edible	food & stimulants
Pipturus argenteus WEDD.	Urticaceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	edible	food & stimulants
Polyscias cumingiana (C.PRESL) FERN.-VILL.	Araliaceae	1	SWA	wP	hedge plant	house & garden
Polyscias scutellaria (BURM.F.) FOSB.	Araliaceae	1	SWA	wP	hedge plant	house & garden
		1	SWA	L	to stimulate fruiting of a banana plant	house & garden
Cocos nucifera L.	Arecaceae	6	TLL/TLT/SWA/NA/AA/APP	W	carving	house & garden
Merremia peltata (L.) MERR.	Convolvulaceae	1	TLL	St	fish poison	house & garden
Calophyllum inophyllum L.	Guttiferae	1	TLL	Sd	toxic for chicken	house & garden
Gyrocarpus americanus JACQ.	Hernandiaceae/ Gyrocarpaceae	6	TLL/TLT/SWA/NA/AA/APP	W	carving	house & garden
Solenostemon scutellarioides L.	Lamiaceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	wP	ornamental plant	house & garden
Barringtonia asiatica (L.) KURZ	Lecythidaceae	1	TLL/AA	Sd	fish poison	house & garden
		1	AA	Frt	fish poison	house & garden
Intsia bijuga (COLEBR.) O. KTZE.	Leguminosae – Caesalpinioideae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	W	carving	house & garden
Derris trifoliata LOUR.	Leguminosae – Papilionoideae	9	AA/ APP/ NA/ SWA/ TLL/ TLT	St	rope for firewood	house & garden
Pterocarpus indicus WILLD.	Leguminosae – Papilionoideae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	W	carving	house & garden
Hibiscus rosa-sinensis L.	Malvaceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	wP	ornamental plant	house & garden
Hibiscus tiliaceus L.	Malvaceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	W	carving	house & garden
Ficus wassa ROXB.	Moraceae	1	TLT	St	to stimulate fruiting of a watermelon plant	house & garden
Vitex trifolia L. ssp. *trifolia*	Verbenaceae	6	AA/ APP/ NA/ SWA/ TLL/ TLT	W	outrigger canoes	house & garden
Graptophyllum pictum (L.) GRIFF.	Acanthaceae	1	SWA	wP	protection against black magic	*Kastom*

scientific name	family	[1]UR	[2]POC	[3]PPU	use	sociocultural relevance
Cordyline fruticosa (L.) A. CHEV.	Agavaceae	1	TLL	L	*Kastom* plant (dye for hair when gaining rank)	*Kastom*
		3	TLL/SWA/AA	wP	several *Kastom* purposes	*Kastom*
Polyscias scutellaria (BURM.F.) FOSB.	Araliaceae	1	SWA	L	poisoned food	*Kastom*
Garuga floribunda DECNE.	Burseraceae	1	TLL	L	ciguatera	*Kastom*
Ipomoea indica (BURM.F.) MERR.	Convolvulaceae	1	SWA	Lat/St	poisoned food	*Kastom*
Luffa cylindrica (LOUR.) ROEM.	Cucurbitaceae	1	SWA	iB	lovesickness	*Kastom*
Dracaena fragrans (L.) KER - GAWL.	Dracaenaceae	1	SWA	yL	poisonous plant used to commit suicide	*Kastom*
Codiaeum variegatum (L.) BL.	Euphorbiaceae	1	AA/ APP/ NA/ SWA/ TLL/ TLT	wP	*Kastom* plant	*Kastom*
Calophyllum inophyllum L.	Guttiferae	1	TLL	Frt	game "sut 'em"	*Kastom*
Gyrocarpus americanus JACQ.	Hernandiaceae/ Gyrocarpaceae	1	TLL	iB	used to tame pigs	*Kastom*
Hibiscus rosa-sinensis L.	Malvaceae	1	TLL	Fl	children, that don't speak	*Kastom*
Donax cannaeformis (G. FORST.) K. SCHUM.	Marantaceae	1	NA	dd/rw/L	children, that don't speak	*Kastom*
Ficus septica BURM.F.	Moraceae	1	SWA	L	children's' diseases caused by spirits	*Kastom*
Maesa ambrymensis GUILL.	Myrsinaceae	1	NA	L	infant crying caused by magic	*Kastom*
Macropiper latifolium (L.F.)	Piperaceae	1	SWA	Frt	black magic	*Kastom*
	Piperaceae	1	NA	L	*Kastom* plant	*Kastom*
Pometia pinnata J.R. FORST. & G. FORST.	Sapindaceae	1	SWA	yL	pain caused by magic	*Kastom*
		1	TLL	L	jealousy (of women)	*Kastom*
Vitex trifolia L. ssp. *trifolia*	Verbenaceae	1	SWA	L	infant crying	*Kastom*
Hornstedtia sp.	Zingiberaceae	1	APP	L	grass skirts	*Kastom*

[1]UR: number of use reports, [2] POC: place of collection; [3] PPU: plant part used, AA: Aneityum, Anelcauhat, APP: Aneityum, Port Patrick, BML: Banks Islands, Moto Lava, NA: North Ambrym, SWA: Southwest Ambrym, TLL: Torres Islands, Loh, Lungharigi; TLT: Torres Islands, Loh, Telaklak; dd/rw: dewdrop/rainwater, Fl: flower, Frt: fruit, iB: inner bark, L: leaf, Lat: latex, Rh: rhizome, Sd: seed, St: stem, W: wood, wP: whole plant, yL: young leaf

1.5 SELECTION OF PLANTS FOR THE SCREENING REGIMEN

There are four basic approaches to select a plant for a pharmacological study: the ethnomedicinal, the phytochemical, the taxonomic, the random approach, or a combination of several criteria [453]. In the ethnomedicinal tactic credibility is given to the traditional use, in the phytochemical particular compound types are regarded to be interesting in a given biological context and plants likely to contain this sort of compounds are collected, and finally in the taxonomic approach plants of a given genus or family are selected. In the random approach all available species are collected irrespective prior knowledge and experience.[454] A retrospective analysis of the NCI program showed that the percentage of active leads based on ethnomedicine was above that based on taxonomy and random.[455]

In this study a combination of the mentioned criteria was used to select plants for the intended screening regimen:

(1) Ethnomedicinal method: In the interviews it has been chosen to target plant species which have been claimed by the healers to be pharmacologically active in a clearly defined therapeutical context (in this study we focused on remedies with immunomodulatory properties). This improved the chance to obtain good interview results, because as in many parts of the world healers are often reluctant to give information on their secrets as a whole. Furthermore the permission to collect information for this study was limited by the Vanuatu Cultural Centre to well known and widely used plant species and preparations, because traditional knowledge in this place is a very touchy issue and subject to restrictions due to the cultural *Kastom* system. Knowledge is usually inherited from generation to generation, given from mother to daughter and father to son and most likely staying in one family. Sometimes, if a consexual heir is not at hand, namely that there simply is no male descendant in a family or there is one, who does not intend to follow in his father's footsteps, these rules can be changed and knowledge can be passed on inter-sexually from father to daughter or mother to son or even to third parties. When visiting Espiritu Santo I was told a story about a unique case in which wisdom of a male healer from Northern Ambrym was given to a female American scientist. She had to undergo several procedures, including the ingestion of a highly hallucinatic secret drug while staying alone in the jungle for several days This was called *kakae* (eat) *tambu-faea* (taboo fire; restricted for the use of men of a very high status), regrettably yielding in only very little information about secret plants and special healing procedures hardly worth mentioning.

(2) Phytochemical and taxonomic methods: Plants bearing interesting compounds such as alkaloids, sesquiterpene lactones, or lignans were chosen by former literature study of genera and families. Detailed information on each plant is found in "Results Ethnobotany" and in Tab. 23 all plants collected for the screening regimen are listed with the reason(s) for their selection.

Tab. 23 Plants collected for the screening regimen and reasons for their selection

scientific name	PPU/C[1]	reason for collection
ANACARDIACEAE *Dracontomelon vitiense* ENGL.	iB	The antibacterial activity shown for *D. dao* and antimalarial activities shown for other members of the family[265] (taxonomic affiliation).
APOCYNACEAE *Tabernaemontana pandacaqui* LAM. I	L	Use against "skin cancer" and wounds, biological activities have already been demonstrated for other members of the genus and membership to the Apocynaceae, a family rich in alkaloids (ethnobotanical use, taxonomic affiliation, and phytochemical composition). Collected twice (I + II) because one plant has been misidentified in the filed as a second species due to a lack of flowers and because no latex was present in the second species.
Tabernaemontana pandacaqui LAM. II	L	
ASTERACEAE *Bidens pilosa* L.	wP	Ethnobotanical use (against cough) and misidentification in the field as another not yet investigated Asteraceae (ethnobotanical use).
EUPHORBIACEAE Acalypha grandis BENTH.	L	Ethnobotanical use (against sore throat, gonorrhoea) and biological activities already demonstrated for other members of the genus (ethnobotanical use and taxonomic affiliation).
Macaranga dioica MUELL. ARG.	iB L	Ethnomedicinal use (wounds), phytochemical composition, and the mentioned biological activities already proven for other members of the genus (ethnobotanical use, taxonomic affiliation, and phytochemical composition).
Macaranga tanarius (L.) MUELL. ARG.	L	Ethnomedicinal use (several dermatological complaints), phytochemical composition, and the mentioned biological activities already proven for other members of the genus (ethnobotanical use, taxonomic affiliation, and phytochemical composition).
GYROCARPACEAE/ HERNANDIACEAE *Gyrocarpus americanus* JACQ.	L	Wound-healing properties described in Vanuatu's and other ethnopharmacopoeia(s) and alkaloid- and flavonoid content expected for a member of the Hernandiaceae family (ethnobotanical use, taxonomic affiliation, and phytochemical composition).
LEGUMINOSAE – CAESALPINIOIDEAE *Intsia bijuga* (COLEBR.) O. KTZE.	L	Cytotoxic activities shown for other members of the family (taxonomic affiliation).
MELIACEAE *Dysoxylum arborescens* (BL.) MIQ.	L	Promising activities as cytotoxic agents proven for other members of the genus and expected alkaloid content (taxonomic affiliation and phytochemical composition).
MYRTACEAE *Syzygium malaccense* (L.) MERR. & L.M. PERRY	L	Use in Vanuatu's ethnopharmacopoeia (mouth infections) and proven biological activities of other members of the genus (ethnobotanical use and taxonomic affiliation).
PHYLLANTHACEAE *Baccaurea stylaris* MUELL. ARG.	iB L	Ethnobotanical use (against cold), biological activities demonstrated for the tribe Antidesmateae (ethnobotanical use and taxonomic affiliation).
PIPERACEAE *Macropiper latifolium* (L.F.)	St	Ethnobotanical use as an antibacterial agent against conjunctivitis, and close relationship to *Piper methysticum* J.R. & G. FORST., a popular stimulant[211] whose roots have shown several biological activities (ethnobotanical use and taxonomic affiliation).

scientific name	PPU/C[1]	reason for collection
RUBIACEAE *Aidia racemosa* (CAV.) D.D. TIRVENG.	L	Antimicrobial activities shown for other *Aidia* species and because of its affiliation to the alkaloid-bearing family Rubiaceae (taxonomic affiliation and phytochemical composition).
RUTACEAE *Euodia latifolia* DC.	L	Ethnomedicinal use (against cough), activities of other *Euodia sp.* in various biological tests, and phytochemical composition of the genus (ethnobotanical use, taxonomic affiliation, and phytochemical composition).
SAPINDACEAE *Allophylus timoriensis* DC. BL.	L	Ethnobotanical use against kidney pain.
SPARRMANNIACEAE *Grewia inmac* GUILL.	L	Use as "aelan panadol®" in Vanuatu's ethnopharmacopoeia, activities of other members of the genus *Grewia* in various test systems and phytochemical composition expected for a member of this genus (ethnobotanical use, taxonomic affiliation, and phytochemical composition).
URTICACEAE *Pipturus argenteus* WEDD.	iB	Ethnobotanical use against boils and biological activities of *P. albidus* (ethnobotanical use and taxonomic affiliation).
ZINGIBERACEAE *Zingiber zerumbet* (L.) SM.	Rh	This plant was misidentified in the field as an *Alpinia sp*. and was therefore collected due to a broad spectrum of biological activities demonstrated for other *Alpinia sp*. and the phytochemical composition expected for a member of this genus (taxonomic affiliation and phytochemical composition).

[1]PPU/C: plant part used and collected; iB: inner bark, L: leaves, Rh: rhizome, St: stem; wP: whole plant

2. BIOLOGICAL TESTS

2.1 CYTOTOXICITY ASSAY

SELECTION OF INOCULATION DENSITIES

Prior to inclusion of cell lines in the screening panel their growth and compatibility with the screening model had to be determined, including the comparison of the linearity of the MTT-generated optical density signal with the cell number in the assay. Cell growth was characterized over three days and from these data the specific inoculation density selected for each cell line was that which produced an optical density signal above the noise level of the assay and within the linear range of the MTT-signal and which was closest to cell densities used in the NCI60 *in vitro* screen (see EXPERIMENTAL PART) (data not shown).

DETERMINATION OF THE SUITABLE DRUG-INCUBATION TIME

The cytotoxic activities of the plant extracts were both tested after incubation periods of 48 h (data not shown) and 72 h. An incubation time of 72 h was finally chosen due to less variation of the optical density either within or between the experiments and the resulting better reproducibility of the data.

INTERACTION OF EXTRACTS AND MTT IN CELL-FREE SYSTEM

The secondary plant metabolites present in the extracts tested in this study did not show any interaction with the MTT assay in a cell-free system (data not shown).

POSITIVE CONTROL FOR THE CYTOTOXICITY ASSAY

A positive control had to be established for the screening to confirm, that the basic conditions of the experiment were able to produce a positive result, even if none of the samples actually did. For each cell line the IC_{50} of podophyllotoxin or parthenolide, respectively has been determined as described in the EXPERIMENTAL PART - section. Parthenolide was used in two cases, because no reasonable value could be achieved with podophyllotoxin. A corresponding dose response analysis with DMSO was also included to make sure, that the DMSO-dose used to solubilise the positive control had no influence.

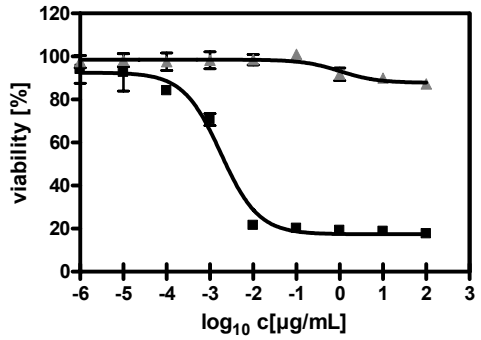

Fig. 16 Dose response curve for 786-0-cells incubated with (■) podophyllotoxin in DMSO for 72 h and corresponding curve for (▲) DMSO. Data shown as means ± SD (*n*=3)

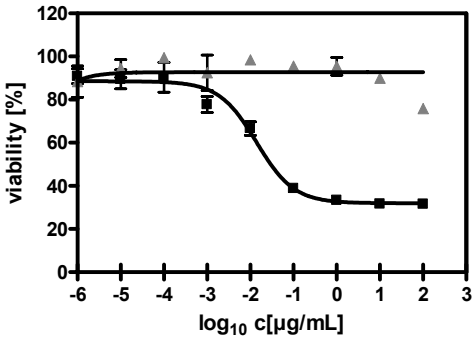

Fig. 17 Dose response curve for A549-cells incubated with (■) podophyllotoxin in DMSO for 72 h and corresponding curve for (▲) DMSO. Data shown as means ± SD (*n*=3)

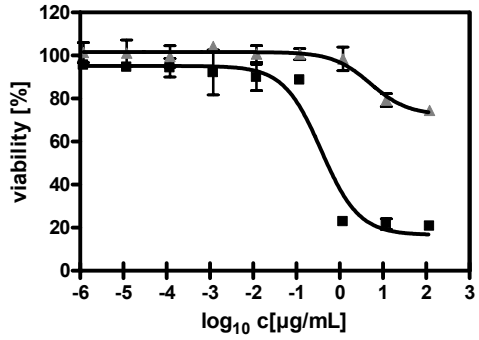

Fig. 18 Dose response curve for HT 29-cells incubated with (■) podophyllotoxin in DMSO for 72 h and corresponding curve for (▲) DMSO. Data shown as means ± SD (*n*=3)

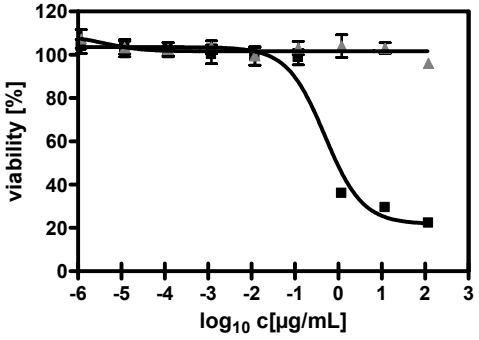

Fig. 19 Dose response curve for MCF7-cells incubated with (■) podophyllotoxin in DMSO for 72 h and corresponding curve for (▲) DMSO. Data shown as means ± SD (*n*=3)

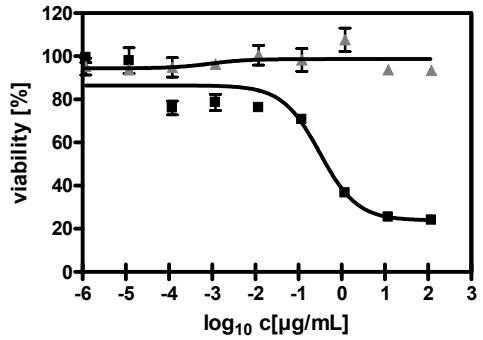

Fig. 20 Dose response curve for OVCAR-3:NIH-cells incubated with (■) podophyllotoxin in DMSO for 72 h and corresponding curve for (▲) DMSO. Data shown as means ± SD (*n*=3)

