Antimicrobial Lipids from Plants and Marine Organisms

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Medicinal plants and marine organisms are natural sources of many antimicrobial compounds. Plant components with antimicrobial activity include alkaloids, sulfur-containing compounds, diterpenes/terpenoids, fatty acids (FA), some carbohydrates, steroidal glycosides, and phenolic compounds. Both primary and secondary metabolites are “generally recognized as safe” (GRAS) substances and the chance of triggering antimicrobial resistance is low. The most studied antimicrobial compounds of marine origin are peptides and alkaloids, contrarily to lipids. However, lipids are ubiquitously distributed in the different marine phyla, being quite abundant in some of them. Besides, several lipid classes from marine organisms have been recognized by their biological activity with a high potential to discover new antimicrobial compounds.

fatty acid | lipid extract | lipidomics | macroalga | marine invertebrate | mechanism of action | microalga | minimum inhibitory concentration | monoacylglycerol | natural antimicrobial

1. Introduction

The consumption of antibiotics in the world population is alarming. In 2016, the top five World Health Organization (WHO)’s major antibiotic consuming countries were Brazil, Turkey, Iran, Russia, and France, by decreasing order [1]. In Brazil, more than 2000 metric tons of antibiotics were consumed annually, followed by ca. 1000 metric tons in Turkey and Iran [1].

Both misuse and overuse of antibiotics has led to the development of antimicrobial resistance (AMR) in microorganisms, which has been a global problem and a growing threat for many years. Antimicrobial resistant microbes are found in people, animals, food, and the environment (hospital or other health care facilities, water, soil and air). Because of AMR, several disease conditions are becoming harder to treat, as tuberculosis, pneumonia, blood poisoning, gonorrhea, and foodborne diseases [2]. AMR leads to higher medical costs, prolonged hospital stays, and increased mortality, causing an economic burden for health care systems. The major cause of AMR is mostly due to misuse of antibiotics.

A number of 700,000 deaths occur worldwide because of drug-resistant diseases [3]. Tuberculosis causes 1.8 million deaths per year, while multidrug-resistant (MDR) tuberculosis causes 250,000 deaths per year and is a

global priority for research and development. Gram-negative bacteria can cause death in days because of the lack of treatment options. By 2050, it is foreseen that drug-resistant diseases could cause 10 million deaths each year [3]. In 2017, the WHO identified a priority list of highly antimicrobial-resistant pathogenic microorganisms, also known as superbugs, that have developed survival mechanisms to circumvent the action of last-line antimicrobials (isoniazid, rifampicin, fluoroquinolone, carbapenem, third-generation cephalosporin, or vancomycin) [4]. There are twelve bacteria that have critical and high priority for treatment discovery, besides *Mycobacterium tuberculosis*, the causing agent of tuberculosis, including the "ESKAPE" pathogens: *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and Enterobacteriaceae [5]. Superbugs cause 33,000 deaths each year, in Europe, by antibiotic-resistant bacterial infections. Italy is the European country with one-third of all cases (11,000 deaths in total), followed by France (more than 5500 deaths) and Germany (with 2300 deaths) [6][7].

The world now lives the so-called "post-antibiotic era." The current guidelines and recommendations from the WHO claim for an interconnected action and national action plans in a multisectoral and sustained "One Health" approach. This is aimed to tackle AMR and achieve the United Nations' Sustainable Development Goals for 2030 toward humans, food and feed, plants and crops, environment, terrestrial and aquatic animals [8].

According to a recent WHO's report, there are 252 antimicrobial agents in preclinical pipeline, being developed to treat WHO's priority pathogens, but at very early stages of development [9]. Even so, very few target the most critical resistant Gram-negative bacteria, thus, they will generate little benefit over existing treatments [9]. As such, it appears that the future will come up with an increased need for new compounds with antimicrobial activity and combined therapeutic strategies, which can be effective against superbugs and bring revenue to the pharmaceutical industry. At the same time, several alternative approaches to conventional antibiotics have been extensively studied, not only to be used in the clinical field but also in animal health, control insect pest, protect agricultural crops, improve food safety, and water disinfection. Developing strategies include antimicrobial peptides (AMP), phage therapy, photodynamic antimicrobial chemotherapy (PACT), nanoparticles, probiotics, lysins, antibodies, quorum sensing inhibitors, and immunotherapeutic agents [5][10][11][12][13][14]. Combination therapy or multi-target approaches are being developed to hinder antibiotic resistance or to sensitize microorganisms to antibiotic action [15]. Another strategy to overcome AMR is the combination of conventional antibiotics with other molecules, as natural products and/or antimicrobials from natural sources, as plants and marine organisms, to enhance the antimicrobial effect against a wide range of pathogens.

Medicinal plants and marine organisms are natural sources of many antimicrobial compounds [14][16][17][18]. Plant components with antimicrobial activity include alkaloids, sulfur-containing compounds, diterpenes/terpenoids [19], fatty acids (FA) [20][21][22], some carbohydrates [23], steroidal glycosides, and phenolic compounds [24]. Both primary and secondary metabolites are "generally recognized as safe" (GRAS) substances and the chance of triggering antimicrobial resistance is low [25]. Simultaneously, marine organisms, mainly slow-moving or sessile, have developed adaptive defense mechanisms to protect themselves against pathogenic microorganisms. In some cases, marine organisms maintain associations with microbiota, being bacterial symbionts responsible by the synthesis of antimicrobial molecules [26][27].