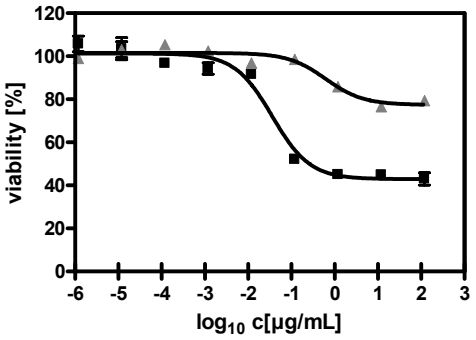

Fig. 21 Dose response curve for PC-3-cells incubated with (■) podophyllotoxin in DMSO for 72 h and corresponding curve for (▲) DMSO. Data shown as means ± SD (*n*=3)

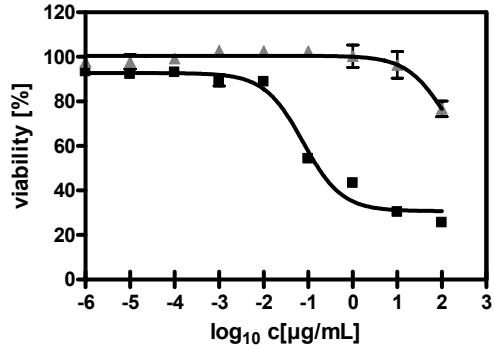

Fig. 22 Dose response curve for SK-MEL-28-cells incubated with (■) parthenolide in DMSO for 72 h and corresponding curve for (▲) DMSO. Data shown as means ± SD (*n*=3)

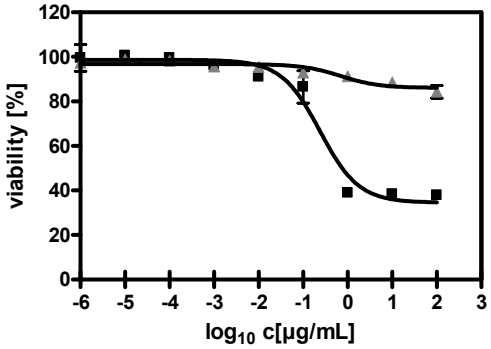

Fig. 23 Dose response curve for SNB-19-cells incubated with (■) parthenolide in DMSO for 72 h and corresponding curve for (▲) DMSO. Data shown as means ± SD (*n*=3)

RESULTS OF THE SCREENING FOR CYTOTOXICITY

In the following the results of the viability assays are presented.

Altogether about 7% of the extracts showed good, 30% moderate, and 62% no cytotoxic activity at all, whereas 85% of the methanolic extracts and 58% of ethyl acetate extracts, but only 45% of the dichloromethane extracts were inactive.

Renal cancer cell line 786-0

19% of the dichloromethane (DCM)-, 11% of the ethyl acetate (EtOAc)-, and 13% of the methanolic (MeOH)-extracts showed growth inhibition of more than 50% at a concentration of 50 µg/mL (data not shown), at 25 µg/mL only 10% of the DCM-, one EtOAc-extract, and none of the MeOH-extracts remained active (Fig. 24).

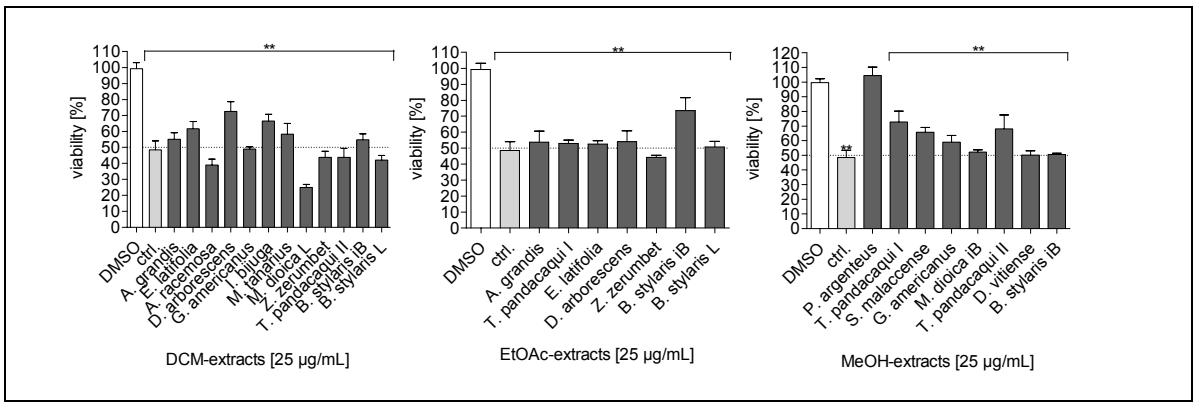

Fig. 24 Results of the cytotoxicity Assay for 786-0. Incubation with 25 µg/mL plant extract for 72 h. Data as means ± SD (*n*=4); passage 5 - 15; ***p*<0.01 in comparison with DMSO-control (Dunnett's multiple comparison test). Ctrl.: positive control podophyllotoxin [0.005 ± 0.0005 µM].

The leaf extracts of *Tabernaemontana pandacaqui* LAM. II, *Macaranga dioica* MUELL. ARG., *Gyrocarpus americanus* JACQ., *Aidia racemosa* (CAV.) DD. TIRVENG., and *Baccaurea stylaris* MUELL. ARG. and the rhizome extract of *Zingiber zerumbet* (L.) SM. showed good cytotoxic effects with IC_{50}-values ranging between 0.2 and 6.8 µg/mL (Fig. 25, Tab. 24), whereas selective activity against this cell line could be shown for *T. pandacaqui*, *G. americanus*, and *A. racemosa*.

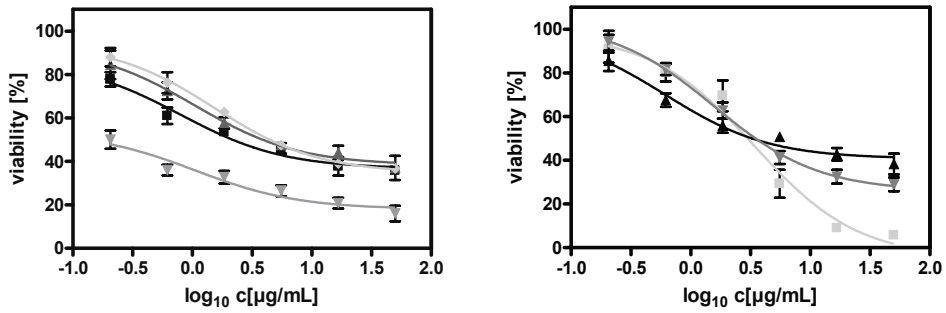

Fig. 25 Dose response curves for 786-0-cells, incubated with extracts for 72 h. Data shown as means ± SD (*n*=4). (■) *A. racemosa* CAV. DD. TIRVENG.. DCM-extract (leaves), (▲) *G. americanus* JACQ. DCM-extract (leaves), (▼) *M. dioica* MUELL. ARG. DCM-extract (leaves), (◆) *T. pandacaqui* LAM. II DCM-extract (leaves), (■) *Z. zerumbet* (L.) SM DCM-extract (rhizome), (▲) *Z. zerumbet* (L.) SM EtOAc-extract (rhizome), (▼) *B. stylaris* MUELL. ARG. DCM-extract (leaves)

Lung cancer cell line A549

While 22% of the DCM-, 10% of the EtOAc-, and 3% of the MeOH-extracts still displayed a decrease of viability greater than 50% at 50 µg/mL (data not shown), only 8% of the DCM-extracts and two of the EtOAc- or none of the MeOH-extracts, respectively showed the same effects at a lower concentration (Fig. 26).

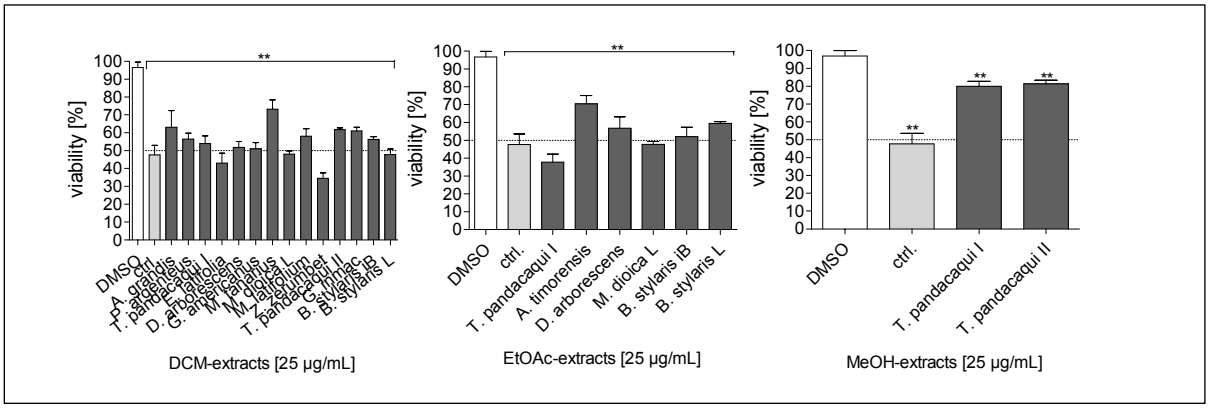

Fig. 26 Results of the cytotoxicity Assay for A549. Incubation with 25 µg/mL plant extract for 72 h. Data as means ± SD (*n*=4); passage 5 - 15; ***p*<0.01 in comparison with DMSO-control (Dunnett's multiple comparison test). Ctrl.: positive control podophyllotoxin [0.038 ± 0.005 µM].

The leaf extracts of *Tabernaemontana pandacaqui* LAM. I, *Macaranga dioica* MUELL. ARG., *Baccaurea stylaris* MUELL. ARG., and *Euodia latifolia* DC, the extract of the inner bark of *Macaranga dioica* MUELL. ARG., and the rhizome extract of *Zingiber zerumbet* (L.) SM. ranged between 1.4 and 14.2 µg/mL (

Fig. 27, Tab. 24), while *T. pandacaqui* and *E. latifolia* also demonstrated selective activity against this cell line.

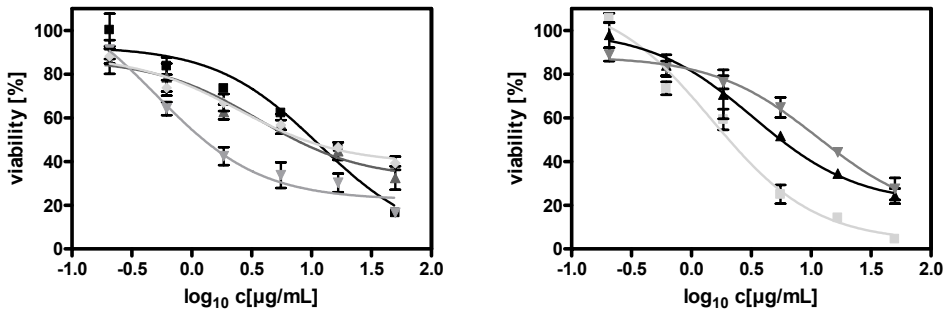

Fig. 27 Dose response curves for A549-cells, incubated with extracts for 72 h. Data shown as means ± SD (*n*=4). (■) *E. latifolia* DC. DCM-extract (leaves), (▲) *M. dioica* MUELL. ARG. DCM-extract (inner bark), (▼) *M. dioica* MUELL. ARG. DCM-extract (leaves), (◆) *M. dioica* MUELL. ARG. EtOAc-extract (leaves), (■) *Z. zerumbet* (L.) SM. DCM-extract (rhizome), (▲) *B. stylaris* MUELL. ARG. DCM-extract (leaves), (▼) *T. pandacaqui* LAM. I DCM-extract (leaves)

Colon cancer cell line HT-29

24% of the DCM-, 16% of the EtOAc-, and 8% of the MeOH-extracts showed good cytotoxic effects at a drug concentration of 50 µg/mL (data not shown), whereas only 8% of the DCM-extracts, and one EtOAc-extract remained active at a lower concentration (Fig. 28).

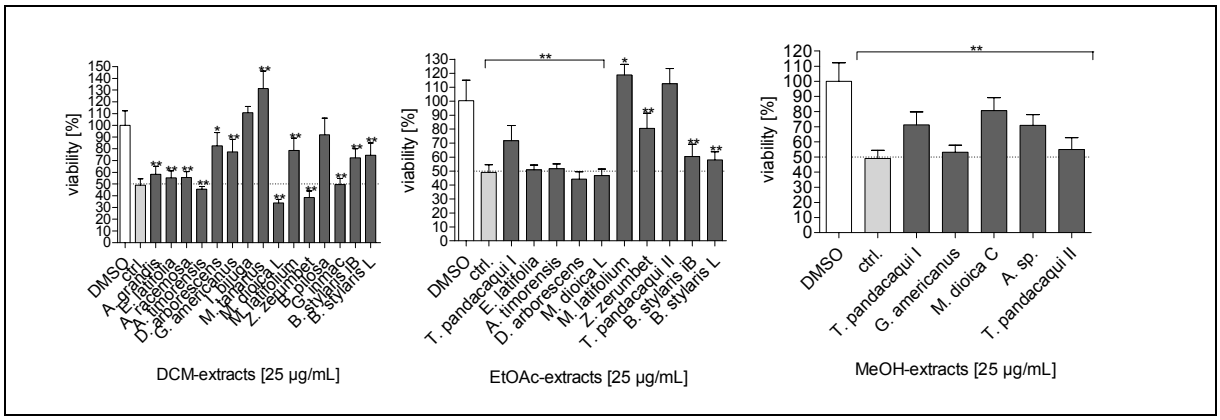

Fig. 28 Results of the cytotoxicity Assay for HT-29. Incubation with 25 µg/mL plant extract for 72 h. Data as means ± SD (n=4); passage 5 - 15; **p<0.01 and* p<0.1 in comparison with DMSO-control (Dunnett's multiple comparison test). Ctrl.: positive control podophyllotoxin [0.624 ± 0.017 µM].

The leaf extracts of *Macaranga dioica* MUELL. ARG., *Dysoxylum arborescens* (BL.) MIQ., *Allophylus timoriensis* DC. BL., and *Grewia inmac* GUILL., and the rhizome extract of *Zingiber zerumbet* (L.) SM. possessed an IC_{50} between 3.3 and 15 µg/mL, see Fig. 29 and Tab. 24, with *D. arborescens*, *A. timoriensis*, and *G. inmac* showing activities only on this cell line.

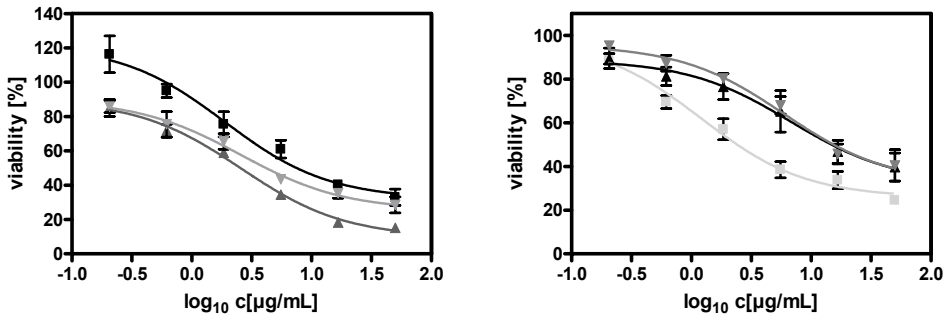

Fig. 29 Dose response curves for HT 29-cells, incubated with extracts for 72 h. Data shown as means ± SD (n=4). (■) *A. timoriensis* DC. BL. DCM-extract (leaves), (▲) *Z. zerumbet* (L.) SM. DCM-extract (rhizome), (▼) *G. inmac* GUILL. DCM-extract (leaves), (■) *M. dioica* MUELL. ARG DCM-extract (leaves), (▲) *M. dioica* MUELL. ARG. EtOAc-extract (leaves), (▼) *D. arborescens* (BL.) MIQ. EtOAc-extract (leaves)

Breast cancer cell line MCF7

While 13% of the DCM-, 21% of the EtOAc-extracts, and one MeOH-extract still showed a good decrease of viability at 50 µg/mL (data not shown), only 3% of the DCM-, 6% of the EtOAc-, and none of the MeOH-extracts remained active at a lower concentration (Fig. 30).

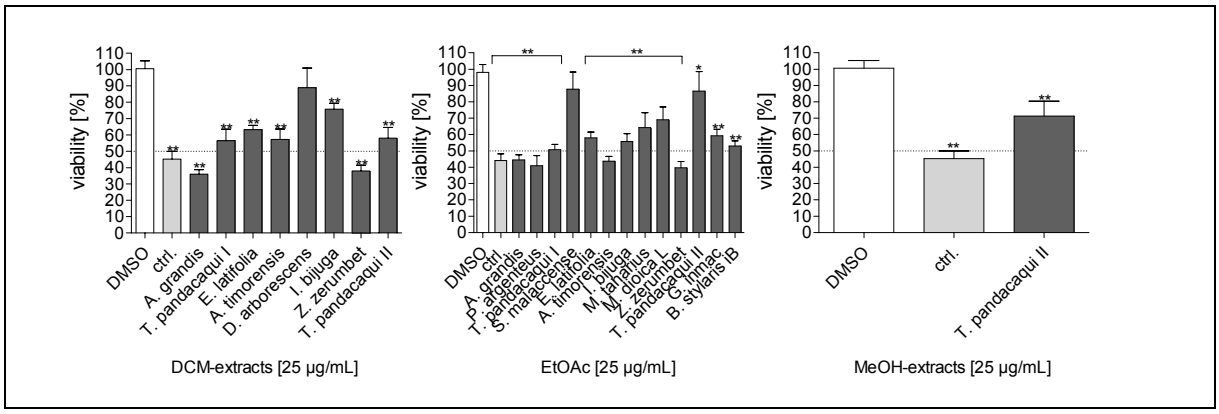

Fig. 30 Results of the cytotoxicity Assay for MCF7. Incubation with 25 µg/mL plant extract for 72 h. Data as means ± SD (*n*=4); passage 5 - 15; ***p*<0.01 and **p*<0.1 in comparison with DMSO-control (Dunnett's multiple comparison test). Ctrl. positive control podophyllotoxin [0.961 ± 0.041 µM].

The leaf extract of *Allophylus timoriensis* DC. BL., the extract of the inner bark of *Pipturus argenteus* WEDD., and the rhizome extract of *Zingiber zerumbet* (L.) SM. showed good cytotoxic effects with an IC_{50} ranging between 1.4 and 13.7 µg/mL (Fig. 31 and Tab. 24), whereas the extracts of *Acalypha grandis* BENTH., *Allophylus timoriensis* DC. BL., and the extract of the inner bark of *Pipturus argenteus* WEDD. also displayed selective activity against this cell line. The effect of *Z. zerumbet* has previously been described for this cell line.[335]

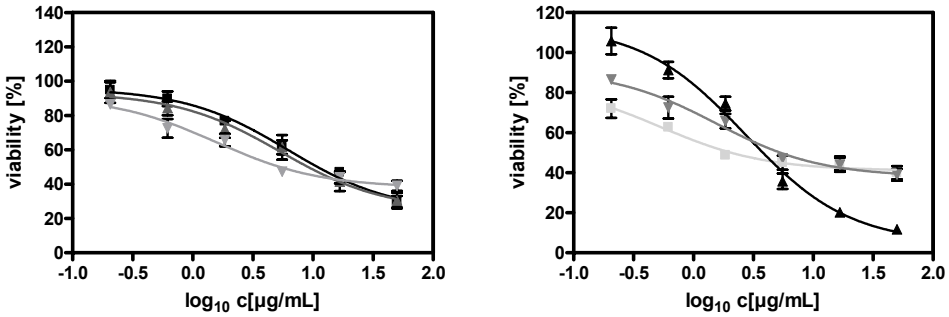

Fig. 31 Dose response curves for MCF7-cells, incubated with extracts for 72 h. Data shown as means ± SD (*n*=4). (■) *A. grandis* BENTH. DCM-extract, (▲) *A. grandis* BENTH. EtOAc-extract, (▼) *A. timoriensis* DC. BL. EtOAc-extract, (■) *P. argenteus* WEDD. EtOAc-extract, (▲) *Z. zerumbet* (L.) SM. DCM-extract, (▼) *Z. zerumbet* (L.) SM EtOAc-extract

Ovarian cancer cell line OVCAR-3:NIH

14% of the DCM-, 11% of the EtOAc-, and only one MeOH-extract(s) displayed cytotoxic effects at 50 µg/mL (data not shown), but only 3% of the DCM- and none of the other extracts kept this effect at a lower drug concentration (Fig. 32).

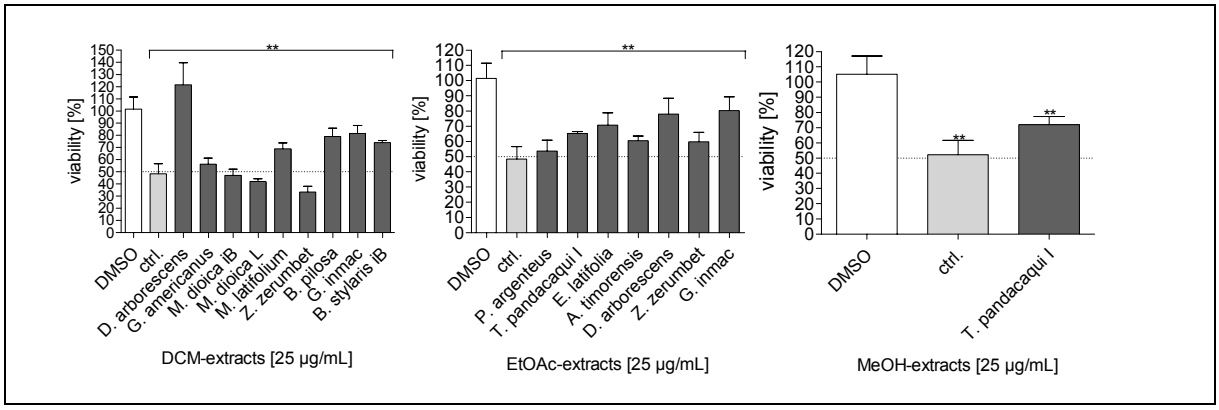

Fig. 32 Results of the cytotoxicity Assay for OVCAR-3:NIH. Incubation with 25 µg/mL plant extract for 72 h. Data shown as means ± SD (*n*=4); passage 5 - 15; ***p*<0.01 in comparison with DMSO-control (Dunnett's multiple comparison test). Ctrl.: positive control podophyllotoxin [0.778 ± 0.021 µM].

Only three extracts showed strong cytotoxic impact with an IC_{50} between 5.0 and 14.1 µg/mL, namely the extracts of inner bark and leaves, respectively of *Macaranga dioica* MUELL. ARG., and the rhizome extract of *Zingiber zerumbet* (L.) SM., whereas no selective activities could be observed (Fig. 33 and Tab. 24).

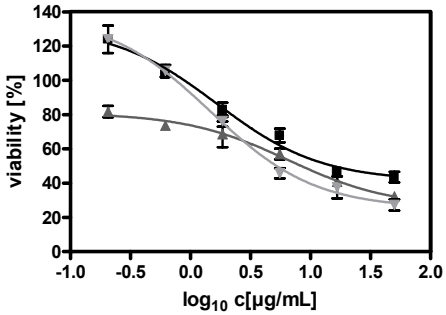

Fig. 33 Dose response curves for OVCAR-3:NIH-cells, incubated with extracts for 72 h. Data shown as means ± SD (*n*=4). (□) M. dioica MUELL. ARG. DCM-extract (inner bark), (▲) M. dioica MUELL. ARG. DCM-extract (leaves), (▼) Z. zerumbet (L.) SM. DCM-extract (rhizome)

Prostate cancer cell line PC-3

While 24% of the DCM-, 13% of the EtOAc- and 6% of the MeOH-extracts still strongly lowered the viability of this cell line PC-3 (data not shown), this effect could only be shown for 2% of the DCM- and 5% of the EtOAc-extracts at 25 µg/mL (Fig. 34).

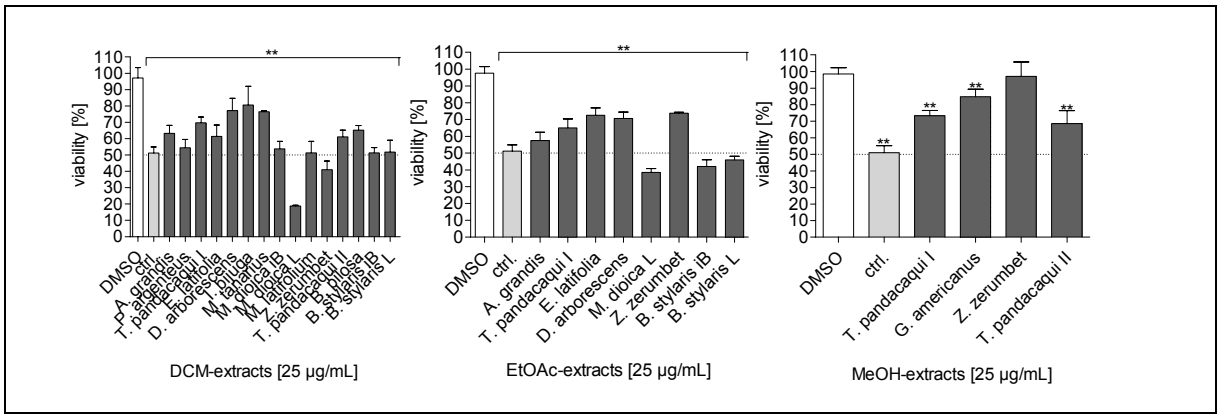

Fig. 34 Results of the cytotoxicity Assay for PC-3. Incubation with 25 µg/mL plant extract for 72 h. Data as means ± SD (*n*=4); passage 5 - 15; ***p*<0.01 in comparison with DMSO-control (Dunnett's multiple comparison test). Ctrl.: positive control podophyllotoxin [0.455 ± 0.024 µM].

The leaf extracts of *Macaranga dioica* MUELL. ARG. and *Baccaurea stylaris* MUELL. ARG., the extract of the inner bark of *Baccaurea stylaris* MUELL. ARG., and the rhizome extract of *Zingiber zerumbet* (L.) SM. demonstrated good cytotoxic effects with an IC_{50} ranging between 0.4 and 12.6 µg/mL, with the leaf extracts and the extract of the inner bark of *Baccaurea stylaris* MUELL. ARG. demonstrating effects only on this cell-line (Fig. 35 and Tab. 24).

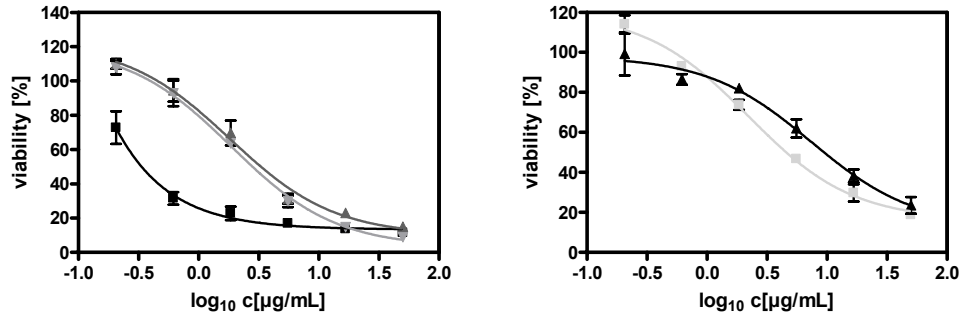

Fig. 35 Dose response curves for PC-3-cells, incubated with extracts for 72 h. Data shown as means ± SD (*n*=4). (■) *M. dioica* MUELL. ARG. DCM-extract (leaves), (▲) *M. dioica* MUELL. ARG. EtOAc-extract (leaves), (▼) *Z. zerumbet* (L.) SM. DCM-extract (rhizome), (■) *B. stylaris* MUELL. ARG. EtOAc-extract (inner bark), (▲) *B. stylaris* MUELL. ARG. EtOAc-extract (leaves)

Melanoma cell line SK-Mel-28

10% of the DCM-, 14% of the EtOAc-, and 5% of the MeOH-extracts were shown to strongly inhibit cell growth at a drug concentration of 50 µg/mL (data not shown), whereas this effect only remained for one DCM-, EtOAc- or MeOH-extract, respectively at a lower drug concentration of 25 µg/mL (Fig. 36).

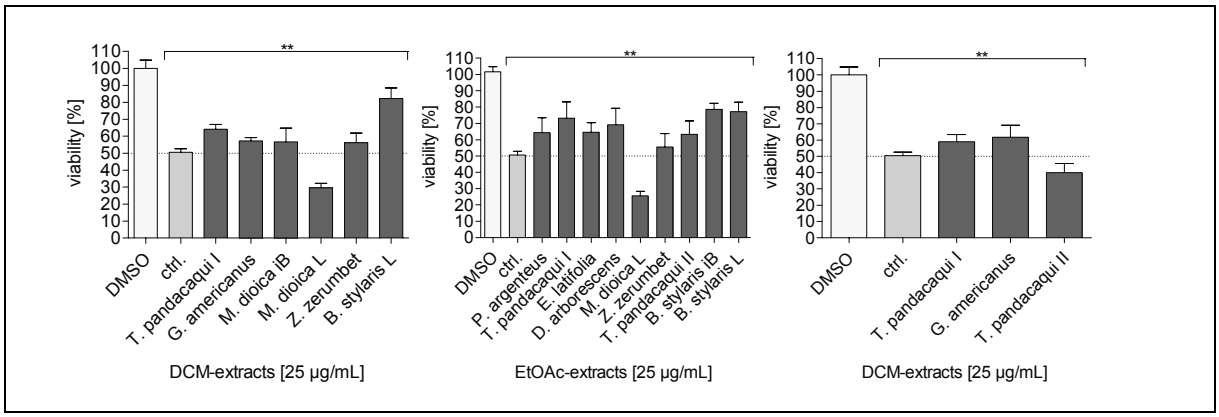

Fig. 36 Results of the cytotoxicity Assay for SK-Mel-28. Incubation with 25 µg/mL plant extract for 72 h. Data as means ± SD (n=4); passage 5 - 15; $^{**}p<0.01$ in comparison with DMSO-control (Dunnett's multiple comparison test). Ctrl.: positive control parthenolide [0.427 ± 0.035 µM].

The leaf extracts of *Tabernaemontana pandacaqui* LAM. II and *Macaranga dioica* MUELL. ARG. displayed IC_{50}-values between 0.1 and 14.5 µg/mL and the only active MeOH-extract in the whole study, namely that of *Tabernaemontana pandacaqui* LAM. II was selective for this cell line (Fig. 37 and Tab. 24).

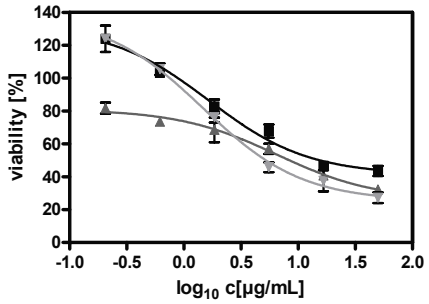

Fig. 37 Dose response curves for SK Mel 28-cells, incubated with extracts for 72 h. Data shown as means ± SD (n=4). (■) *M. dioica* MUELL. ARG. DCM-extract (leaves), (▲) *M. dioica* MUELL. ARG. EtOAc-extract (leaves), (▼) *T. pandacaqui* LAM. II MeOH-extract (leaves)

Glioblastoma cell line SNB-19

Whereas still 17% of the DCM-, 13% of the EtOAc-, and 3% of the MeOH-extracts were able to reduce the cell viability more than 50% at 50 µg/mL, none of the extracts kept the same effect at a lower concentration of 25 µg/mL (Fig. 38).

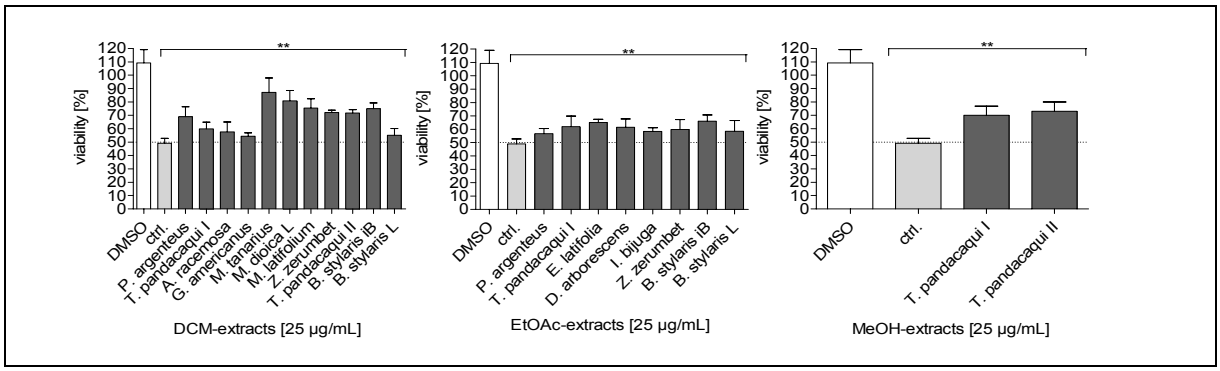

Fig. 38 Results of the cytotoxicity Assay for SNB-19. Incubation with 25 µg/mL plant extract for 72 h. Data as means ± SD (*n*=4); passage 5 - 15; ***p*<0.01 in comparison with DMSO-control (Dunnett's multiple comparison test). Ctrl.: positive control parthenolide [0.780 ± 0.063 µM].

In Fig. 39 the results of the viability assay are summarised. The colour coding indicates the IC_{50}-range, whereas extracts with an IC_{50} >50 µg/mL, which are considered as inactive in this study are marked light grey, extracts with an IC_{50} between 25 and 50 µg/mL, considered as moderately active, in medium grey, and extracts with an IC_{50} < 25 µg/mL, considered as active, in dark grey. The exact IC_{50} values were determined for the active extracts and are displayed in Tab. 24.