2. Antimicrobial Lipids from Plants

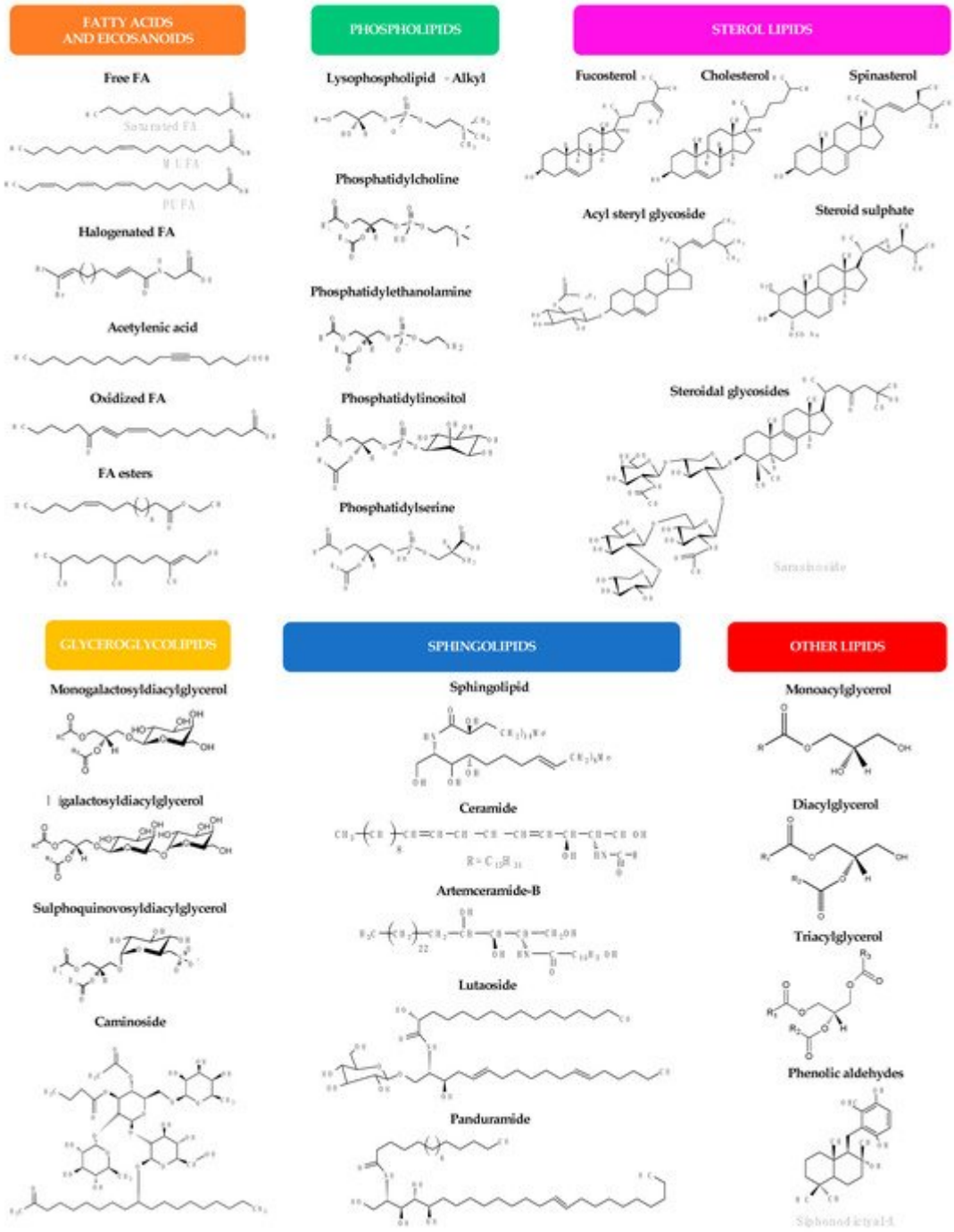
Over the evolution, higher plants have developed several resilience strategies that allow them to resist or escape external attacks (e.g., microorganisms, pathogens, and predators). Their innate immune system had to be equipped with highly complex mechanisms of resistance and survival. The defense mechanisms of plants are unique and consist of both physical barriers and production of secondary metabolites. Plant secondary metabolites are formed in particular biosynthetic pathways by means of substrate-specific enzymes. The precursors of these secondary metabolites stem from primary metabolites, such as amino acids, FA, sugars, or acetyl-CoA. Some of the secondary metabolites serve as constitutive chemical barriers against the microbial attack (phytoanticipins) while others serve as inducible antimicrobials (phytoalexins) [28].

Oxylipins are a large family of plants' secondary metabolites derived from PUFA that make part of their immune system and play key roles as antimicrobial agents. They are formed through enzymatic or radical oxidation of FA 18:2 and 18:3, in order to protect plants against pests and pathogens [29]. The enzymatic biosynthesis of these molecules is triggered by an alpha-dioxygenase (DOX) and by lipoxygenases (LOX) [30][31] that lead to the formation of the different types of molecules, including hydroxy-, hydroperoxy-, divinyl-, oxo-, and keto-derivatives of FA. Oxylipins are formed during abiotic and biotic stresses [32]. They are plant signaling molecules that can induce cell death and have an effect on the growth of eukaryotic microbes [29]. A deeper knowledge on plant response to stresses at molecular, physiological and metabolic levels will allow the development of new plant-derived antimicrobial molecules for use in the clinical field and as biopesticides [32].

The search for novel antimicrobials has led to exploring also amide derivatives of FA because they are natural self-defense agents in plants. FA amides are bioactive lipids [33] formed by the amidation of long chain saturated and unsaturated FA (UFA) [34]. They have higher antimicrobial activity against yeasts and bacteria than unmodified FA [35]. Amide derivatives of FA possess a broad bioactivity against different pathologic conditions (bacterial and parasitic infections, cancer, inflammation, etc.,) and their mechanisms of action imply protein synthesis inhibition and membrane leakage [36]. Also, microorganisms inside healthy plant tissues are unique to explore novel bioactive compounds. The FA and their amides from plant's endogenous microorganisms have been scarcely reported despite being bioactive in a variety of processes and should be more explored as new therapeutic agents [36].

Lipids represent up to 7% of the dry weight of the leaves of higher plants and are important constituents of cell membranes, chloroplasts, and mitochondria [37]. Besides their structural function as main constituents of cell membranes, they have functional roles in plants (intracellular mediators, extracellular signalers, inter-species communication, and plant defense) and also serve as energy reserves (namely in seeds during germination) [21]. Palmitic acid (16:0) is the major saturated FA in leaf lipids. On the other hand, chloroplast membranes can have up to 90% α-18:3 FA in some lamellae [21]. FA exist in plants mainly linked to more complex molecules, as acylglycerols, esterified to a glycerol backbone in the form of triacylglycerols, sterol esters, MAG and diacylglycerols, phospholipids, or glycolipids. Several lipid classes, besides FA and MAG, have been identified in a diverse group of higher plants and tested for their antimicrobial activity, as will be detailed in the next sub-

sections. **Figure 1** illustrates the chemical structures of the different lipid classes with antimicrobial activity isolated from natural sources.



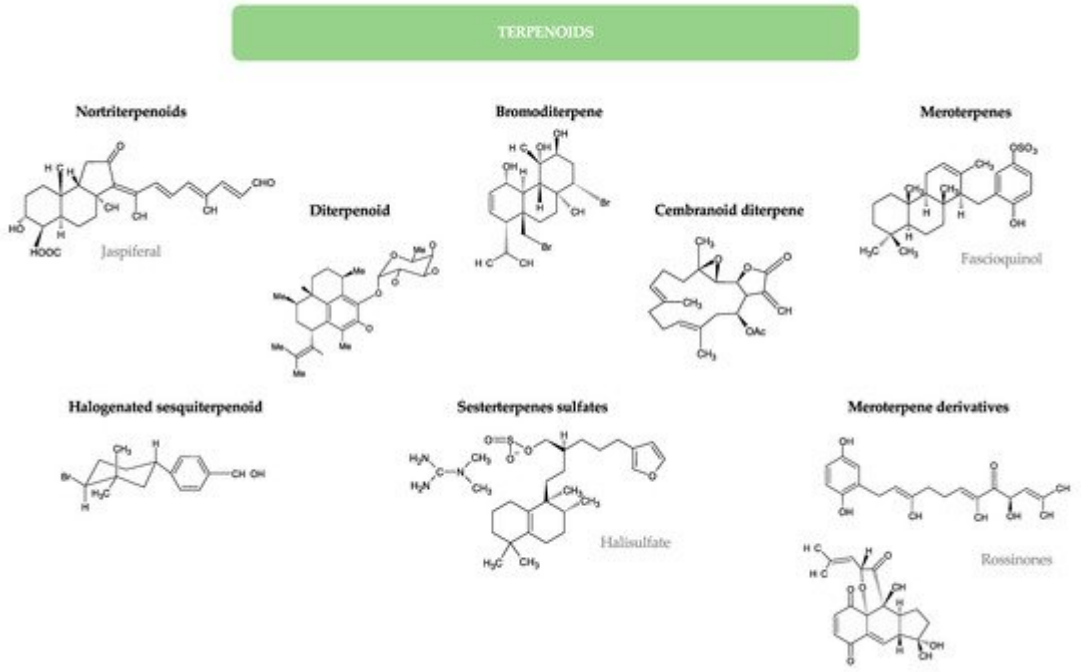


Figure 1. Chemical structures of the different lipid classes isolated from natural sources with antimicrobial activity.