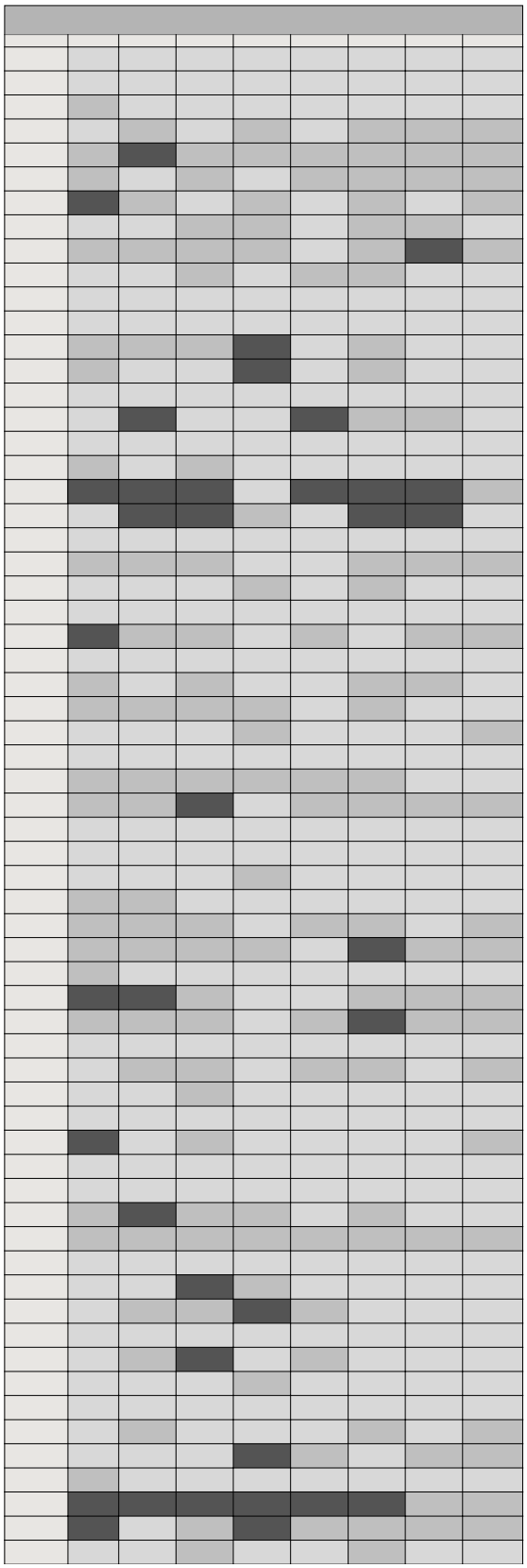

Fig. 39 Activity pattern for the plant extracts tested on eight cell-lines.

Tab. 24 *In vitro* cytotoxicity of the active plant extracts (IC_{50} in µg/mL; means ± SD; *n*=4)

786-0	**IC_{50}±SD**
Aidia racemosa (CAV.) DD. TIRVENG. DCM	3.540 ± 0.522
Baccaurea stylaris MUELL.ARG. DCM (leaves)	3.993 ± 0.379
Gyrocarpus americanus JACQ. DCM	4.544 ± 0.462
Macaranga dioica MUELL. ARG. DCM (leaves)	0.226 ± 0.024
Tabernaemontana pandacaqui LAM. II DCM	4.616 ± 0.656
Zingiber zerumbet (L.) SM. DCM	3.635 ± 0.371
EtOAc	6.792 ± 0.874
A549	
Baccaurea stylaris MUELL.ARG. DCM (leaves)	6.630 ± 0.931
Macaranga dioica MUELL. ARG. DCM (inner bark)	13.54 ± 1.036
Macaranga dioica MUELL. ARG. DCM (leaves)	1.443 ± 0.160
Macaranga dioica MUELL. ARG. EtOAc (leaves)	12.92 ± 1.290
Tabernaemontana pandacaqui LAM. I EtOAc	13.46 ± 0.983
Euodia latifolia DC. DCM	14.21 ± 0.890
Zingiber zerumbet (L.) SM. DCM	2.805 ± 0.389
HT-29	
Allophylus timoriensis DC. BL. DCM	10.93 ± 1.168
Dysoxylum arborescens (BL.) MIQ. EtOAc (leaves)	14.99 ± 2.308
Grewia inmac GUILL. DCM	4.570 ± 0.408
Macaranga dioica MUELL. ARG. DCM (leaves)	3.173 ± 0.455
Macaranga dioica MUELL. ARG. EtOAc (leaves)	14.99 ± 2.308
Zingiber zerumbet (L.) SM. DCM	3.332 ± 0.312
MCF7	
Acalypha grandis BENTH. DCM	13.72 ± 1.383
Acalypha grandis BENTH. EtOAc	9.960 ± 1.146
Allophylus timoriensis DC. BL. EtOAc	4.863 ± 0.563
Pipturus argenteus WEDD. EtOAc	1.630 ± 0.221
Zingiber zerumbet (L.) SM. DCM	4.128 ± 0.565
EtOAc	1.373 ± 0.176
OVCAR-3:NIH	
Macaranga dioica MUELL. ARG. DCM (inner bark)	14.06 ± 1.547
Macaranga dioica MUELL. ARG. DCM (leaves)	10.14 ± 1.412
Zingiber zerumbet (L.) SM. DCM	5.003 ± 0.402
PC-3	
Baccaurea stylaris MUELL.ARG. EtOAc (inner bark)	5.043 ± 0.337
Baccaurea stylaris MUELL.ARG. EtOAc (leaves)	12.61 ± 1.789
Macaranga dioica MUELL. ARG. DCM (leaves)	0.435 ± 0.062
Macaranga dioica MUELL. ARG. EtOAc (leaves)	3.288 ± 0.0438
Zingiber zerumbet (L.) SM. DCM	3.275 ± 0.445
SK-Mel-28	
Macaranga dioica MUELL. ARG. DCM (leaves)	0.088 ± 0.01
Macaranga dioica MUELL. ARG. EtOAc (leaves)	1.510 ± 0.082
Tabernaemontana pandacaqui LAM. II MeOH	14.52 ± 0.296

2.2 ANTIBACTERIAL AND ANTIFUNGAL ASSAYS

None of the extracts has shown significant antibacterial activities, neither against the Gram-positive *Staph. aureus* nor the Gram-negative *E. coli*, only the DCM-extract of the inner bark of *D. vitiense* has displayed moderate activity against *Staph. aureus* in a pre-screening, which did not qualify it for a second screen. Furthermore none of the extracts was able to significantly inhibit the growth of *Aspergillus fumigatus*, *Candida albicans*, and *Microsporum canis*, only the methanolic extract of the inner bark of *M. dioica* has shown moderate activity against *C. albicans*, but did also not qualify for a second screen. The DCM extract of the inner bark and the EtOAc-extracts of both, the inner bark and the leaves of *B. stylaris* have shown moderate activities against *Trichophyton rubrum* but did not qualify for a re-screen either.

Tab. 25 *In vitro* activities against selected bacteria and fungi (IC_{50} in µg/mL; *n*=1)

			IC_{50} [µg/mL]		
scientific name	**PPU**	**SOE**	**Sa**	**Ca**	**Tr**
ANACARDIACEAE					
Dracontomelon vitiense ENGL.	iB	DCM	5.78	-	-
EUPHORBIACEAE					
Macaranga dioica MUELL.ARG.	iB	MeOH	-	8.24	-
PHYLLANTHACEAE					
Baccaurea stylaris MUELL.ARG.	iB	DCM	-	-	9.39
		EtOAc	-	-	5.51
	L	EtOAc	-	-	8.81
Ampicillin			0.179		
Flucytosine				0.293	
Econazole					0.025
Doxycyclin (*E. coli*): 0.671 µg/mL					
Terbinafine (*A. fumigatus*): 0.803 µg/mL					
Terbinafine (*M. canis*): 0.102 µg/mL					

PPU: plant part used; iB: inner bark, L: leaf; SOE: solvent of extraction; DCM: dichloromethane, EtOAc: ethyl acetate, MeOH: methanol; Sa: *Staph. aureus*, Ca: *Candida albicans*, Tr: *Trichophyton rubrum*

2.3 ANTIPROTOZOAL ASSAYS

Eleven of 63 extracts tested have shown strong (IC_{50}<5 µg/mL) or moderate (IC_{50} 5-15 µg/mL) activity against one or two of the protozoa tested. Five of 63 extracts have demonstrated moderate activity against *Trypanosoma brucei brucei*, 15 extracts have shown effects on *Trypanosoma cruzi*, with eight extracts exhibiting strong and three moderate activities, and finally eleven extracts displayed activity against *Plasmodium falciparum*, three of them strong and eight moderate. None of the extracts tested was effective against *Leishmania infantum*.

The extracts showing the best effects which may serve as candidates for further investigation are highlighted in grey.

Tab. 26 *In vitro* activity against selected protozoal organisms (IC_{50} in µg/mL; means ± SD; *n*=3-4)

scientific name	PPU	solvent of extraction	Tbb IC_{50}±SD [µg/mL]	MRC-5SV2 IC_{50}±SD [µg/mL]
Macaranga dioica MUELL. ARG.	L	EtOAc	7.88 ± 0.17	6.96 ± 0.64
Gyrocarpus americanus JACQ.	L	MeOH	6.46 ± 0.55	-
Dysoxylum arborescens (BL.) MIQ.	L	DCM	8.23 ± 0.24	7.77 ± 0.74
		EtOAc	8.30 ± 1.04	-
Euodia latifolia DC.	L	DCM	8.28 ± 0.62	8.29 ± 0.43
Tamoxifen				11.1 ± 0.14
Suramin			0.06 ± 0.002	
	PPU	**solvent of extraction**	**Tc IC_{50}±SD [µg/mL]**	**MRC-5SV2 IC_{50}±SD [µg/mL]**
Tabernaemontana pandacaqui LAM. I	L	DCM	7.30 ± 1.55	6.82 ± 0.25
		EtOAc	7.27 ± 1.21	-
Tabernaemontana pandacaqui LAM. II	L	DCM	1.53 ± 0.21	7.99 ± 0.67
Macaranga dioica MUELL. ARG.	L	EtOAc	2.22 ± 0.38	6.96 ± 0.64
Gyrocarpus americanus JACQ.	L	MeOH	6.69 ± 1.28	-
Intsia bijuga (COLEBR.) O. KTZE.	L	EtOAc	2.45 ± 0.60	9.71 ± 2.29
Dysoxylum arborescens (BL.) MIQ.	L	DCM	6.86 ± 1.35	7.77 ± 0.74
		EtOAc	2.23 ± 0.05	-
Baccaurea stylaris MUELL. ARG.	iB	DCM	3.15 ± 0.33	-
		EtOAc	1.72 ± 0.50	9.20 ± 1.70
Macropiper latifolium (L.F.)	St	EtOAc	6.61 ± 0.40	-
		MeOH	4.87 ± 0.67	-
Euodia latifolia DC.	L	DCM	6.55 ± 0.79	8.29 ± 0.43
		EtOAc	7.64 ± 0.62	8.41 ± 0.80
Zingiber zerumbet (L.) SM.	Rh	DCM	2.52 ± 0.87	8.03 ± 0.15
Benznidazol			1.96 ± 0.14	
	PPU	**solvent of extraction**	**Pf IC_{50}±SD [µg/mL]**	**MRC-5SV2 IC_{50}±SD [µg/mL]**
Dracontomelon vitiense ENGL.	iB	DCM	8.18 ± 1.03	6.82 ± 0.25
Acalypha grandis BENTH.	L	MeOH	11.80 ± 2.04	-
Macaranga dioica MUELL. ARG.	L	EtOAc	11.48 ± 1.20	6.96 ± 0.64
Gyrocarpus americanus JACQ.	L	MeOH	1.59 ± 0.38	-
Dysoxylum arborescens (BL.) MIQ.	L	DCM	8.85 ± 0.25	7.77 ± 0.74
		EtOAc	2.58 ± 0.78	-
Baccaurea stylaris MUELL. ARG.	iB	DCM	8.94 ± 0.76	-
		EtOAc	4.30 ± 0.43	9.20 ± 1.70
Euodia latifolia DC.	L	DCM	8.30 ± 1.43	8.29 ± 0.43
		EtOAc	14.94 ± 2.72	8.41 ± 0.80
Zingiber zerumbet (L.) SM.	Rh	DCM	6.85 ± 0.93	8.03 ± 0.15[23]
Chloroquine			0.04 ± 0.002	

[1]PPU: plant part used; iB: inner bark, L: leaves, St: stem, Rh: rhizome; DCM: dichloromethane, EtOAc: ethyl acetate, MeOH: methanol; Tbb: *Trypanosoma brucei brucei*, Tc: *Trypanosoma cruzi*, Pf: *Plasmodium falciparum*

All five extracts being moderately effective against *Trypanosoma brucei brucei* have only shown very low selectivity as they exhibited moderate or good activities against

Trypanosoma cruzi and *Plasmodium falciparum* as well. The best value was gained by the MeOH-extract of *Gyrocarpus americanus* JACQ. with an IC_{50} of 6.46 ± 0.55 µg/mL and no cytotoxic activity. Three extracts have shown good and specific activities against *Trypanosoma cruzi*, the DCM-extract of *Tabernaemontana pandacaqui* LAM. II (most effective/ 1.53 ± 0.21 µg/mL), the EtOAc-extract of *Intsia bijuga* (COLEBR.) O. KTZE. (2.45 ± 0.6 µg/mL), and the MeOH-extract of *Macropiper latifolium* (L.F.) (4.87 ± 0.67 µg/mL). The high cytotoxicity of the extracts of *T. pandacaqui* and *I. bijuga* suggest that the observed activity is maybe due to their cytotoxicity. Only the last extract showed no cytotoxic activity and is therefore a good candidate for further studies. Three extracts have demonstrated moderate and specific activity against the same parasite, namely the DCM- and the EtOAc-extract of *Tabernaemontana pandacaqui* LAM. I (7.3 ± 1.55 µg/mL or 7.27 ± 1.21 µg/mL, respectively), and the EtOAc-extract of *Macropiper latifolium* (L.F.) (6.61 ± 0.40 µg/mL). Both are good candidates for further investigation, as their activity is not caused by cytotoxicity against the MRC5-SV2 host cells. Five have shown good but aspecific effects against *T. cruzi*, namely the EtOAc-extracts of *Dysoxylum arborescens* (BL.) MIQ. (2.23 ± 0.05 µg/mL), *Macaranga dioica* MUELL. ARG. (leaves) (2.22 ± 0.38 µg/mL), the DCM- and EtOAc-extract of *Baccaurea stylaris* MUELL. ARG. (3.15 ± 0.33 µg/mL and 1.72 ± 0.50 µg/mL, respectively), and the DCM-extract of *Z. zerumbet* (L.) SM. (2.52 ± 0.87 µg/mL), with the EtOAc-extract of *D. arborescens* and the DCM-extract of *B. stylaris* being non cytotoxic.

Three extracts namely the MeOH-extract of *Gyrocarpus americanus* JACQ. and the EtOAc-extracts of *Dysoxylum arborescens* (BL.) MIQ. and *Baccaurea stylaris* MUELL. ARG. were able to significantly kill *Plasmodium falciparum* with IC_{50s} of 1.59 ± 0.38 µg/mL, 2.58 ± 0.78 µg/mL, or 4.30 ± 0.43 µg/mL, respectively, with the extracts of *G. americanus* and *D. arborescens* showing no cytotoxic effects. The extract of *G. americanus*, which only showed moderate effects on the two *Trypanosoma* species, could be a promising candidate for further investigation. The MeOH-extract of *Dracontomelon vitiense* ENGL. (8.18 ± 1.03 µg/mL) and DCM-extract of *Acalypha grandis* BENTH. (11.80 ± 2.04 µg/mL) were only moderately active, but at least displayed specific activity against only one protozoal test organism and the extract of *A. grandis*, which in addition did not display any cytotoxic activity, could be a possible candidate for further investigation.

2.4 INFLICTIONS OF THE CENTRAL NERVOUS SYSTEM – PRELIMINARY RESULTS

TESTING FOR NEW ACHE- AND BCHE-INHIBITORS

In this pre-test five extracts have shown more than 70% inhibition of the activity of acetylcholinesterase and six extracts have shown similar effects on the activity of butyrylcholinesterase and could therefore be candidates for further investigation in order to

discover new lead molecules for the development of new drugs. As this assay has been performed only once yet, the results first have to be confirmed before a final statement can be made, but they were included in the thesis to roughly outline some further possibilities of the plants tested.

Tab. 27 Activity of the extracts as AChE- and BChE-inhibitors (*n*=1) (preliminary results)

scientific name	PPU	solvent	inhibition of AChE [%]	inhibition of BChE [%]
ANACARDIACEAE				
Dracontomelon vitiense ENGL.	iB	MeOH	60.0	91.8
ASTERACEAE				
Bidens pilosa L.	wP	MeOH	36.5	99.7
EUPHORBIACEAE				
Macaranga dioica MUELL. ARG.	iB	MeOH	69.1	92.5
	L	MeOH	62.8	-45.4
MELIACEAE				
Dysoxylum arborescens (BL.) MIQ.	L	MeOH	68.1	37.8
MYRTACEAE				
Syzygium malaccense (L.) MERR. & L.M. PERRY	L	MeOH	57.9	87.7
PIPERACEAE				
Macropiper latifolium (L.F.)	St	MeOH	64.2	-39.5
RUTACEAE				
Euodia latifolia DC.	L	MeOH	14.9	69.5
URTICACEAE				
Pipturus argenteus WEDD.	iB	MeOH	82.9	80.5

PPU: plant part used/ iB: inner bark, L: leaves, St: stem, wP: whole plant; MeOH: methanol; AChE: acetylcholinesterase, BChE: butyrylcholinesterase

Although the preliminary data look promising, the results shown here should be viewed as work in progress data only, since there is no sufficient statistical basis to them yet. However, some alkaloids have been isolated as natural AChE- and BChE inhibitors. Their incidence and their contribution to the effects observed for some of the extracts tested could be assumed, as alkaloids were actually isolated from one species (*Bidens pilosa*[456]), or are most likely to be present in the plants tested due to their occurrence in other members of the same genus: e.g. *Dracontomelon mangiferum*[457], *Dysoxylum lenticellare*[440], *Syzygium jambos*[458], *Piper methysticum*[459], and *Euodia rutaecarpa*[301, 304], which already provided the potent AChE inhibitor dehydroevodiamine. Although no alkaloids have been isolated from members of the genera *Macaranga* and *Pipturus* yet, when performing a TLC and spraying the plates with *Dragendorff's* reagent, alkaloids could be detected in the methanolic extracts of both plants (not shown).