2.1. Extraction and Isolation of Plant Lipids

Studies that extract or isolate lipids from plants to test their antimicrobial activity are scarce (**Table 1**). The biomass used to extract lipids includes leaves, fruits, seeds, stems, rhizomes, shoots, stem barks, and heartwoods (**Table 1**). Lipid extraction from plants is usually carried out with organic solvents of different polarities (mainly *n*-hexane, $CHCl_3$, CH_2Cl_2, EtOAc, EtOH, BuOH, MeOH, and their mixtures) (**Table 1**). Liquid/liquid extractions or Soxhlet extraction are commonly performed to obtain total lipid extracts [38][39][40][41][42]. Instead of analyzing one lipid class or one lipid molecule, some studies have analyzed the total lipid extracts that were obtained by sequential extraction.

Table 1. Plant potential antimicrobial lipids or lipid-rich extracts, their origin and extraction method grouped by botanic family.

Botanical Name	Family	Common Name	Country of Collection	Plant Part	Extracting Solvent/Method	Isolated Lipids or Lipid Mixtures	Ref.
Sesuvium portulacastrum L.	Aizoaceae	Sea purslane	India	Leaves	MeOH/benzene/sulfuric acid (200:100:10, *v*/*v*)	FAME	[43]
Blutaparon portulacoides (A. St.-Hil.) Mears	Amaranthaceae	Capotiraguá	Brazil	Roots	EtOH	Acyl steryl glycosides (sitosteryl 3-*β*-*O*-glucoside 6′-*O*-palmitate and stigmasteryl 3-*β*-*O*-glucoside 6′-*O*-palmitate)	[44]
Arthrocnemum indicum (Willd.) Moq., *Salicornia*		Glasswort for *Salicornia* genus, herbaceous	India	Shoots of *A. indicum* and *S. brachiata*, and	Dry MeOH/benzene/sulfuric acid (200:100:10, *v*/*v*)	FAME	[45]

Botanical Name	Family	Common Name	Country of Collection	Plant Part	Extracting Solvent/Method	Isolated Lipids or Lipid Mixtures	Ref.
brachiata Roxb., *Suaeda maritima* (L.) Dumort. and *Suaeda monoica* Forsk.		seepweed for *S. maritima*, and South-Indian seepweed for *S. monoica*		leaves of *S. maritima* and *S. monoica*			
Alternanthera brasiliana		Brazilian joyweed	Brazil	Root, stem and leaves	EtOH and EtOAc	Linoleate oxylipins	[46]
Phoenix dactylifera L.	Arecaceae	Date palm	India	Seeds	$CHCl_3$ and acetone	Sterol and triterpenes	[47]
Asphodelus aestivus Brot.	Asphodelaceae (formerly Liliaceae)	Summer asphodel	Turkey	Seeds	Petroleum ether with Soxhlet extractor	FA (C4:0, 6:0, 8:0, 10:0, 16:0, 18:0, 21:0, 24:0, 14:1, 15:1, 18:1n9t, 20:1, 24:1, 18:2, 18:2n6t, 18:2n6c, 20:2n6, 20:3n3, 22:6n3, and others unidentified)	[38]
Artemisia incisa Pamp.	Asteraceae		Pakistan	Roots	MeOH and recovered after elution on a SiO_2 column with CH_2Cl_2/MeOH (9:1, *v*/*v*) following previous elution with *n*-hexane/EtOAc (5:4, *v*/*v*)	Artemceramide-B	[48]
Pteranthus dichotomus Forssk. (also known as *P. echinatus* Desf.)	Caryophyllaceae		Algerian Sahara	Aerial parts	MeOH/H_2O (80:20, *v*/*v*). Aqueous phase extracted successively with petroleum ether, EtOAc and *n*-BuOH. EtOAc fraction contained the sterols and steryl glycoside. BuOH fraction contained the glyceroglycolipids and the cerebroside.	BuOH fraction contained the compounds: 1-*O*-palmitoyl-3-*O*-(6-sulfo-α-D-quinovopyranosyl)-glycerol, 1,2-di-*O*-palmitoyl-3-*O*-(6-sulfo-α-D-quinovopyranosyl)-glycerol and soya cerebroside I. EtOAc fraction contained the compounds: stigmat-7-en-3-ol, spinasterol, *β*-sitosterol and *β*-sitosterol-3-*O*-glycoside	[49]
Cucumis sativus L.	Cucurbitaceae	Cucumber	China	Stems	$CHCl_3$ fraction of the crude methanolic extract	Sphingolipids [(2*S*,3*S*,4*R*,10*E*)-2-[(2′*R*)-2-hydroxytetracosanoylamino]-1,3,4-octadecanetriol-10-ene, 1-*O*-*β*-D-glucopyranosyl-(2*S*,3*S*,4*R*,10*E*)-2-[(2′*R*)-2-hydroxytetracosanoylamino]-1,3,4-octadecanetriol-10-ene and soya-cerebroside I]	[50]

Botanical Name	Family	Common Name	Country of Collection	Plant Part	Extracting Solvent/Method	Isolated Lipids or Lipid Mixtures	Ref.
Excoecaria agallocha	Euphorbiaceae	Blind-your-eye mangrove	India	Leaves	Dry MeOH, benzene and sulfuric acid (200:100:10, *v*/*v*)	FAME	[51]
Albizia adianthifolia (Schumach) and *Pterocarpus angolensis* (DC)	Fabaceae	Flat crown Albizia and African teak, respectively	Nigeria and Botswana, respectively	Heartwood of *A. adianthifolia* and stem bark of *P. angolensis*	*n*-hexane, $CHCl_3$, MeOH, and 10% MeOH (aq)	*n*-hexadecanoic acid (palmitic acid); oleic acid; chondrillasterol; stigmasterol, 24S 5α-stigmast-7-en-3-ol; 9,12-octadecadienoic acid (*Z*,*Z*)-, methyl ester; *trans*-13-octadecanoic acid, methyl ester; tetradecanoic acid; hexadecanoic acid, methyl ester; octadecanoic acid	[52]
Baphia massaiensis		Jasmine pea	Botswana	Seeds	*n*-hexane/1-propanol (3:1, *v*/*v*) with Soxhlet extractor	Seed oil (total FA)	[53]
Cassia tora L. (or *Senna tora* L. Roxb.)		Sickle Senna	India	Leaves and stem	Petroleum ether with Soxhlet extractor	FA (the major were palmitic acid, linoleic acid, linolenic acid, margaric acid, melissic acid, and behenic acid)	[39]
Trigonella foenum-graecum L.		Fenugreek	India	Seeds	Supercritical fluid extraction (40–60 °C and 10–25 Mpa)	Conjugated linoleic acid methyl ester, saturated FAME, steroids	[54]
Quercus leucotrichophora A. Camus	Fagaceae	Banjh oak	India	Fruits	85% aqueous EtOH. Ethanolic extract fractionated with hexane and EtOAc using Soxhlet extractor. Hexane extract was analyzed.	FAME	[40]
Quercus leucotrichophora A. Camus		Banjh oak	Garhwal region of Himalaya	Leaves and bark	MeOH	FA; linoleic acid in stem bark and leaves extracts and *cis*-vaccenic acid in stem bark	[55]
Vitex altissima L., *V. negundo* L. and *V. trifolia* L.	Lamiaceae	Peacock chaste tree, Chinese chaste tree, and simpleleaf chastetree, respectively	India	Leaves	Dry MeOH/benzene/sulfuric acid (200:100:10, *v*/*v*)	FAME	[56]
Linum usitatissimum L.	Linaceae	Common flax or linseed	Algeria	Seeds	Petroleum ether with Soxhlet extractor	FAME	[41]