PRELIMINARY RESULTS OF THE NMDA-ASSAY

Five extracts have shown effects as possible NMDA-receptor antagonists in a pre-screening. As the SD values are still much too high in some cases, the results were only included to

carefully point out some additional options of these plants, but these values have to be verified before a final statement on their usefulness in the given context can be made.

Tab. 28 Activity of the extracts as NMDA-receptor antagonists (*n*=2) (prelimiinary results)

scientific name	PPU	solvent	excitotoxicity at 50 µg/mL [%]	excitotoxicity at 10 µg/mL [%]
ANACARDIACEAE				
Dracontomelon vitiense ENGL.	iB	MeOH	32.2 ± 13.1*	70.1 ± 17.9*
LEGUMINOSAE CAESALPINIOIDEAE				
Intsia bijuga (COLEBR.) O. KTZE.	L	MeOH	28.7 ± 4.9	77.8 ± 23.4*
MYRTACEAE				
Syzygium malaccense (L.) MERR. & L.M. PERRY	L	MeOH	49.6 ± 18.0*	103.7 ± 7.4
PHYLLANTHACEAE				
Baccaurea stylaris MUELL. ARG.	iB	DCM	43.2 ± 17.1*	99.0 ± 8.1
URTICACEAE				
Pipturus argenteus WEDD.	iB	MeOH	27.8 ± 6.7*	83.9 ± 10.3

*SD value >20% (has to be repeated); PPU: plant part used/ iB: inner bark, L: leaves/ DCM dichloromethane, MeOH: methanol

Only a few natural or naturally derived products with properties as NMDA receptor antagonists are known to date, therefore the identification of the bioactive compounds in the extracts tested would maybe open up new vistas in the development of new drugs for inflictions of the CNS such as *Morbus Alzheimer* or *Morbus Parkinson*.

3. ISOLATION PROCEDURE

When the chemical composition of a plant is unknown, the isolation procedure can be based on how the plant is used in folk medicine, or several extraction procedures with solvents of increasing polarity can be performed. [453] In Vanuatu plants are generally used freshly and this state was not convenient for the collected material due to transport issues and so the latter was chosen.

Usually a good way to isolate a biologically active compound from an extract is the so called bioactivity-guided fractionation, in which every fraction obtained during the extraction process is submitted to a chosen bioassay in order to follow the activity. This method was not applied to the present survey, because *Baccaurea stylaris* MUELL. ARG., the plant chosen for phytochemical purification was not investigated due to a promising activity in a bioassay, but due to the fact, that the genus is only poorly studied and though we were interested in novel compounds. As some interesting compounds have already been isolated from other members of the tribe Antidesmateae, e.g. alkaloids, a lupeolactone, and triterpenoids[87] this plant was considered as a perfect match in this context.

4. STRUCTURE ELUCIDATION

Compound D5G2 was the dominating secondary metabolite in the DCM-extract of *B. stylaris* and was obtained as yellow, glassy oil with aromatic smell, UV: λ_{max} 240 nm. Its ^{13}C-NMR spectrum exhibited 20 carbon signals, which were sorted by an ^{1}H,^{13}C-HSQC experiment into three CH_3, six CH_2, six CH and five quaternary carbons. The low resolution EI-MS showed a molecular ion at *m/z* 316 indicating together with the ^{13}C data a molecular formula of $C_{20}H_{28}O_3$.

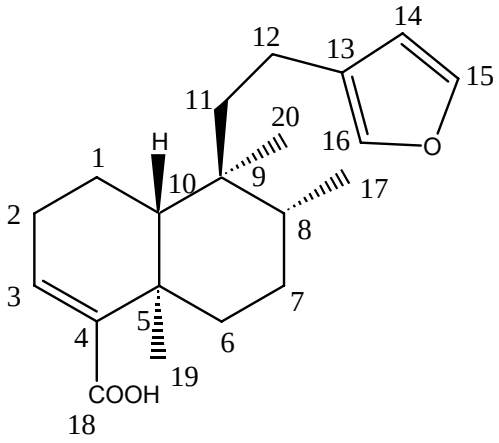

Fig. 40 D5G2, hardwickiic acid

The ^{13}C NMR and ^{1}H spectra exhibited the presence of a 3-substituted furan moiety with characteristic carbon signals at δ_C 111.0 (C-14, *d*), 125.6 (C-13, *s*), 138.4 (C-16, *d*) and 142.7 (C-15, *d*) and the respective proton signals at δ_H (H-14), (H-16) and H-(H-15), see Tab. 29 and Tab. 30. Other NMR signals were in agreement with the presence of a diterpene with neoclerodane skeleton bearing a carboxyl group (C-18, 172.8) at position C-4. Comparison of the spectroscopic data with literature values revealed that compound D5G2 is identical with hardwickiic acid first isolated from *Hardwickia pinnata* (Leguminosae - Caesalpinioideae)[460], This was confirmed by extensive use of 2D NMR especially ^{1}H,^{1}H-COSY, ^{1}H,^{13}C-HSQC, ^{1}H,^{13}C-HMBC, and ^{1}H,^{1}H-ROESY. Up to now (-)-hardwickiic acid was also isolated from or detected in several other plants like *Salvia divinorum* (Lamiaceae)[461], *Solidago rugosa* (Asteraceae),[462] and *Echinodorus grandiflorus* (Alismataceae).[463] Besides the more common (-)-hardwickiic acid, also the (+)-hardwickiic acid has been isolated from natural sources like copaiba oil (*Copaifera officinalis*, Leguminosae – Caesalpinioideae),[464] the optical rotation has to be determined before exact identification can be performed. Interestingly some biological investigation on (-)-hardwickiic acid has been done and revealed potent antibacterial activity against *Bacillus subtilis* and *Mycobacterium smegmatis*[465], which which was not observed against *Staph. aureus* and *E. coli* used in this study (2.2 Antibacterial and Antifungal Assays).

Tab. 29 ^{1}H-NMR spectral data of compound D5G2 and D6.1G2 (δ ppm, m, J in Hz)

proton	D5G2	D6.1G2
H-1	2.43, m, 1H; 1.13, m, 1H	2.35, m, 1H; 1.85, m, 1H
H-2	2.35, m, 1H; 2.20, m, 1H	1.96, m, 1H; 1.60, m, 1H
H-3	6.85, t, *J* = 3.8, 1H	4.54, m, 1H
H-6	1.68, m, 1H; 1.57, m, 1H	2.05, m, 1H; 1.47, m, 1H
H-7	1.47, m, 2H	1.71, m, 1H; 1.38, m, 1H
H-8	1.58, m, 1H	1.71, m, 1H
H-10	1,40, m, 1H	2.40, m, 1H
H-11	1.71, m, 1H; 1.50, m, 1H	5.35, m, 1H
H-12	2.30, m, 1H; 2.22, m, 1H	2.25, m, 1H; 2.15, m, 1H
H-14	6.25, d, *J* = 0.9, 1H	6.30 d, *J* = 0.9, 1H
H-15	7.34, t, *J* = 1.6, 1H	7.38, t, *J* = 1.6, 1H
H-16	7.20, br s, 1H	7.38, br s, 1H
H-17	0.83, d, *J* = 6.5, 3H	0.80, d, *J* = 6.5, 3H
H-19	1.26, s, 3H	5.13, s, 1H
H-20	0.76, s, 3H	5.27, s, 1H

The more polar compound D6.1G2, a white amorphic powder; m.p. ± SD: 152.4 ± 0.071°C; UV: λ_{max} 235 nm, was also identified as a neoclerodane derivative with furan moiety by ^{1}H-and ^{13}C-NMR analysis. The low resolution EI-MS showed a molecular ion peak at *m/z* 374 indicating together with the ^{13}C-NMR spectrum a molecular formula of $C_{21}O_6H_{26}$. Interestingly in both spectra the proton and carbon signals of the methyl groups C-19 (δ_C 20.6, δ_H 1.26, s, 3H) and C-20 (δ_C 20.6, δ_H 0.76, s, 3H) were lacking and substituted by two methine signals resonating at δ_C 100.7 (δ_H 5.27, s, 1H) δ_C 104.3 (δ_H 5.13, s, 1H). Further remarkable differences were the lacking of a double bond between C-3 and C-4, the presence of a methyl ester (OCH_3 resonating at δ_H 3.70, s, 3H and δ_C 51.6) and a downfield shift of C-5 (δ_C 44.0 instead of δ_C 37.8) and C-9 (δ_C 50.3 instead of δ_C 38.6), as well as the presence of an hydroxyl substitution in the side chain which shifted the signal of H-11/C-11 from δ_H to and from δ_C 17.5 to 74.9. Extensive 2D NMR analysis (^{1}H,^{1}H-COSY, ^{1}H,^{13}C-HSQC, ^{1}H,^{13}C-HMBC and ^{1}H,^{1}H-ROESY) revealed the presence of the structure given in Fig. 41. This is to the best of our knowledge a new natural compound, which we named baccauric acid methyl ester.

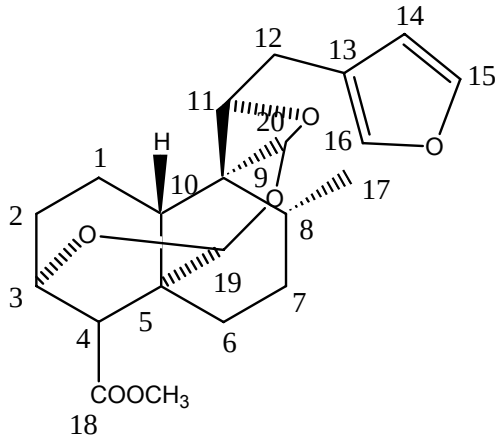

Fig. 41 D6.1G2, baccauric acid methyl ester

Tab. 30 ^{13}C-NMR spectral data of compound D5G2 and D6.1G2 (δ ppm, m)

carbon	D5G2	D6.1G2
C-1	35.8, *t*	20.2, *t*
C-2	18.3, *t*	26.5, *t*
C-3	140.2, *d*	75.7, *d*
C-4	141.5, *s*	54.0, *d*
C-5	37.8, *s*	44.3, *s*
C-6	38.8, *t*	31.5, *t*
C-7	27.3, *t*	30.4, *t*
C-8	36.3, *d*	37.4, *d*
C-9	38.6, *s*	50.3, *s*
C-10	46.7, *d*	38.8, *d*
C-11	17.5, *t*	74.9, *d*
C-12	27.5, *t*	38.5, *t*
C-13	125.6, *s*	127.1, *s*
C-14	111.0, *d*	108.6, *d*
C-15	142.7, *d*	143.4, *d*
C-16	138.4, *d*	139.3, *d*
C-17	16.0, *q*	16.9, *q*
C-18	172.8, *s*	170.7, *s*
C-19	20.6, *q*	104.3, *d*
C-20	18.2, *q*	100.7, *d*
OCH_3	-	51.6, *q*

For all other isolated compounds mentioned in the extraction scheme (Fig. 14) structure elucidation is in progress.

DISCUSSION, CONCLUSION AND PERSPECTIVES

This thesis combines an ethnobotanical survey on a South Pacific island with molecular structure elucidation and modern pharmacological screening methods. During five months of fieldwork plants traditionally used in Vanuatu's ethnopharmacopoeia were documented. 27 healers were interviewed about plants, treatment methods, healing concepts, and diseases. The correct identification of the species in the field, essential for their selection for the screening regimen, was performed using a self-made field guide, because identification literature is barely available for this region. This situation was complicated by discrepancies between our Linnean and the folk taxonomy system, as the healers classified the plants exclusively by their leaves and were not able to give information on flowers, which some plants were lacking. The disease aetiology of Vanuatu's ethnomedicine is also quite different from the Western one; so sometimes careful questioning was necessary to find suitable Western counterparts for some folk diseases. Nevertheless, 420 individual use reports on 130 taxa were documented and subjected to a qualitative and quantitative analysis. The reports were divided into 17 categories of use and grouped according to their medicinal affiliation or sociocultural relevance, showing that dermatological and gastrointestinal complaints, followed by respiratory ailments and diseases related to the urogenital system were illnesses most commonly indicated, reflecting a prevalence of these illnesses in the study areas. 18 plants with indications towards immunomodulatory effects were selected on site and material of 21 plant parts was collected

One of the plants collected, *Baccaurea stylaris* MUELL. ARG. (Phyllanthaceae) was also selected for a phytochemical investigation yielding seven pure compounds. Two of these compounds could be identified to date as diterpenoids with a neoclerodane skeleton. Among them, the already known hardwickiic acid first isolated from *Hardwickia pinnata* (Leguminosae - Caesalpinioideae) and a new compound, also a neoclerodane derivative with a furan moiety which we named baccauric acid methyl ester. The structural relative Salvinorin A from *Salvia divinorum* which is said to be the first naturally occurring non-nitrogenous opioid-receptor subtype-selective agonist.[466] is the most potent naturally occurring hallucinogen known to date.[467] It would now be highly interesting to investigate, if the pure compounds isolated from *B. stylaris* would be able to show similar effects on κ-opioid receptors.

The screening regimen performed in this study comprised - besides a preliminary screening for drugs which may be effective against *Alzheimer's* disease - antibacterial, antifungal, and antiprotozoal assays, and a cytotoxicity screening on a variety of human cancer cell lines.

Although the preliminary data for the cholinesterase assays look promising, the results should be viewed as work in progress data only, since there is no sufficient statistical basis to

them yet. However, alkaloids already isolated as natural AChE- and BChE inhibitors may contribution to the effects observed for some of the extracts tested, as alkaloids either actually were isolated from one species (*Bidens pilosa*[456]), or are most likely to be present in the plants tested due to their occurrence in other members of the same genus or close relatives: e.g. *Dracontomelon mangiferum*[457] in case of *D. vitiense*, *Dysoxylum lenticellare*[440] for *D. arborescens*, *Syzygium jambos*[458] in case of *S. malaccense*, *Piper methysticum*[459] for *Macropiper latifolium*, and *Euodia rutaecarpa*[301, 304] (in case of *E. latifolia*), which already provided the potent AChE inhibitor dehydroevodiamine. Although no alkaloids have been isolated from members of the genera *Macaranga* and *Pipturus* yet, when performing a TLC and spraying the plates with *Dragendorff's* reagent, alkaloids could be detected in the methanolic extracts of both *Macaranga dioica* and *Pipturus argenteus*.

None of the extracts has shown significant antibacterial activities, neither against the Gram-positive *Staph. aureus* nor the Gram-negative *E. coli*, only *Dracontomelon vitiense* has displayed moderate activity against *Staph. aureus* in a pre-screening, which did not qualify it for a second screen. Unfortunately it was not possible to include other bacteria into the screening regimen, which would have been more promising, like *Streptococcus pyogenes*, a very common cause of skin infections, *Haemophilus influenzae*, *Streptococcus pneumoniae*, or *Pneumococcus sp.,* possible agents for respiratory complaints, or *Shigella sp*., *Campylobacter sp.*, *Salmonella sp*., *Vibrio cholerae,* or *Yersinia sp*. which may be causes of severe forms of diarrhoea. Antibacterial[264] and antifungal[263] activities, as demonstrated for *Dracontomelon dao* could not be observed in the same intensity for *D. vitiense*, but as already mentioned the bacteria most likely causing that form of diarrhoea against which *D. vitiense* is used in Vanuatu's ethnopharmacopoeia could not be included into the screening regimen, so the efficacy of the folk use could neither be proven nor disproven. Antimicrobial and antifungal effects as demonstrated for *P. albidus*[224, 225] could not be shown for *Pipturus argenteus*, but the sticky sap which is applied to wounds may contribute to the healing by formation of an occlusive layer like a band-aid.[224, 225]

Furthermore none of the extracts was able to significantly inhibit the growth of *Aspergillus fumigatus* and *Microsporum canis*, only the inner bark of *Macaranga dioica* has shown moderate activity against *Candida albicans*, and both, inner bark and leaves of *Baccaurea stylaris* against *Trichophyton rubrum*, but did not qualify for a second screen. Fungal infections seem to be rather uncommon in Vanuatu and were never mentioned by a healer. Only one case of ringworm, which is predominantly caused by *Trichophyton rubrum,* was observed in Ambrym, but this disease was not believed to be treatable with traditional medicine, but only by Western medicine.

All five extracts being moderately effective against *Trypanosoma brucei brucei* have only shown very low selectivity as they exhibited moderate or good activities against

Trypanosoma cruzi and *Plasmodium falciparum* as well. *Gyrocarpus americanus* was the most active plant in this context with an IC_{50} of 6.46 ± 0.55 µg/mL, perhaps due to alkaloids already isolated from this species and other members of the Hernandiaceae[203-205]. The use in Vanuatu's ethnopharmacopoeia to tame pigs may also be a result of a high content of alkaloids in this species.