Botanical Name	Family	Common Name	Country of Collection	Plant Part	Extracting Solvent/Method	Isolated Lipids or Lipid Mixtures	Ref.
Scaphium macropodum (Miq.) Beumee ex. Heyne	Malvaceae	Malva nut or Kembang semangkok	Malaysia	Stem bark	MeOH	Methyl hexadecanoate, hexadecanoic acid <*n*->	[57]
Melastoma malabathricum L.	Melastomataceae	Planter's rhododendron or Sendudok	Malaysia	Leaves	MeOH/H_2O (4:1, *v*/*v*), defatted with petroleum ether and extracted with $CHCl_3$. Lipids recovered after elution of the $CHCl_3$ extract by SiO_2 column with $CHCl_3$/acetone/MeOH (10:9:1, *v*/*v*).	Steryl glycoside: *β*-sitosterol 3-*O*-*β*-*D*-glucopyranoside	[58]
Azadirachta indica A. Juss	Meliaceae	Neem	India	Leaves	MeOH. Recovered after elution on a SiO_2 column with $CHCl_3$/MeOH (9:1, *v*/*v*)	SQDG	[59]
Azadirachta indica A. Juss		Neem	India	Leaves	Petroleum ether (60–80 °C) for 24 h and extracted thrice with MeOH for 48 h each time at room temperature	SQDG	[60]
Carapa guianensis Aubl. and *Carapa vasquezii* Kenfack		Andiroba	Brazil	Seed oil	*n*-hexane with Soxhlet extractor	FA, FAME, squalene, *β*-sitosterol	[42]
Ficus lutea Vahl	Moraceae	Giant-leaved fig or Lagos rubbertree	Cameroon	Woods	CH_2Cl_2/MeOH (1:1, *v*/*v*) and elution with EtOAc/10% MeOH	Glycosphingolipid [1-*O*-*β*-D-glucopyranosyl-(2*S*,3*R*,5*E*,12*E*)-2*N*-[(2′*R*)-hydroxyhexadecanoyl]-octadecasphinga-5,12-dienine] named lutaoside	[61]
Ficus pandurata Hance		Fiddle leaf fig	Egypt	Fruits	70% MeOH. MeOH extract fractionated on a SiO_2 column and purified by semi-preparative HPLC to afford pure ceramides	Ceramides [panduramides A-D, and newbouldiamide]	[62]
Kunzea ericoides (A. Rich) J. Thompson	Myrtaceae	Kanuka (Maori), white manuka (Maori) or the white tea tree (English)	Australia	Leaves and twigs	CH_2Cl_2:MeOH (1:1, *v*/*v*), CH_2Cl_2:MeOH (2:1, *v*/*v*) and CH_2Cl_2 (neat)	Steryl esters, triacylglycerols, free FA, sterols, and phospholipids	[63]

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and *Terminalia chebula* with EtOAc [66] and leaves of candle bush (*Senna alata*) and rhizomes of fingerroot (*Kaempferia pandurata*) with EtOH [67]. *β*-sitosterol 3-*O*-*β*-D-glucopyranoside, a steryl glycoside, was obtained from the leaves of Sendudok (*Melastoma malabathricum*) with $CHCl_3$/acetone/MeOH [58] and the acyl steryl glycosides sitosteryl 3-*β*-*O*-glucoside 6'-*O*-palmitate and stigmasteryl 3-*β*-*O*-glucoside 6'-*O*-palmitate were obtained from the roots of capotiraguá (*Blutaparon portulacoides*) with EtOH [44]. Glyceroglycolipids, namely sulfoquinovosyldiacylglycerols (SQDG) were retrieved from neem (*Azadirachta indica*) leaves by extracting with MeOH and separating by SiO_2 column chromatography with $CHCl_3$/MeOH [59] or extracted with petroleum ether and re-extracted with MeOH [60].

In the group of sphingolipids, different chemical structures were identified belonging to different subclasses: ceramides and glycosphingolipids, also known as cerebrosides (**Figure 1** and **Table 1**). Artemceramide-B was identified from the roots of *Artemisia incisa* after extraction with MeOH and recovered by SiO_2 column chromatography after elution of the extract with CH_2Cl_2/MeOH following previous elution with *n*-hexane/EtOAc [48]. A cerebroside (soya-cerebroside I), a sphingolipid glycoside (1-*O*-*β*-D-glucopyranosyl(2*S*,3*S*,4*R*,10*E*)-2-[(2'*R*)-2-hydroxytetracosanoylamino]-1,3,4-octadecanetriol-10-ene), and its aglycone form (2*S*,3*S*,4*R*,10*E*)-2-[(2'*R*)-2-hydroxytetra-cosanoylamino]-1,3,4-octadecanetriol-10-ene) were isolated from the stems of cucumber (*Cucumis sativus*) by $CHCl_3$ fractionation of the methanolic extract [50]. New glycosphingolipids were isolated and

Botanical Name	Family	Common Name	Country of Collection	Plant Part	Extracting Solvent/Method	Isolated Lipids or Lipid Mixtures	Ref.
Pentagonia gigantifolia Ducke	Rubiaceae		Peru	Roots	95% EtOH. EtOH extract was fractionated on a SiO_2 column using $CHCl_3$/MeOH from 0% to 100% MeOH. Fraction eluted with 2% MeOH/$CHCl_3$ was separated on C18 SiO_2 using 85% to 90% MeOH.	[61] Acetylenic acids: 6-octadecynoic acid and 6-nonadecynoic acid	[64]
					MeOH at 60 °C, suspended in water and successively		