Extracts of *Tabernaemontana pandacaqui* II, *Intsia bijuga*, and *Macropiper latifolium* displayed good and selective impact against *Trypanosoma cruzi*, but the high cytotoxicity of the first two extracts suggest that the observed activity is perhaps only a result of their strong cytotoxicity against the host cell line MRC5-SV2. Only the methanolic extract of *Macropiper latifolium* with an IC_{50} of 4.87 ± 0.67 µg/mL showed no cytotoxic effects and might warrant further investigations. The EtOAc-extracts of *Tabernaemontana pandacaqui* I (7.27 ± 1.21 µg/mL), and *Macropiper latifolium* (6.61 ± 0.40 µg/mL) demonstrated moderate but specific activity which is not caused by cytotoxic effects, so these extracts should also be investigated further. The two *Tabernaemontana pandacaqui* probes, initially collected as different species in Loh or Ambrym, respectively have displayed differing spectra of efficacy, most likely being due to variabilities in the composition of secondary plant metabolites often developed by species growing in a differing ecologic environment.

Extracts of *Baccaurea stylaris* (as previously shown for other members of the tribe Antidesmatoideae),[90, 91, 468] *Dysoxylum arborescens*, and *Gyrocarpus americanus* were strongly but aspecifically active against *Plasmodium falciparum* with IC_{50s} of 4.30 ± 0.43 µg/mL, 2.58 ± 0.78 µg/mL, or 1.59 ± 0.38 µg/mL, respectively, with the second and third extract displaying no cytotoxicity. Antimalarial activity has previously been observed for another member of the genus *Dysoxylum*, *D. fraseranum* and said to be due to the presence of limonoids often found in this family.[469] The extract of *G. americanus* whose antimalarial activity may be due to alkaloids already isolated from this species and other members of the Hernandiaceae,[203-205] which only showed moderate effects on the two *Trypanosoma* species, but very good antiplasmodial activity, should be investigated further to isolate the active compounds and test their impact in against *P. falciparum.* Extracts of *Dracontomelon vitiense* (8.18 ± 1.03 µg/mL) and *Acalypha grandis* (11.80 ± 2.04 µg/mL) were only moderately active, but at least displayed specific activity with the extract of *A. grandis* showing no cytotoxic potential. Antimalarial effects were previously described for other members of the Anacardiaceae, where *D. vitiense* belongs to,[264] perhaps due to triterpenoids and flavonoids often found in Anacardiaceae[469, 470] and also for another member of the genus *Acalypha*, *A. guatemalensis,*[294] so this could be an interesting candidate for further investigation with the aim to isolate the active principle, too.

At last, the extracts were subjected to a molecular targeted screening on various human cancer cell lines, a smaller version of the NCI60 screen.

15 extracts displayed significant cytotoxic activities specific for only one cell line. Extracts of *Tabernaemontana pandacaqui* II and *Gyrocarpus americanus* displayed cytotoxic effects selective for the renal cell line 786-0. Here again it was also seen, that the two *T. pandacaqui* probes exhibited different activities against the eight tumour cell lines tested. A brief literature research comparing the relevant oncogenic mutations of these cell lines revealed, that only here the *von Hippel-Lindau* (VHL) tumour suppressor gene which is involved in angiogenesis is silenced[471]. A shortage of oxygen causes the increase of the active form of HIF-1 (hypoxia-inducible factor 1) which in turn stimulates the transcription of *VEGF* (vascular endothelial growth factor) and other genes that play a key part in angiogenesis. *VHL* among others is involved in the degradation of HIF-1. A loss-of-function of this gene leads to high levels of HIF 1, which in turn trigger the continual overproduction of VEGF, resulting in the development of in particularly hemangioblastomas, tumours containing dense masses of blood vessels[472]. Although the molecular mechanisms by which *VHL* loss leads to tumorigenesis are not yet fully understood, it may be a possible target of compounds present in the extracts in the future.

T. pandacaqui I was shown to selectively decrease the viability of lung cancer cell line A549 cells. In this cell line a gain-of-function of the *K-Ras* (v-Ki-ras2 Kirsten rat sarcoma viral oncogene homologue) gene, involved in receptor tyrosine-kinase signalling and a loss-of-function mutation of *STK11*, a gene coding for a serine/threonine kinase were observed.[471]

Extracts of *Dysoxylum arborescens*, *Allophylus timoriensis*, and *Grewia inmac* have demonstrated selective cytotoxic effects on colon cancer HT-29 cells, with *G. inmac* with an IC_{50} of 4.57± 0.408 µg/mL showing the best effect. Loss-of-function mutations of both the tumour suppressor gene *SMAD4* MAD, mothrs against DPP homologue 4), playing a role in TGF*β* (transforming growth factor *β*) signaling and *APC* (adenomatous polyposis coli), involved in the Wnt signaling pathway were found to be specific for this cell line[471]. The extract of *Dysoxylum kuskusense*[442, 443] has also previously demonstrated the cytotoxicity against HT-29, with diterpenoids isolated as the active principle. It would be interesting to research, if the same or related compounds could be responsible for the effect observed here. Another member of the genus *Grewia*, *G. bilamellata* has shown cytotoxic effects against KB-cells[398], with triterpenoids and lignans isolated as the active compounds, which could be expected in *G. inmac*, too, therefore a bio-activity guided fractionation of this extract would be highly interesting.

Extracts of *Acalypha grandis*, *Allophylus timoriensis*, and *Pipturus argenteus* were shown to significantly and specifically decrease the viability of breast cancer MCF7 cells, *P. argenteus* showing the best effects with an IC_{50} of 1.63 ± 0.221 µg/mL. *Acalypha. wilkesiana*, is used in the Nigerian ethnopharmacopoeia for the empirical treatment of breast cancer[236] and so a further investigation of *A. grandis*, perhaps in comparison with *A. wilkesiana* could be

interesting. Cytotoxicity against murine P388 lymphoma cells has been demonstrated for *A. siamensis*, with a tetraterpene isolated as the active principle, therefore tetraterpenoids could be suspected in *A. grandis*, too.[295] By comparison of the eight cell lines tested no mutation specific for this cell line was found. The same was observed for the prostate cancer cell line PC-3, where the extracts of *Baccaurea stylaris* leaves and bark displayed good cytotoxic effects, with the extract of the inner bark being more effective with an IC_{50} of 5.043 ± 0.337 µg/mL.

Only the methanolic extract of *Tabernaemontana pandacaqui* showed cytotoxic effects against the melanoma cell line SK-Mel-28 with an IC_{50} of 14.52 ± 0.296 µg/mL. Interestingly the latex of this plant is indeed used to cure “skin cancer” in Vanuatu’s ethnopharmacopoeia, which in this case might argue for cancer in terms of cancer known in the Western medicine. Even more interesting, only in this cell line the *EGFR* (epidermal growth factor receptor) tyrosine kinase domain is affected by two in-frame deletions[471], leading to an constant over-activation and thus rendering the receptor independent from normal EGF signalling necessary for growth control. Similar mutations have been found in different non-small cell lung cancer cell lines and some gliomas.[473, 474]. One could now assume, that SK-Mel-28 cells are dependent on this oncogenic signalling of the EGFR and that compounds in the plant extract were somehow able to inhibit this signalling process. A quick approach to test this hypothesis would be to make use of the commercially available EGFR inhibitor erlotinob (Roche) to verify the prediction of a strong sensitivity to such drugs. Also the molecular tools to further decipher the mode of action within the EGF signalling pathway (such as antibody against phosphorylated EGFR and downstream MAPKinases) are already at hand.

These results nicely demonstrate the power of screening of well characterized cancer cell lines, as they provide the unique opportunity for the fast connection of effects from novel chemical compounds to the wealth of readily available molecular knowledge.

We could show in this study that the approach of finding active leads on an ethnobotanical basis was successful, as many plants open up new opportunities for further investigations. Of particular interest would be the isolation of structures responsible for the strong antimalarial activity of *Gyrocarpus americanus* and the anti-trypanosomal of *Macropiper latifolium* and the investigation of molecular mechanisms forming the basis of the effects of *D. arborescens* and *G. inmac* on HT-29-, *A. grandis* on MCF7-, and *T. pandacaqui* II on SK-Mel-28-cells. Furthermore the pure compounds isolated from *B. stylaris* should be tested for their ability as κ-opioid receptor agonists.

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KEY TO PLANT LIST AND PLANT LIST

Abbreviations of the plant parts used, the preparations and application modes as follows:

Abbreviations of the plant parts used

dd/rw	dewdrops/ rainwater	Rh	rhizome
Fl	flower	Rt	root
Fr	frond	sap	sap (watery)
Frt	fruit	Sd	seed
iB	inner bark	Sh	shoot
L	leaf	St	stalk/ stem
Lat	latex	W	wood
LG	leaf gall	wP	whole plant
oB	outer bark	yL	young leaves

Abbreviations of preparations

BL	boil	MwS	mix with saltwater
BN	burn	MwW	mix with water
CH	chew	RbH	rub in hands
CHL	chill	SKC	special Kastom ceremony
CK	cook	SQ	squeeze
CLL	collect liquid	SQiCW	squeeze in coconut water
F	fresh	SQiS	squeeze in saltwater
G	ground	SQiW	squeeze in water
MwCM	mix with coconut milk	T	toast
Mw CW	mix with coconut water	WiL	wrap into leaf

Abbreviations of application modes

AF	add food	CHwCM	chew with coconut milk
AO	add oil	HD	hair dye
AS	apply steam	HW	head wash
B	bath	KHG	Kastom, house & garden
C	cataplasm	L	local
CH	chew	MW	mouth wash
CHS	chew and spit (healer)	P	plant
D	drink	R	rub (massage)
E	eat	SKC	special Kastom ceremony
EW	eye wash	Sm	smell

Abbreviations of origins

AA	Aneityum Anelghowhat	SWA	Southwest Ambrym
APP	Aneityum Port Patrick	TLL	Torres Islands (Loh, Lungharigi)
BML	Banks Islands (Moto Lava)	TLT	Torres Islands (Loh, Telaklak)
NA	North Ambrym		

Abbreviations of languages

B	Bislama
E	English
F	French
IK	Indass Khermo (language of Aneityum)
LBML	language Banks Moto Lava
LNA	language North Ambrym
N	Newaweteme (language in Lungharigi and Telaklak, Loh, Torres Islands)
R	Rallglëin (language Southwest Ambrym)

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
ACANTHACEAE								
Graptophyllum pictum (L.) GRIFF. [3076-10]	*G. pictum* var. *pictum, G. hortense, Justicia pictum*	limälar, limilar (R)	caricature plant (E)	SWA	L	SQiW	D	hypotension
					wP	-	P	protection against black magic
					sap	MwW	D	anaemia
Strobilanthes reptans ENGL red variety [0386-2.2].	*Hemigraphis reptans*	rämämap (LNA)	blakgras (B)	NA	L	SQiW	D	anaemia
				TLL	L	SQiW	D	tonic for children
AGAVACEAE								
Cordyline fruticosa (L.) A. CHEV. [1786-10]	*C. terminalis, Taetsia fruticosa, Convallaria fruticosa*	nitschatimi (IK), neggurrie (N)	cordyline, ti, ki, lily-palm, dracaena palm, good luck plant, tree-of-kings (E), nara (B)	AA	L	F	CH	leprosy in the mouth
				TLL	L	SQiW	HD	Kastom plant (dye for hair when gaining rank)
				TLL/SWA/AA	wP	-	P	several Kastom purposes
AMARANTHACEAE								
Achyranthes aspera L. [2286-1.2.1]	*A. indica*	nabudschata (IK)	chaff-flower weed, achyranthes weed (E), nokorin (B)	AA	L	RbH, SQ	D	asthma
				APP	L	SQ	L	boils
Achyranthes aspera L. (red variety) [2286-1.2.2]	*A. indica*	nabudschata (IK)	chaff-flower weed, achyranthes weed (E), nokorin (B)	AA	L	SQiW	D	increases fertility in woman
AMARYLLIDACEAE								
Crinum asiaticum L. [2176-17]	*C. pedunculatum*	wael litainbop (R), naha (IK)	grand crinum, white crinum, white crinum-lily, Asiatic lily, poison-bulb lily, beach lily (E), lili (B)	SWA/NA	L	SQiW	D	indigestion
				SWA	Lat	MwW	D	to cause emesis
					Lat	F	L	ear ailments
				AA	Rt	BL	MW	toothache
Crinum xanthophyllum HANNIBAL, 1972 [2966-7]	*C. pedunculatum* var. *xanthophyllum, C. asiaticum* (misapplied)	nemuelake (N), naha (IK), litainbop (R)	golden-leaf crinum-lily, golden-leaf crinum (E), lili (B)	TLL	St	G, SQiW	HW	headache
					L	T, SQ	L	ear ailments
				AA	L	T, SQ	D	asthma
					sap	MwW	D	ciguatera
				SWA	St	F	C	fractures
					Lat	F	L	warts

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
Hippeastrum puniceum (LAM.) URBAN [2966-1]	-	nemwelaque (N)	no popular name	TLL	L	T, SQ	L	ear ailments
ANACARDIACEAE								
Dracontomelon vitiense ENGL. [0186-12]	-	rämil (LNA)	dragon plum (E), prunier dragon (F), nakatambol (B)	NA	iB	WiL, T, SQiW	D	severe illness with bloody faeces
					Frt	F	E	edible
ANNONACEAE								
Annona muricata L. [1176-2]	-	no local name	soursop, guanabana, (prickly) custard apple, bullock's heart (E), cachiman, corossol (F), saosop, korosol, karasol (B)	TLL	L	BL, CHL	B	scabies
				SWA	L	BL, CHL	B	scabies
				TLL	Frt	F	E	edible
Cananga odorata (LAM.) HOOK.F. & THOMSON [1176-4]	*Canangium odoratum*	neviaou (N)	ylang ylang, perfume tree (E), ylang ylang (F), nandingori, nidingro (B)	TLL	Fl	F	AO	scents coconut oil
					iB	SQiW	D	postpartum abdominal pain (to expulse placenta)
APOCYNACEAE								
Alstonia vitiensis SEEM. [1786-3]	-	nätiädäl (IK)	no popular name	AA	L	SQiW	D	contraceptive
Kopsia flavida BL. [0176-4]	-	tewawetäl (N)	no popular name	TLL	yL	F	CH	cough
Tabernaemontana pandacaqui LAM. [2966-2] and [2576-10]	*T. obtusciuscula, T. excavatia, T. orientalis, Ervatamia obtusciuscula, Ervatamia orientalis, Ervatamia pandacaqui*	newawedäl (N), "wael litschi" ("R"), inmathethi (IK)	no popular name	TLL (I)	Lat	F	L	centipede bites
				SWA (II)	Lat	F	D	tuberculosis
				AA	L	F	L	wounds
					L	SQiW	D	"skin cancer" (severe wounds?)
					St	F	CH	influences sex of embryo during pregnancy in favour of girl
ARACEAE								
Epipremnum pinnatum (L.) ENGL. [2866-7]	*E. aureum, E. mirabilis, Dracontium pertusum, Pothos pinnatum, Pothos aureum, Rhaphidophora pertusa, Rhaphidophora vitiensis, Scindapsus aureus*	nekamuro/nekaumro (N)	philodendron, devil's ivy, taro vine, pothos, golden pothos (E), rop blong pik (B)	TLL/ TLT	St	SQ	L	stops bleeding
				SWA	L	SQiW	D	amenorrhoea
				TLL	Sh	F	CH	abortive
ARALIACEAE								
Polyscias cumingiana (C.PRESL) FERN.-VILL. [2176-13.1]	*P. filicifolia* (MOORE EX FOURNIER) BAILEY	räpi (R)	(fern leaf) panax, angelica, chotto, fern leaf aralia (E), nalaslas, nanalas (B)	SWA	L	F	E	edible
					wP	-	P	hedge plant
					L	CK	E	influences sex of embryo during pregnancy in favour of girl

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
Polyscias samoensis (A.GRAY) HARMS [1886-5.1]	-	näthoiatmas (IK)	no popular name	AA	L	G, MwCW	D	ciguatera
Polyscias scutellaria (BURM.F.) FOSB. [2176-13.2]	*P. pinnata* J.R. & G.FORST., *P. balfouriana* (HORT. EX ANDRE) BAILEY, *P. tricochleata* (MIQ.) FOSB., *Nothopanax tricochleatum* MIQ.	räpi (R)	large-leaf panax (E), nalaslas (B)	SWA	L	CK	E	edible
					wP	-	P	hedge plant
					L	BN	AF	poisoned food
					L	F	KHG	to stimulate fruiting of a banana plant
					L	CK	E	influences sex of embryo during pregnancy in favour of girl
ARECACEAE								
Cocos nucifera L. [0386-2.1]	-	lihol, natora (LNA)	coconut palm, coco palm, coco tree, coconut tree, cocoa nut (old English), cocoanut (old English), porcupine wood (E), cocotier (nucifère/ porte-noix), noix de coco (F), natora, kokonas, kavra, kavura, navara, samsam (B)	NA	oB	BN	L	wounds
				TLL/TLT/SWA/NA/AA/APP		F	KHG	carving
					Sd	F	E, D	edible
					Frt	F	E, D	edible
				SWA	iB	SQiW	D	back pain
ASCLEPIADACEAE								
Hoya vanuatensis [2576-9]	-	rämümürtschul (R)	no popular name	SWA	L	SQiW	D	facilitates childbirth