Botanical Name	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (in mm) or Other	Isolated Lipids or Lipid Mixtures	Ref.
Sesuvium portulacastrum L.	G(+) bacteria: *Bacillus subtilis* NCIM 2063, *B. pumilus* NCIM 2327, *Micrococcus luteus* NCIM 2376 and *S. aureus* NCIM 2901; G(-) bacteria: *P. aeruginosa* NCIM 5031, *K. pneumoniae* NCIM 2957 and *E. coli* NCIM 2256. Ten isolates of MRSA and of MRSA NCTC 6571. Human pathogenic yeast type fungi: *Candida albicans*, *C. krusei*, *C. tropicalis* and *C. parapsilosis* and mould fungi: *Aspergillus niger*, *A. flavus*, and *A. fumigatus*	Inhibition zone (IZ) by disk diffusion test and minimum inhibitory concentration (MIC) by broth macrodilution method	Ciprofloxacin for bacteria, methicillin, oxacillin and vancomycin for MRSA and amphotericin-B for fungi	MIC: 0.25 mg/mL for *B. subtilis*, 0.5 mg/mL for *S. aureus*, MRSA, *P. aeruginosa*, *K. pneumoniae* and *C. albicans*, and 1.0 mg/mL for *E. coli*; MBC: 0.5 mg/mL for *B. subtilis*, 1.0 mg/mL for *S. aureus*, MRSA and *K. pneumoniae*, and 2.0 mg/mL for *P. aeruginosa* and *E. coli*; MFC: 1 mg/mL for *C. albicans*	FAME	[43]
Blutaparon portulacoides (A. St.-Hil.) Mears	*Trypanosoma cruzi*, *Leishmania amazonensis*, *S. aureus* ATCC 25923 and 7+ penicillinase producer, *Streptococcus epidermidis* (6ep), *E. coli* ATCC 10538, *Streptococcus mutans* (9.1), *Streptococcus sobrinus* (180.3)	Crude extracts and isolated compounds added to the trypomastigote-containing blood samples and incubated 24 h at 4 °C. Trypanocidal activity evaluated by counting the remaining trypomastigotes. *L. amazonensis* amastigote viability assessed colorimetrically by the reduction of a tetrazolium salt (MTT). Antimicrobial activity measured by the well-diffusionmethod in double layer	Gentian violet for trypanocidal activity and gentamicin for antibacterial assays	MIC: 100–500 µg/mL in *T. cruzi* trypomastigotes and 14–500 µg/mL in *L. amazonensis* amastigotes; 50 µg/mL in *E. coli*, *S. aureus* ATCC 25923, *S. aureus* (7+) and 500 µg/mL in *S. epidermidis*, *S. mutans*, and *S. sobrinus*	Acyl steryl glycosides (sitosteryl 3-*β*-*O*-glucoside 6'-*O*-palmitate and stigmasteryl 3-*β*-*O*-glucoside 6'-*O*-palmitate)	[44]

Botanical Name	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (in mm) or Other	Isolated Lipids or Lipid Mixtures	Ref.
Arthrocnemum indicum (Willd.) Moq., *Salicornia brachiata* Roxb., *Suaeda maritima* (L.) Dumort. *and Suaeda monoica* Forsk.	G(+) bacteria: *B. subtilis* NCIM 2063, *B. pumilus* NCIM 2327, *M. luteus* NCIM 2376, and *S. aureus* NCIM 2901; G(-) bacteria: *P. aeruginosa* NCIM 5031, *K. pneumoniae* NCIM 2957, and *E. coli* NCIM 2256; ten isolates of MRSA and of MRSA NCTC 6571; yeasts (*C. albicans, C. krusei, C. tropicalis,* and *C. parapsilosis)* and molds (*A. niger*, *A. flavus,* and *A. fumigatus*)	Disk diffusion method and broth macrodilution method	Ciprofloxacin for bacteria, methicillin, oxacillin and vancomycin for MRSA and amphotericin-B for fungi	MIC of 0.06 mg/mL of *S. brachiata* extracts against *B. subtilis*, *S. aureus,* and MRSA, and 0.5 mg/mL against *P. aeruginosa*; MIC of 0.5 mg/mL of all FAME extracts against *E. coli* and *K. pneumoniae*; MBC of 0.1 mg/mL of *S. brachiata* extracts against *P. aeruginosa* and of 1.0 mg/mL of all FAME extracts against *E. coli* and *K. pneumoniae*	FAME	[45]
Alternanthera brasiliana	*E. coli* ATCC 25922, *B. subtilis* ATCC 6623, *P. aeruginosa* ATCC 15442, *M. luteus* ATCC 9341, and *S. aureus* ATCC 25923	Microdilution broth method according to NCCLS standardization	Tetracycline and norfloxacin	MIC: 50 µg/mL against *B. subtilis*, *M. luteus,* and *S. aureus*	Linoleate oxylipins	[46]
Phoenix dactylifera L.	*Bacillus cereus* and *E. coli*	Disk diffusion method	Streptomycin	20 mm against *E. coli* and 17 mm against *B. cereus* at 1 mg/mL of the acetone extract	Sterol and triterpenes	[47]
Asphodelus aestivus Brot.	G(+) bacteria: *S. aureus* ATCC 6538-p, *E. faecalis* ATCC 29212; G(-) bacteria: *E. coli* ATCC 29998, *K. pneumoniae* ATCC 13883, *P. aeruginosa* ATCC 27853); yeasts: *C. albicans* ATCC 10239 and *C. krusei* ATCC 6258	Disk diffusion method and broth microdilution tests according to the recommendations of Clinical and Laboratory Standards Institute (CLSI)	Ampicillin, ciprofloxacin and fluconazole	MIC: 512 µg/mL against *S. aureus*, *E. faecalis*, *K. pneumoniae,* and *C. albicans*	FA (4:0, 6:0, 8:0, 10:0, 16:0, 18:0, 21:0, 24:0, 14:1, 15:1, 18:1n9t, 20:1, 24:1, 18:2, 18:2n6t, 18:2n6c, 20:2n6, 20:3n3, 22:6n3, and others unidentified)	[38]
Artemisia incisa Pamp.	*S. epidermidis* and *S. aureus*	Agar well diffusion method and MIC determined by a referenced method	Streptomycin and tetracycline	*S. epidermidis* (0.0157 mg/mL) and *S. aureus* (0.0313 mg/mL)	Artemceramide-B	[48]
Pteranthus dichotomus Forssk. (also known as *P. echinatus* Desf.)	*S. aureus* ATCC 25923, *E. coli* ATCC 25922, *K. pneumoniae* ESBL, and *Enterobacter sp.* ESBL	Disk diffusion method	Gentamicin and ampicillin	*P. dichotomus* BuOH extracts at 0.25 g/mL (8 mm against *E. coli*, *K. pneumoniae* ESBL); *P. dichotomus* EtOAc extract at 0.5 g/mL (7 mm against *E. coli*), at 65 mg/mL (8.33 mm against *S. aureus*), and at	BuOH fraction contained 1-*O*-palmitoyl-3-*O*-(6-sulfo-α-D-quinovopyranosyl)-glycerol, 1,2-di-*O*-palmitoyl-3-*O*-(6-sulfo-α-D-quinovopyranosyl)-glycerol and soya cerebroside I. EtOAc fraction contained stigmat-7-en-3-ol, spinasterol, *β*-sitosterol and *β*-sitosterol-3-*O*-glucoside	[49]

Botanical Name	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (in mm) or Other	Isolated Lipids or Lipid Mixtures	Ref.
				0.25 g/mL (7 mm against *Enterobacter sp.* ESBL)		
Cucumis sativus L.	Phytopathogenic fungi (*Pythium aphanidermatum*, *Botryosphaeria dothidea*, *Fusarium oxysporum* f.sp. *cucumerinum,* and *Botrytis cinerea*); phytopathogenic bacteria [G(-): *Xanthomonas vesicatoria* ATCC 11633, *Pseudomonas lachrymans* ATCC 11921, and G(+) *B. subtilis* ATCC 11562]	Mycelial radial growth inhibition assay and antifungal activity (pour plating method in potato dextrose agar medium) for fungi and agar-well diffusion assay for bacteria	Carbendazim for fungi and streptomycin sulfate for bacteria	5.5–100 inhibitory rate of mycelia growth inhibitory activity; IC_{50} of *B. subtilis* (50.2–110.9 µg/mL), *X. vesicatoria* (25.6–64.5 µg/mL), *P. lachrymans* (15.3–37.3 µg/mL) for sphingolipids	Sphingolipids [(2*S*,3*S*,4*R*,10*E*)-2-[(2′*R*)-2-hydroxytetracosanoylamino]-1,3,4-octadecanetriol-10-ene, 1-*O*-*β*-D-glucopyranosyl-(2*S*,3*S*,4*R*,10*E*)-2-[(2′*R*)-2-hydroxytetracosanoylamino]-1,3,4-octadecanetriol-10-ene and soya-cerebroside I]	[50]
Excoecaria agallocha	G(+) bacteria: *B. subtilis* NCIM 2063, *B. pumilus* NCIM 2327, *M. luteus* NCIM 2376, *S. aureus* NCIM 2901; G(-) bacteria: *P. aeruginosa* NCIM 5031, *K. pneumoniae* NICM 2957, and *E. coli* NCIM 2256; yeasts: *C. albicans*, *C. krusei*, *C. tropicalis,* and *C. parapsilosis*	Disk diffusion method for antibacterial and antifungal susceptibility tests; MIC tested in Mueller-Hinton broth for bacteria and yeast nitrogen base for yeasts by two-fold serial dilution method	Ciprofloxacin and amphotericin B	MIC: 0.125 mg for *B. subtilis* and *S. aureus*, 0.5 mg for *P. aeruginosa* and *K. pneumoniae*, and 1.0 mg for *E. coli*; MBC: 0.25 mg for *B. subtilis* and *S. aureus*, 1.0 mg for *P. aeruginosa* and *K. pneumoniae*, and 2.0 mg for *E. coli*; MFC: 1 mg for *C. albicans*, *C. krusei* and *C. parapsilosis*	FAME	[51]
Albizia adianthifolia (Schumach) and *Pterocarpus angolensis* (DC)	Bacteria (*E. coli*, *P. aeruginosa*, *B. subtilis*, *S. aureus*) and yeast (*C. albicans*)	Modified agar overlay method	Chloramphenicol for bacteria and miconazole for fungi	MIQ: 1 µg of *n*-hexane and $CHCl_3$ extracts of *A. adianthifolia* against *E. coli*; 50 µg of *n*-hexane and $CHCl_3$ extracts of *A. adianthifolia* against *P. aeruginosa*; 50 µg of $CHCl_3$ extract of *P. angolensis* against *B. subtilis* and 100 µg of *n*-hexane extract of *P. angolensis* against *B. subtilis* and *C. albicans*	*n*-hexadecanoic acid (palmitic acid); oleic acid; chondrillasterol; stigmasterol, 24S 5α-stigmast-7-en-3-ol; 9,12-octadecadienoic acid (*Z*,*Z*)-, methyl ester; *trans*-13-octadecanoic acid, methyl ester; tetradecanoic acid; hexadecanoic acid, methyl ester; octadecanoic acid	[52]
Baphia massaiensis	*E. coli*, *B. subtilis, P. aeruginosa*, *S. aureus,* and *C. albicans*	Agar well diffusion method	Not mentioned	10 mm of inhibition zone against *E. coli* and *S. aureus*, and 16 mm against *B. subtilis*	Seed oil (total FA)	[53]

Botanical Name	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (in mm) or Other	Isolated Lipids or Lipid Mixtures	Ref.
Cassia tora L. (or *Senna tora* L. Roxb.)	MRSA, MSSA, *B. subtilis*, and *P. aeruginosa*	Broth microdilution method	Ampicillin	MIC for all bacteria between 125–1000 µg/mL	FA (the major were palmitic acid, linoleic acid, linolenic acid, margaric acid, melissic acid, and behenic acid)	[39]
Trigonella foenum-graecum L.	G(-) bacteria: *E. coli* and *P. aeruginosa*; G(+) bacteria: *S. aureus* and *Streptococcus pyogenes*; acid-fast bacteria: *M. tuberculosis*; fungi: *C. albicans*, *A. niger* and *A. clavatus*; parasite *Plasmodium falciparum* (etiological agent of malaria)	Antimicrobial activity assessed by broth dilution method, anti-tuberculosis activity assessed by the slope method, in vitro anti-malarial assay according to a microassay protocol	Gentamycin, chloramphenicol, ciprofloxacin and norfloxacin for bacteria; isoniazid and rifampicin for mycobacteria; nystatin and greseofulvin for fungi; chloroquine and quinine as anti-malarials	MIC values of 100, 250, 125 µg/mL towards *E. coli*, *S. aureus,* and *S. pyogenes* and *P. aeruginosa*, respectively. MFC value of 250 µg/mL of *C. albicans*. MIC value of 100 µg/mL toward *M. tuberculosis* and of 0.29 µg/mL toward *P. falciparum*	Conjugated linoleic acid methyl ester, saturated FAME, steroids	[54]
Quercus leucotrichophora, A. Camus	G(+) bacteria: *B. subtilis* and *S. aureus*; G(-) bacteria: *P. aeruginosa* and *E. coli*	Disk diffusion method for antibacterial susceptibility tests; MIC was tested in Mueller-Hinton broth for bacteria by two-fold serial dilution method	Ciprofloxacin	MIC: 0.125 mg/mL for *B. subtilis* and *S. aureus*; 0.5 mg/mL for *P. aeruginosa* and 1.0 mg/mL for *E. coli*	FAME	[40]
Quercus leucotrichophora A. Camus	G(-) bacteria: *E. coli* MTCC-582 and *P. aeruginosa* MTCC-2295; G(+) bacteria: *S. aureus* MTCC-3160, *B. subtilis* MTCC-441 and *S. pyogenes* MTCC-1924	Disk diffusion method	Ampicillin	IZ of both extracts against all microorganisms: 8.53 ± 0.50 to 19.07 ± 0.31 mm	FA; linoleic acid in stem bark and leaves extracts and *cis*-vaccenic acid in stem bark	[55]
Vitex altissima L., *V. negundo* L. and *V. trifolia* L.	*Culex quinquefasciatus* (early fourth-instar larvae)	Larvicidal activity analyzed according to standard procedures (WHO-VBC 81.807, 1981)	Not mentioned	*V. trifolia* (LC_{50} = 9.26 ppm and LC_{90} = 21.28 ppm)	FAME [1]	[56]
Linum usitatissimum L.	*A. flavus* MTTC 2799 and *A. ochraceus* CECT 2092 [50]	Determination of percent mycelial inhibition by growth radial technique on solid medium and by biomass technique on liquid medium	Not mentioned	Antifungal index of FAME in solid medium: 54.19 ± 0.85 at 10 µL in *A. flavus* and 40.48 ± 0.12 at 90 µL for *A. ochraceus* at 90 µL	FAME [46]	[41]
Scaphium macropodum (Miq.)	*Mycobacterium smegmatis*, *E. coli*, *S. typhimurium*, *B. subtilis*, and *S. aureus*	Inhibitory activity of the extract by disk diffusion	Ampicillin and rifampicin	IZ of 10.67 ± 0.58 mm in *S. aureus* and of 9 mm	Methyl hexadecanoate, hexadecanoic acid <*n*->	[57]