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
ASTERACEAE								
Ageratum conyzoides L. [1786-15]	-	noragidi (IK)	ageratum, goat weed (E)	AA	L	SQ	L	wounds
Bidens pilosa L. [1686-1.2]	-	nilbuthou (IK)	beggar's-tick, Spanish needles, cobbler's pegs (E)	AA	Sh	SQiW	D	cough
Mikania micrantha KUNTH. [3076-3]	-	no local name	mile a minute, mikania weed (E), maelminit, (grew) wandei, amerika, merikanrop, tudei, rop blong amerika (B)	SWA	L	SQ	L	conjunctivitis
					sap	SQ	L	boils
					L	SQiW	D	fever
					L	SQiW	D	dengue fever
					L	SQiW	D	diarrhoea
				TLL	L	G, SQiW	L	scabies
					L	G, SQiW	L	insect bites
				BML	L	F	L	wounds
					L	RbH	L	wounds
					L	WiL, T	L	wounds
				AA	L	BL	AS	cold
					L	SQiW	D	cough
				TLL/NA	wP	SQ	L	stops bleeding
Synedrella nodiflora (L.) GAERTN. [1686-1.1]	*S. vialis, Calyptocarpus nodiflora, Verbesina nodiflora*	intäbasiät itounga (IK)	nodeweed, synedrella, cinderella weed (E)	AA	L	RbH	L	toothache
Vernonia cinera (L.) LESS. [1886-1.1]	*V. cinerea* var. *parviflora, V. parviflora, Conyza cinerea*	-	little ironweed (E)	AA	L	SQ	L	boils
					L	SQ	L	wounds

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
ATHYRIACEAE								
Diplazium latifolium MOORE [0386-1.9]	-	libarr (R)	no popular name	SWA	Fr	F	C	wounds
BURSERACEAE								
Canarium vulgare LEENH. [1886-5.3]	*C. indicum, C. commune*	nangae, nang(a)i, nat tri (IK)	pili/ kanari nut, Java/ native almond (E), nangae, nang(a)i, nat tri (B)	AA	L	G, MwCM, MwS	D	diarrhoea
					L	G, MwCM	D	ciguatera
				TLL/TLT/SWA/NA/AA/APP	Sd	F	E	edible
				APP	L	CH, MwCW	D	ciguatera
Garuga floribunda DECNE. [2966-6]	*G. abilo* MERR., *G. littoralis* MERR., *G. pacifica* BURKILL	neradou (N)	namalaos/ namalaus (B)	TLL	L	CK	AF	ciguatera
CARICACEAE								
Carica papaya L. [3076-8]	*C. vulgaris*	hialwi (N), nässä (IK)	pawpaw, papaya (E), papaye(r) (F), popo, papae (B)	SWA	Fl	BL	D	hepatitis
				BML	Rt	F	CHwCM	"HIV" 1st stage
					Frt	F	E	edible
				AA	Fl	F	CH	ciguatera
COMBRETACEAE								
Terminalia catappa L. [2966-3]	-	netelihe (N)	sea/ tropical/ Indian/ country/ coastal/ Malabar almond, olive bark tree (E), badamier, myrobolan (F), natapoa, natavoa, natalie (B)	TLL	L	BL	MW	toothache
				AA/ APP/ NA/ SWA/ TLL/ TLT	Sd	F	E	edible
CONVOLVULACEAE								
Ipomoea indica (Burm.f.) MERR. [3066-3]	*I. indica* var. *indica, I. acuminata, I. congesta, I. insularis, I. learii, Pharbitis insularis, Convolvulus indica*	nagawul (N), hauwä (R), inmouwat (IK)	common morning-glory, blue morning-glory, blue dawn-flower (E)	TLL	wP	SQ	D	cough
				SWA	Lat	MwW	D	laxative
					Lat	MwW	D	poisoned food
					Fl	SQiW	D	facilitates childbirth
				AA	Lat	F	L	stops bleeding
Ipomoea littoralis (L.) BL. [0876-1.2]	*I. denticulata, I. forsteri, Convolvulus littoralis*	nerauwul (N)	coastal morning-glory (E)	TLL	L	SQiW	D	cough
					L	SQiW	D	bronchitis
Ipomoea pes-caprae (L.) R. BR. [2866-4]	*I. biloba, I. (pes-caprae) brasiliensis*	nerre (N), nahou (IK)	beach morning glory (E), kabis blong solwota (B)	TLL	L	T	C	boils
				AA	St	F	SKC	severe abdominal pain during pregnancy caused by spirits
Merremia peltata (L.) MERR. [3066-1]	*M. nymphaeifolia, Ipomoea peltata, Operculina peltata, Convolvulus peltata*	negedenuo (N)	peltate morning glory (E)	TLL	St	G	KHG	fish poison

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
Operculina turphetum (L.) SILVA MANSO [0876-2.10]	*O. turpethum* var. *Ventricosa, O. ventricosa*	netekulkwäl (N)	ventricose morning-glory (E)	TLT	Sh	F	CH	abdominal pain
Stictocardia campanulata (HALLIER F.) MERR. [2176-11]	*Ipomoea campanulata*	haubahub (R), räbau (LNA)	no popular name	SWA	L	SQiW	D	pain of the spleen
					L	SQiW	D	tonic for babies
				NA	St	BN	L	"skin cancer" (severe wounds?)
					St	BN	L	wounds
					St	BN, MwW	D	inflammation in the urogenital system
CUCURBITACEAE								
Cucurbita pepo L. [2766-8]	-	nevinrao (LBML)	(autumn/ summer) pumpkin, winter squash, bapken (E), citrouille (F), pamken (B)	BML	L	RbH, SQ	L	ear ailments
					St	T	AS	ear ailments
				AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	CK	E	edible
Luffa cylindrica (LOUR.) ROEM. [3076-5]	*L. aegyptiaca, L. insularum, Momordica cylindrica* L., *Momordica luffa*	haukonkon, lärumohonon (R)	smooth (loofah), dishcloth/ rag gourd, vegetable sponge (E), loofah (F)	SWA	L	SQiW	D	"cancer"
					iB	SQiW	D	lovesickness
Luffa sp. [0186-7]	-	haukonkon (LNA)	no popular name	NA	L	F	L	scabies
Zehneria sp. [2176-6]	-	rärumohonon/ räparip hangal (R)	no popular name	SWA	L	SQiW	D	cough
					L	SQiW	D	facilitates childbirth
CYCADACEAE								
Cycas seemannii A.BRAUN [0876-2.4]	*C. circinalis*	nepäpä (N)	queen sago-palm, sago palm, cycad (E)	TLT	L	T, G	L	sting of stonefish
Cycas weinmannii [2966-5]	-	namwale (N)	no popular name	TLL	L	T, SQ	L	centipede bites
DIOSCOREACEAE								
Dioscorea bulbifera L. [0876-2.7]	*D. sativa*	nerachamete (N), woyip (LNA)	(aerial/bitter/ air/ bulbil/ common) yam, devil's/ air-potato (E), igname (F), yam (B)	TLT	St	WiL, T	CHS	ear ailments
				NA	L	WiL, T, SQiW	B	wounds
					L	CK	E	edible
DRACAENACEAE								
Dracaena angustifolia ROXB. [1686-1.12]	-	nisbähäin (IK)	no popular name	AA	L	SQiW	D	ciguatera (to stimulate emesis)
Dracaena fragrans (L.) KER - GAWL. [2176-5]		litoltol (R)	no popular name	SWA	yL	SQiW	D	poisonous plant used to commit suicide

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
Sansevieria trifasciata PRAIN [2186-1.1]	*Sansevieria trifasciata var. trifasciata, Sansevieria trifasciata var. laurentii* (yellow margins), *Sansevieria zeylanica*	-	snake plant, Angola hemp, bowstring hemp, devil's-tongue, mother-in-law's tongue, good-luck plant, lucky plant (E)	AA	L	T, SQ	L	ear ailments
EUPHORBIACEAE								
Acalypha grandis BENTH. [2766-1.1]	-	yangyang (LBML), ringring (N)	navlag (B)	BML	L	F	CH	sore throat
				TLT	L	SQiW	D	gonorrhoea
Acalypha wilkesiana MUELL. ARG. [2766-1.2]	*A. tricolor*	ringring, neljaboth (N), yangyang (LBML)	beefsteak plant, copperleaf ,Fijian fire bush, Jacob's coat (E)	TLL	L	F	CH	aphthous ulcers
				AA	L	SQ	L	aphthous ulcers
				BML	L	SQ	L	conjunctivitis
Chamaesyce hirta L. [2286-1.1]	*Euphorbia pilulifera, Euphorbia hirta*	dissä (IK)	hairy spurge, garden spurge, asthma plant (E), red gras (B)	AA	L	F	CH	asthma
Codiaeum variegatum (L.) BL. [1786-7]	*C. variegatum* var. *variegatum, Croton variegatum, Croton pictum*	inlobot tschaub (IK)	(variegated) croton, croton shrub croton (E), nanggaria, nagiria, nagaria, lif kala, kala lif (B)	AA	L	T, SQiW	D	migraine headache
				AA/ APP/ NA/ SWA/ TLL/ TLT	wP	-	P	Kastom plant
Euphorbia cyathophora L., MURR. [2286-2]	*E. heterophylla , Poinsettia cyathophora*	no local name	Mexican fire-plant, Mexican fireweed, wild poinsettia (E)	AA	Frt	F	E	diarrhoea
Excoecaria agallocha L. [1886-4.1]	-	nedet-he (IK)	palétuvier, aveuglant (F), natongtong blong solwota (B)	AA	Lat	F	L	wounds
Macaranga dioica MUELL. ARG. [2176-7L2]	*Mappa tannaensis, Ricinus dioicus*	nähäwanatschill, nähiväing (IK), leviunu/ livinu hanläla (R)	navenu(e), brata blong burao,nafanhu, nafenua (B)	AA	iB	F	SKC	migraine headache
					yL	WiL, T	C	wounds
				SWA	yL	WiL, T, SQ	D	hypertension
					iB	SQiW	B	wounds
					L	SQ	L	wounds
					L	WiL, T	C	wounds
				NA	yL	SQiW	D	hypertension
Macaranga tanarius (L.) MUELL. ARG. [2176-7L1]	-	livinu/ leviunu tahor (R), nehivaing (IK), nevingne (N)	navenu (B)	SWA/NA	yL	WiL, T	C	sunburn
					yL	WiL, T	C	wounds
				SWA	yL	SQ	C	stops bleeding
				AA	iB	BL, CHL	MW	toothache
				TLL	L	RbH, SQ	D	asthma (babies)

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
scientific plant name not known 1 [0276-2]	-	nehiäm (N)	-	TLL	L	SQiW	C	boils
					L	SQiW	C	sunburn
					L	SQiW	C	various skin diseases
scientific plant name not known 2 [1176-10]	-	nemeturiäm (N)	-	TLL	L	SQiW	C	boils (painful)
GOODENIACEAE								
Scaevola taccada ROXB. [2866-3]	*S. frutescens, S. koenigii, S. sericea, Lobelia taccada*	nenglau (N), nanath (IK)	half flower shrub, sea lettuce shrub, scaevola (E)	TLL	L	BL, CHL	B	scabies
				AA	L	BL	D	tonic
					iB	BL	D	tonic
GUTTIFERAE								
Calophyllum inophyllum L. [2866-8]	-	nepugure (N)	tamanu, beach mahogany, pacific mahogany, Polynesian mahogany, beauty leaf, Alexandrian laurel, kamani (E), tamanou (F), tamanu (blong solwota), nambakura, na(m)bangura (B)	TLL	Fl	F	AO	scents coconut oil
					Frt	G	AO	Tamanu oil (anti-inflammatory properties)
					Frt	F	KHG	game "sut 'em"
					Sd	F	KHG	toxic for chicken
Garcinia sp. [1786-4]	-	inmobolhat (IK)	no popular name	AA	L	F	CH	liver pain
HERNANDIACEAE/ GYROCARPACEAE								
Gyrocarpus americanus JACQ. [0476-2.1]	-	nowe (N)	canoe tree (E), kanutri, kenutri, naove (B)	TLL	L	SQ	L	wounds
					iB	SQ	AF	used to tame pigs
				TLL/TLT/SWA/NA/AA/APP	W	F	KHG	carving
LAMIACEAE								
Hyptis pectinata (L.) POIT. [1786-16]	-	nälchagbäw (IK)	no popular name	AA	L	SQ	C	circumcision wounds
Salvia sp. [1176-12]	-	no local name	stinggras (B)	TLL	wP	BL, CHL	D	indigestion
					wP	BL, CHL	D	gastritis, stomach-ache, ulcers
					wP	BL, CHL	B	scabies
					wP	BL, CHL	B	boils
					wP	BL, CHL	B	wounds
					wP	BL, CHL	D	menses pain

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
Solenostemon scutellarioides L. [2766-10]	*Coleus blumei, Coleus scutellarioides, Ocymum scutellarioides, Plectranthus scutellarioides*	nemeligevot (N)	coleus (E), lif kala, kala lif (B)	TLL	L	RbH	C	fractures
					L	SQiW	D	anaemia
					L	SQ	D	leukaemia and sepsis
				AA/ APP/ NA/ SWA/ TLL/ TLT	wP	-	P	ornamental plant
LAURACEAE								
Cassytha filiformis L. [0576-1]	-	-	cassytha, devil's twine, love vine, dodder laurel (E)	TLL	wP	G, T, SQiW	D	postpartum abdominal pain (to expulse placenta)
LECYTHIDACEAE								
Barringtonia asiatica (L.) KURZ [2866-6]	*B. butonica, B. speciosa, Mammea asiatica*	nüt (N), neteng (IK)	barringtonia, box-fruit tree, heart tree, poison fish tree, sea putat, yum-yum tree (E), chapeae d'évêque (F), fisposentri, navele blong solwota (B)	TLL/AA	Sd	G	KHG	fish poison
				AA	Frt	G	KHG	fish poison
				AA	iB	SQiW	MW	toothache
Barringtonia edulis SEEM. [2876-1]	-	livuwob (R), fetofeto (IK)	bush nut, edible barringtonia, nut tree (E), navel, noix de brousse (F), navel(e) wud (B)	SWA	iB	BL, CHL	MW	toothache
					Frt	F	E	edible
					iB	BL, CHL	D	cough
LEGUMINOSAE - CAESALPINIOIDEAE								
Intsia bijuga (COLEBR.) O. KTZE. [2176-1]	*Afzelia bijuga, Intsia madagascariensis*	lehumo (R)	cohu, ifil/ ipil (tree), (Moluccan) ironwood, kwila, (island/ pacific) teak (E), cohu, faux teak (F), natora, tik (B)	SWA	L	SQiS, WiL	D	to defeat infections
					L	SQiS, WiL	D	diabetes
					iB	SQiS, WiL	D	to defeat infections
					iB	SQiS, WiL	D	diabetes
					iB	SQiCW	D	asthma
				AA/ APP/ NA/ SWA/ TLL/ TLT	W	F	KHG	carving
LEGUMINOSAE – MIMOSOIDEAE								
Entada pursaetha DC. [1786-13]	-	inhätäliñga (IK)	no popular name	AA	L	SQiW	D	severe pain during pregnancy
					Frt	F	E	edible

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
LEGUMINOSAE – PAPILIONOIDEAE								
Derris trifoliata LOUR. [0876-1.1]	*D. uliginosa*	netüwe (N)	Kastom penicillin (B)	TLL	L	F	CHS	boils
					L	F	CHS	carbuncles
					L	F	CHS	abscesses
				AA/ APP/ NA/ SWA/ TLL/ TLT	St	F	KHG	rope for firewood
Desmodium incanum (SW.) DC. [1886-2.3]	*D. canum*, *Hedysarum incanum*	nälnjabuit (IK)	creeping beggarweed, kaimi clover, Spanish clover (E)	AA	L	F	CH	diarrhoea
Erythrina variegata L. [2176-8]	*E. indica, E. picta, E. variegata orientalis, E. variegata parcellii*	rärar/ lirar (R), nerare (N)	coral bean, (Indian) coral tree, crab's claw, tiger's claw (E), narara (B)	SWA	L	SQiW	D	cough
				TLL	iB	SQiW	D	chest pain (adiposity; angina pectoris?)
					iB	T, SQ	D	asthma
					yL	F	CH	postpartum abdominal pain (to expulse placenta)
Inocarpus fagifer PARK. [3066-6]	*I. edulis, I. fagiferus*	nemegwe (N)	Polynesian/ Tahitian chestnut (E), châtaignier (de tahiti), mapé (F), namamb(w)e, nawemba, nawembe (B)	TLL	Sd	G, SQiW	D	protein intoxication after consumption of too much seafood (flatulence + pain)
				AA/ APP/ NA/ SWA/ TLL/ TLT	Sd	CK	E	edible
Mucuna gigantea (WILLD.) DC. [2576-6]	*Mucuna gigantea gigantea*, *Dolichos gigantea*	habba (R)	sea bean (E)	SWA	sap	F	L	sting of *Dendrocnide moroides*
Pterocarpus indicus WILLD. [2176-18]	-	läsumol (R), nagautewa (IK)	blue water, narra tree, new guinea rosewood, padouk, sang dragon (E), bluwota, nananar(a), navilae (B)	SWA	yL	SQiW	D	pain
				AA	iB	BL	D	anaemia
				AA/ APP/ NA/ SWA/ TLL/ TLT	W	F	KHG	carving
Pueraria lobata (WILLD.) OHWI [3066-4]	*P. harmsii, P. montana* var. *lobata*	netü (N), ya (R)	no popular name	TLL	L	G, MwCW, BL	D	asthma
				SWA	L	SQiW	D	hepatitis
Vigna luteola (JACQ.) BENTH. [0386-1.7]	*Phaseolus luteolus*	ya (R)	(string) bean (E), haricot (vert), flageolet (F), ariko, (wael) bin (B)	SWA	L	SQiW	D	hepatitis
					Sd	CK	E	edible
MALVACEAE								
Hibiscus rosa-sinensis L. [2966-4]	-	(ne)tewäwiäiw (N)	red hibiscus, Chinese hibiscus, Chinese rose-mallow, blacking plant (E), haebiskis (B)	TLL	Fl	BL, CHL	EW	conjunctivitis
					Fl	F	AF	children, that don't speak
				AA/ APP/ NA/ SWA/ TLL/ TLT	wP	-	P	ornamental plant