Overhauser effect spectroscopy-NOESY, heteronuclear single quantum coherence-HSQC, and heteronuclear multiple bond correlation-HMBC) have been used for the identification of artemceramide-D [48] and glyceroglycolipids [60]. Other methods are regularly used for the analysis of lipid extracts or their fractionation, such as TLC [41][58][50][63], column chromatography as mentioned above, or paper chromatography, but the information is very limited [58]. Analysis of FA is mostly performed by GC-FID or GC-MS, after derivatization. Total lipid extracts or lipid fractions are subjected to derivatization techniques using acid or alkaline hydrolysis or transmethylation to obtain FAME.

To identify and/or quantify mixtures of compounds, simpler techniques can be applied as biochemical assays using colorimetric tests, as for instance, for sterols' and steryl glycosides' identification and quantification [67][58][60]. The data obtained for compounds' identification in these studies on antimicrobial plant lipids are normally compared with data reported in the literature, especially for spectroscopic data [60][65].

2.2. Susceptibility Testing, Inhibitory, and Microbicidal Activities of Plant Lipids

Several microbial strains were used in plant lipid studies, comprising Gram-positive bacteria, Gram-negative bacteria, acid-fast bacteria, yeasts, filamentous fungi, parasitic protozoa, and some MDR strains and/or hospital isolated strains, such as MRSA (**Table 2**).

Botanical Name	Tested (Micro)Organisms [65]	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (in mm) or Other	Isolated Lipids or Lipid Mixtures [48]	Ref.
Beumee ex. Heyne		method; broth microdilution assay (MTT assay) was used to determine the MIC; MBC was determined via streak plate method		in *P. aeruginosa* at 0.25 [46]mg/mL. *S. aureus* showed the lowest MIC (0.78 mg/mL) and MBC (3.13 mg/mL). For *M. smegmatis*, MIC value was 3.13 mg/mL and MBC was 25 mg/mL [45]		
Melastoma malabathricum L.	*S. aureus* ATCC 25923, *B. cereus* ATCC 10876, *P. aeruginosa* ATCC 17853, *S. typhi* laboratory strain	[48] Disk diffusion method	Rifampicin	*P. aeruginosa* (9 mm at 0.25 mg/mL), *S. aureus* (7 mm, 1 mg/mL), *S. typhi* (9 mm at 1 mg/mL), *B. cereus* (10.5 mm at 2 mg/mL)	Steryl glycoside: *β*-sitosterol 3-*O*-*β*-D-glucopyranoside	[58]
Azadirachta indica A. Juss	Multidrug-resistant clinical isolates of *S. aureus*, *Salmonella enterica* serovar *typhi*, *S. dysenteriae*, *E. coli*, *Vibrio cholerae*, *K. pneumoniae,* and *P. aeruginosa*	MIC determined by microbroth dilution method and antibacterial sensitivity of SQDG determined by disk diffusion method (CLSI protocol)	Not mentioned [46]	MIC of 32 µg/mL for *S. typhi* and two isolates of *S. dysenteriae*; MIC of 64 µg/mL for three isolates of *S. typhi*, *E. coli* and *V. cholerae* and 256 µg/mL for *K. pneumoniae*	SQDG	[59]
Azadirachta indica A. Juss [39]	*Raillietina* spp. (helminth parasite)	Ultrastructural changes by scanning electron microscopy	Praziquantel	Anthelmintic activity of SQDG with 0.5 and 1 mg/mL, respectively: paralysis time of 1 h and 0.7 h; death time of 1.6 h and 0.9 h [51]	SQDG	[60]
Carapa guianensis and *Carapa vasquezii*	[52] Phytopathogenic fungi: *A. flavus*, *A. niger,* and *F. oxysporum*	Fungal mycelial growth inhibition trials developed in 96-well microtiter plates adding 10 µL of conidia suspensions (2 × 10^5 conidia mL^{-1}) and 90 µL yeast peptone dextrose. Inhibition of germination observed under light microscopy	20 mM hydrogen peroxide	MIC (µg/mL): 125–250 of *C. guianensis* and [53]6–125 of *C. vasquezii* against the three phytopathogenic fungi	FA, FAME, squalene, *β*-sitosterol	[42]
Ficus lutea Vahl	*Mucor miehei* and *B. subtilis*	Disk diffusion method	Nystatin [52]	IZ of 17 mm for *M. miehei*; of 16 mm for *B. subtilis*; and of 12 mm for *C. albicans* exposed to 40 µg of compound	Glycosphingolipid [1-*O*-*β*-D-glucopyranosyl-(2*S*,3*R*,5*E*,12*E*)-2*N*-[(2′*R*)-hydroxyhexadecanoyl]-	[61]

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of *B. portulacoides* (50 µg/mL) [44]. Also with low MIC values, the FAME extracted from the shoots of *S. brachiata* (0.5 mg/mL) [45] and the FAME and steroids from *Trigonella foenum-graecum* seeds (100 µg/mL) [54]. A MBC range between 1.0 and 2.0 mg/mL was verified for FAME extracts from the leaves of different plants [43][45][51].

Some lipid extracts were found to have low MIC against *P. aeruginosa*, as the FA and their derivatives obtained from the *n*-hexane and $CHCl_3$ extracts of the heartwood of *A. adianthifolia* (50 µg) [52], FAME and steroids from fenugreek seeds (*T. foenum-graecum*, 100 µg/mL) [54], and the SQDG extracted from the neem leaves (*A. indica*, 128 µg/mL) [59]. MBC toward *P. aeruginosa* between 0.1 and 2.0 mg/mL were verified for the extracts of FAME from leaves of different plants [43][45][51], similarly to the findings for the *E. coli* strains.

For strains of *Salmonella typhimurium*, a high MIC value of 25 mg/mL was obtained from the stem bark extract of *S. macropodum* which contained four compounds including two FA (hexadecanoate methyl and hexadecanoic acid <*n*->) [57]. The SQDG extracted from the neem leaves showed antimicrobial activity against MDR strains of *Salmonella typhi* and *Shigella dysenteriae*, both with a MIC range between 32 and 64 µg/mL, and also against MDR strains of *E. coli* (64–128 µg/mL), *P. aeruginosa* (128 µg/mL), *S. aureus* (128–256 µg/mL), and *K. pneumoniae* (256 µg/mL) [59]. Also, identical MIC values (0.5 mg/mL) of FAME extracts [43][45][51] and FA [38] from different plants were observed against *K. pneumoniae*.