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
Hibiscus tiliaceus L. [3076-1]	*H. tiliaceus tiliaceus, H. tiliaceus hastatus,Taliparititi tiliaceum, Taliparititi tiliaceum* var. *tiliaceum*	lipolwär (R), nevar (N)	burao, cottonwood, beach/ tree hibiscus (E), bourao (F), b(u)rao (B)	AA/ APP/ NA/ SWA/ TLL/ TLT	W	F	KHG	carving
				BML	Sh	F	CH	gastritis, stomach-ache, ulcers
				TLL	Sh	G	CH	constipation/ ileus
				SWA	iB	WiL, T, SQiW	D	"cancer"
					L	WiL, T, SQiW	D	"cancer"
					Sh	SQ	C	stops bleeding
					Sh	SQ	C	wounds
Sida rhombifolia L. [1886-2.2]	*S. microphylla, S. rhombifolia rhombifolia*	uagas (IK)	broom weed, Cuba jute, tall-flower sida, paddy's lucerne, Queensland hemp (E)	AA	L	BL	D	diarrhoea
MARANTACEAE								
Donax cannaeformis (G. FORST.) K. SCHUM. [0186-5]	*Actoplanes cannaeformis*	libällabo (LNA)	no popular name	NA	dd/rw	CLL	D	children, that don't speak
MARATTIACEAE								
Marattia smithii METT. EX. KUHN [1786-1]	-	äminäkäi (IK)	no popular name	AA	L	BL, CHL	B	neurodermatitis, infantile eczema
MELIACEAE								
Dysoxylum arborescens (BL.) MIQ. [0476-1.6]	-	nemawte (N)	no popular name	TLL	iB	T, SQiW	D	kidney pain
MORACEAE								
Artocarpus altilis (PARK.) FOSB. [2286-1.3.2]	*A. communis, A. incisa, A. incisus*	inma (IK)	breadfruit (E), fruit de baobab, pain de singe (F), bredfrut (B)	AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	CK	E	edible
					Sd	T	E	edible
				AA	Sh	F	SKC	migraine headache
					Lat	F	L	wounds
Ficus adenosperma MIQ. [1686-1.3]	-	nithidao (IK), linum (R)	no popular name	AA	St	F	CH	headache
				SWA	sap	CLL, MwW	D	albuminuria
Ficus aspera FORST. [1786-17]	-	nautschärob abäng (IK)	no popular name	AA	L	SQ	L	conjunctivitis

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
Ficus septica BURM.F. [2176-2]	-	libälä (R), nälmaha (IK)	no popular name	SWA	L	SQiW	D	asthma
					dd/rw	CLL	L	conjunctivitis
					dd/rw	CLL	D	tonic for children
					L	T, SQiW	D	children's' diseases caused by spirits
					yL	F	CHS	headache
				AA	St	F	CH	headache
Ficus sp. [2576-5]	-	liwirim (R), lipüru (LNA)	no popular name	SWA	Lat	SQiW	D	postpartum abdominal pain (to expulse placenta)
				NA	iB	F	C	burns
Ficus wassa ROXB. [0876-2.12]	-	newuo (N)	nasis, (nam)balanggo (B)	TLT	St	F	KHG	to stimulate fruiting of a watermelon plant
MYRSINACEAE								
Maesa ambrymensis GUILL. [2576-1]	-	liputu (R), tilalamnumnu (LNA)	no popular name	SWA	Frt	F	E	to initiate the menopause
				NA	L	SQiW	D	infant crying caused by magic
MYRTACEAE								
Psidium guaJava L. [2766-5]	-	guap (N), guava (LNA)	apple/ common/ yellow guava (E), gwava (B)	BML	L	F	CH	diarrhoea
				AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	F	E	edible
				NA	L	SQiW	D	severe illness with bloody faeces
Syzygium malaccense (L.) MERR. & L.M. PERRY [3066-2]	*Eugenia malaccensis, Jambosa malaccensis*	negebige (N), hawei (R), injähäl (IK)	Malay/ mountain/ rose apple (E), pommier (canaque) (F), (na)kavika (B)	TLL	L	F	CH	mouth infections
				SWA	L	F	CH	abdominal pain (to cause emesis)
				AA	iB	SQiW	D	ciguatera
				AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	F	E	edible
PANDANACEAE								
Freycinetia tannaensis MARTINELLI [1786-2]	-	näbägchat (IK)	no popular name	AA	L	G	L	fractures
Pandanus tectorius PARK. [2866-5]	*P. odoratissimus, P. chamissonis*	nerongän (N)	pandanus (palm), screw pine/ palm (E), wael pandanas, grastri (B)	TLL	L	F	SKC	headache
					Rt	G	L	lice
				AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	CK	E	edible
					L	F	KHG	weaving

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
PHYLLANTHACEAE								
Baccaurea stylaris MUELL. ARG. [1786-6]	-	nithtschaub (IK)	no popular name	AA	L	BL, CHL	B	asthma
					iB	BL, CHL	B	asthma
					L	BL, CHL	B	cough
					iB	BL, CHL	B	cough
PIPERACEAE								
Macropiper latifolium (L.F.) [2176-10]	*Piper latifolium*	libärarmen (R), newureri (N)	wild kava (E), kava sauvage (F), wael kava (B)	SWA	St	SQ	L	conjunctivitis
					St	SQiW	D	panacea
					Frt	F	E	black magic
					St	F	C	to draw a splinter
				TLL	Rt	SKC	D	ciguatera
				NA	L	F	SKC	Kastom plant
					LG	F	E	influences sex of embryo during pregnancy (girl or boy)
Piper methysticum J. R. & G. FORST. [3076-6]	*Macropiper methysticum*	injäjajän (IK)	kava (B)	SWA	L	WiL, T, SQiW	D	appendicitis
				AA/ APP/ NA/ SWA/ TLL/ TLT	Rt	SKC	D	folk drug
				AA	L	SQiW	D	cough
					Rt	SQiW	D	cough
POACEAE								
Digitaria radicosa PRESL [2766-7]	*D. sanquinalis, D. timoriensis, Panicum radicosa*	no local name	large crab-grass (E), gras (B)	BML	sap	F	L	wounds
Oplismenus hirtellus (L.) P.BEAUV. [1886-2.1]	-	"gras" (IK)	-	AA	Sh	F	CH	cough
Saccharum robustum BRAND. & JESW. EX GRASSL F. [0386-1.6]	-	tschib (R)	sugaken (B)	SWA	St	F	CH	ciguatera
POLYPODIACEAE								
Drynaria rigidula (SW.) BEDD. [1786-11]	-	nässäi (IK)	no popular name	AA	L	BN	L	hair loss
Pyrrosia confluens (R.BR.) CHING [0876-2.8]	-	nobody could remember the vernacular name	no popular name	TLT	Frt	BL, CHL	MW	toothache
RUBIACEAE								
Aidia racemosa (CAV.) D.D. TIRVENG. [0476-1.2]	*Randia racemosa*	nenieum/ nenyeung (N)	nakumlum (B)	TLL	L	BL, CHL	B	scabies
Gardenia tannaensis GUILL. [0876-2.3]	-	nerukka (N)	no popular name	TLT	L	F	AF	constipation

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
Morinda citrifolia L. [3076-9]	*M. citrifolia* var. *citrifolia*	lihokon (R), nouras (IK)	awl tree, Indian mulberry, noni, yaw bush, yellow tree (E), fromager, mûrier Indien, nono (F), yelowud (B)	SWA	L	BL	D	panacea
					Frt	CLL	D	panacea
					L	BL	D	tonic
					Frt	CLL	D	tonic
				AA	Frt	F	E	constipation
RUTACEAE								
Citrus aurantifolia CHRISTM. [nVS]	*C. limetta, C. medica acida, Limonia aurantifolia*	no local name	lemon (tree), lime (E), laem (B)	TLL	Frt	SQ	L	scabies
Euodia latifolia DC. [0276-1]	*Euodia latifolia, Melicope latifolia*	nehine (N)	no popular name	TLL	L	SQiW	D	cough
Micromelon minutum (FORST.F.) WIGHT & ARN. [0876-2.6]	*M. pubescens*	nerrenärre (N)	wael pima (B)	TLT	L	F	CH	toothache
SAPINDACEAE								
Allophylus timoriensis DC. BL. [0476-1.5]	*Al. sublaxus, A. vitiensis, Rumphia timoriensis*	nerriä (N)	allophylus (E)	TLL	L	T, SQ	D	kidney pain
Pometia pinnata J.R. FORST. & G. FORST. [2176-9]	*Nephelium pinnata*	lirra (R), neta(u)we (N)	langsir, native/ oceanic/ pacific lychee, taun (E), nandao, nandau, natau (B)	SWA	yL	T	C	pain caused by magic
					iB	SQiW	D	asthma
				TLL	iB	SQ	L	boils
					yL	F	CH	bloody urine + pain
				TLT/ SWA	L	F	CH	jealousy (of women)
				AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	F	E	edible
SOLANACEAE								
Capsicum frutescens L. [1686-1.5]	-	no local name	bird's-eye chilli, bird's-eye pepper, bird pepper, chilli (pepper), chilli pepper (alternate spelling), hot pepper (E), petit piment, pim d'oiseau, poivre (F), (wael) pima, pimang, tsil (B)	AA	L	F	R	muscle pain
					L	F	R	rheumatism
				APP	Frt	F	L	boils
Physalis angulata L. [2576-11]	*P. minima*	-	annual ground-cherry, cape gooseberry weed wild cape gooseberry (E)	SWA	L	BL	D	dengue fever
SPARRMANNIACEAE								
Grewia inmac GUILL. [1686-1.13]	-	nämdokai (IK)	Kastom penicillin (B)	AA	L	SQ, BL	D	pain/"aelan panadol"
TECTARIACEAE								
Tectaria latifolia (FORST.) COPEL. [2576-8]	-	räbabagongon (R)	no popular name	SWA	Fr	F	O	wounds

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
THELYPTERIDACEAE								
Sphaerostephanos invisus (FORST. F.) HOLTTUM [2766-2]	*Cyclosorus invisus, Nephrodium invisus, Dryopteris invisus*	fern (LBML)	no popular name	BML	Frt	SQ	L	conjunctivitis
ULMACEAE								
Trema orientalis (L.) BL. [0186-3]	*T. orientalis* var. *viridis*	lirpüu (LNA)	trema (E)	NA	iB	SQiW	D and C	fractures
URTICACEAE								
Pipturus argenteus WEDD. [2766-1.9]	*P. argenteus* var. *argenteus, P. propinquus, P. velutinus, Urtica argenteus*	lärumo, lirumo (R), nehieungwi (N)	pipturus (E)	SWA	L	BL	D	hepatitis
					sap	CLL	D	panacea
					Sh	SqiW	D	tonic for children
					iB	SQiW	D	abortive
				BML	iB	F	C	boils
				AA/ APP/ NA/ SWA/ TLL/ TLT	Frt	F	E	edible
VERBENACEAE								
Lantana camara L. [1786-9]	*L. aculeata*	no local name	lantana (weed) (E), blakberi, lantan(a), blarvari (B)	AA	L	SQ	L	wounds
Stachytarpheta cayennensis (RICH.) VAHL [1786-5]	*S. jamaicensis, S. urticifolia* (some authors), *S. urticaefolia* (some authors, alterative spelling), *Verbena cayennensis*	inchäi unasuandan (IK)	blue rat's tail, cayenne/ dark blue snakeweed, false verbena, nettle leaf velvet berry (E), bluflaoa, suga (B)	AA	L	SQ	L	wounds
Vitex trifolia L. ssp. *trifolia* [2176-14]	-	limadnobnob (R)	no popular name	SWA	L	F	Sm	infant crying
				AA/ APP/ NA/ SWA/ TLL/ TLT	W	F	KHG	outrigger canoes
VITACEAE								
Cayratia trifolia (L.) DOMIN. [0186-2]	-	awür (LNA)	no popular name	NA	L	SQiW	D	„cancer" (heart burn?)
					sap	F	L	"skin cancer" (severe wounds?)
					sap	F	L	wounds
VITTARIACEAE								
Vittaria lineata (L.) JE. SMITH [1786-12]	-	nabuthwä (IK)	no popular name	AA	L	G	D	ciguatera
ZINGIBERACEAE								
Alpinia novae-pommeraniae K. SCHUM. [2576-2]	-	libadumäla (R)	no popular name	SWA	St	G	L	toothache
					St	G, MwW	D	chest pain (angina pectoris?)
Zingiber zerumbet (L.) SM. [2576-4]	*Z. fairchildii*, *Amomumzerumbet*; *Scitaminea*	liwolängdob, billo (R)	-	SWA	Rh	G, MwW	D	diabetes

FAMILY SCIENTIFIC NAME [VOUCHER NO.]	SYNONYM(S)	VERNACULAR NAME(S)	POPULAR NAME(S)	ORIGIN	PPU	PREPARATION	MODE OF APPLICATION	USES
Alpinia sp. [1176-3]	-	no local name	wael jinja (B)	TLL	Rh	G, MwW	D	"cancer"
Hornstedtia lycostoma (LAUTERB. & K. SCH.) K. SCH. [1176-8]	-	nehärrdelit (N)	no popular name	TLL	L	SQiW	D	tonic
Hornstedtia sp. [1586-1]	-	nitschisäi (IK)	no popular name	APP	Rh	G, MwW	D	tonic
					Rh	G, MwW	D	diabetes
					Rh	G, MwW	D	"cancer"
					L	F	KHG	grass skirts
PLANT FAMILY NOT KNOWN								
not known 3 [2286-1.4.1]	-	nälmaha (IK)	no popular name	AA	L	F	SKC	severe abdominal pain during pregnancy caused by spirits
not known 4 [2286-1.4.2]	-	näüsärop (IK)	no popular name	AA	L	F	SKC	severe abdominal pain during pregnancy caused by spirits
not known 5 [1886-5.2]	-	nanathoba (IK)	no popular name	AA	L	BL	D	ciguatera
					L	G, MwCW	D	ciguatera

QUESTIONNAIRES

1. PLANT SPECIFIC PART

date	voucher specimen number		
informant-/ collector information			
name	gender	age	profession
taxonomic information			
popular name/s	scientific name/s	synonym/s	plant family
taxonomic indicator (e.g. endemic, invasive)			
information on the specimen			
short description of the plant			
geographical/ geological information			
island	village name	habitat/ vegetation type	
ethnological information			
clan name		chief name	
medicinal/ pharmaceutical information			
uses	plant part/s used		importance
preparation	dosage	application form	application time
effect/s	observation/s	side effect/s	contraindication/s
illustration or picture			notes

Fig. 42 Questionnaire on the plants and their uses

2. INFORMANT-SPECIFIC PART

healers (ethnological aspects)	
Which kind of healer is asked?	
How to become this kind of healer?	
selection of plants Why is a plant used in medicine?	
What are the criteria for plant selection?	
How are medicinal and non-medicinal plants classified?	
How are medicinal plants classified?	Are non-medicinal plants also classified?
classification of illnesses Which illnesses does the healer know?	
diagnosis	
cause/s	symptom/s
concerned persons	prevention
Who may medicate the patient and why?	healing ceremony

Fig. 43 Questionnaire on healers and illnesses

WORD LISTS

INDASS KHERMO, NEWAWETEME, AND RALLGLÉIN

ENGLISH	INDASS KHERMO	NEWAWETEME	RALLGLÉIN
black	napäng	namededüt	märmär
white	náhi	nalül	fifiu
blue	nämälmát	namelerükä	näbnäb
green	nämälmát	namelerükä	girri
brown	numdschin		jäbobo
red	ingap	namemi	fifíri
yellow	injáng	naieng	ngúngo
bark	narasinchräi	neviurerra	hallulíhä
leaf	nerin	nekórrera	räsorro
flower		tewäherera	
stem	nowún	nedédrerra	bädschidä
root	nowán	negerrérra	líbidi
tree	chräi	dedrerra	lihä
sea	íntschab	nebäéwonnä	dä
bush	inlíllidäi	ligaiwón	bubuhórr
yes	maja	ää	mafíttin
no	äo	dadrä	mangalás
1	ití	duwä	súpp
2	ärron	vürruä	ru
3	ässätch (miti)	wetäl	tschull
4		wewät	wírr
5		tewälímä	limm
6		livíssä	milipdsché
7		levürruä	milibrú
8		lewedäl	milipdschul
9		liviwät	milifärr
10		hängewúl	sangawül
I	ánjak	nokkä	ni
you	ák	nikkä	näk
he/ she/ it	án	njä	ngai
we	átschama	deöjöl	ränämdschul
you	´tschoña	gomarr	ngärie
they	árra (>2), ákatscha (2)	nihe	närrilgäbäni
big	albass upni	naluwó	moúgormär
small	haklin	narríri	magegéi
quick	árauru (ak)		korrkorr
come	ajak	vinwe/ vinhe	mä
go	áthiak	vene/ alleven!	jann
good morning	nujaläng dupni		fangfang ränändú
good afternoon			dábliäländú
good night	intschupura dupni		fángrän
good bye	intschupura dupni		
My name is...	nithák...		
Thank you	nahauriníng albáss		sippan tuñgórr/ món
OK	dádo (dupni)		mókonon
What?	nividäi iä?	näwe	mimbä
white man	natimiahí	salül	vändän fifiu

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Regensburg, den _____ _____

Gesine Bradacs