Botanical Name	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (in mm) or Other	Isolated Lipids or Lipid Mixtures	Ref.
					octadecasphinga-5,12-dienine] named lutaoside	[54]
Ficus pandurata Hance	Yeast: *C. albicans* ATCC 90028, *C. glabrata* ATCC 90030, *C. krusei* ATCC 6258, *A. fumigatus* ATCC 90906, MRSA ATCC 33591, *Cryptococcus neoformans* ATCC 90113, *S. aureus* ATCC 2921, *E. coli* ATCC 35218, *K. pneumoniae* ATCC 13883, *P. aeruginosa* ATCC 27853, and *Mycobacterium intracellulare* ATCC 23068); chloroquine sensitive (D6, Sierra Leone) and resistant (W2, Indochina) strains of *Plasmodium falciparum*; parasite: *Leishmania donovani* promastigotes	Modified versions of the NCCLS methods	Antibacterial agent and antifungal agents not mentioned; antimalarial agents: chloroquine and artemisinin; anti-leishmanial agents: pentamidine and amphotericin B	No activity was observed for any compound [65]	Ceramides [panduramides A-D, and newbouldiamide]	[62]
Kunzea ericoides (A. Rich) J. Thompson	*E. coli* ATCC 25922 and *S. aureus* ATCC 25923	Broth microdilution method utilizing the redox dye resazurin	Not mentioned	0.625–10 mg/mL for *S. aureus* and more than 10 mg/mL in *E. coli*	Steryl esters, triacylglycerols, free FA, sterols and phospholipids	[63]
Pentagonia gigantifolia Ducke	*C. albicans* ATCC 90028 and fluconazole-resistant *C. albicans* strains [69]	MIC and MFC determined by using a modified version of the microdilution NCCLS methods; sphingolipid reversal assay	Amphotericin B, fluconazole and flucytosine [70]	*C. albicans* ATCC 90028 (0.52 to 1.04 µg/mL)	Acetylenic acids: 6-octadecynoic acid and 6-nonadecynoic acid [59]	[64]
Hedyotis pilulifera (Pit.) T.N. Ninh	*S. aureus* NBRC 100910, *B. subtilis* NBRC 13719, *M. smegmatis* NBRC 13167	Microdilution method	Ampicillin	Oleanolic acid (MIC value of 2.5 µg/mL against *M. smegmatis*), rotungenic acid (MIC value of 2.5, 2.5, and 1.25 µg/mL against *S. aureus*, *B. subtilis*, and *M. smegmatis*, respectively), rotundic acid (MIC value of 5 µg/mL against *B. subtilis*)	Triterpenoids, steroids, FA, glycolipids, and a ceramide	[65]
Withania somnifera (L.) Dunal, *Euphorbia hirta* L., *Terminalia chebula* Retz.	*E. coli* MTCC 46, *P. aeruginosa* MTCC 1934), *Proteus mirabilis* MTCC 3310, *Raoultella planticola* MTCC 2271, *Enterobacter aerogenes* (now *Klebsiella aerogenes*) MTCC 2822, *B. subtilis* MTCC 121, *S. aureus* MTCC 3160	Disk diffusion method for antibiotic susceptibility testing. Broth microdilution method for determination of MIC values	Streptomycin	MIC: *W. somnifera* leaf (0.039 mg/mL on *P. aeruginosa*); *T. chebula* fruits and stems (0.039 mg/mL on *E. coli*) and *T. chebula* stems and fruits (0.039 mg/mL on *S.*	Sterols fraction [71][72][73]	[66]

However, lipids are ubiquitously distributed in the different marine phyla, being quite abundant in some of them. Besides, several lipid classes from marine organisms have been recognized by their biological activity with a high potential to discover new antimicrobial compounds.

3.1. Marine Algae

Algal biomass is mainly composed by minerals, sugars, proteins, and lipids, that represent 1–15%, depending on the algal species and its habitat. Lipids found in the macroalgae from the three phyla, Rhodophyta, Chlorophyta, and Ochrophyta (**Table 3**), have demonstrated antimicrobial activity against Gram-positive and Gram-negative bacteria, yeasts, and fungi [74][75][76][77][78] (**Table 4**). Most of these antimicrobial lipids were isolated from Rhodophyta and Chlorophyta. While the former shows a high diversity of algal species as source of antimicrobial lipids, studies in Chlorophyta were focused on species belonging to the order Bryopsidales.

Table 3. Algae lipids and lipid-rich extracts with antimicrobial potential, their origin and extraction method.

Scientific Name	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Methods for Compounds Identification	Ref.
Macroalgae–Chlorophyta					

Scientific Name	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Methods for Compounds Identification	Ref.
Caulerpa racemosa	Qionghai, Hainan, China	EtOH (95%). Extract partitioned with EtOAc and *n*-BuOH	SQDG [2S-1,2-di-*O*-palmitoyl-3-*O*-(6'sulfo-α-D-quinovopyranosyl) glycerol]	^{1}H and ^{13}C NMR, ESI-MS	[79]
Caulerpa racemosa, Caulerpa lentillifera	Port Dickson, Malaysia	$CHCl_3$, MeOH	PUFA, MUFA, Terpenoids	LC-MS	[80]
Caulerpa racemosa, Ulva fasciata	Buzios, Rio de Janeiro, Brazil	Acetone insoluble material extracted with $CHCl_3$/MeOH (2:1 and 1:2, *v*/*v*). Lipid extract partitioned on SiO_2 column, eluted with $CHCl_3$, acetone or MeOH	Glycolipid-rich extracts (Sulfoglycolipids, Glycosyldiacylglycerols)	HPTLC	[81]
Caulerpa spp., *Chlorodesmis fastigiata, Halimeda* spp., *Penicillus capitatus, Penicillus dumentosus, Penicillus pyriformis, Rhipocephalus phoenix, Udotea argentea, Udotea cyathiformis, Udotea flabellum, Udotea petiolata*	Bahamas, Florida Keys, Puerto Rico, Belize, Guan, Hawaii, Australia, Mediterranean Sea	CH_2Cl_2. Chlorophylls removed with MgO_3Si. Fractionation with SiO_2 column and purification by HPLC	Sequiterpenoids, Diterpenoids	TLC, NMR, HPLC	[82]
Chaetomorpha linum	IMTA, Mar Piccolo of Taranto, Italy	$CHCl_3$/MeOH (2:1, *v*/*v*), Soxhlet extractor, EtOH (95%)	Lipid extracts	^{1}H and ^{13}C NMR, 1D and 2D NMR, GC-FID, TLC	[83]
Codium amplivesiculatum	Bahía Magdalena, Mexico	CH_2Cl_2/EtOH (97:3, *v*/*v*). Liquid/liquid extraction CH_2Cl_2/H_2O. Fractionation with CH_2Cl_2. Crystallization in hot MeOH	Fraction with clerosterol as main constituent. Isolated clerosterol did not show activity	^{1}H NMR, IR	[84]
Ulva fasciata	Malvan, India	EtOH, fractionated by neutral alumina column with EtOAc/MeOH	Sphingosine (major component: *N*-palmitoyl-2-amino-1,3,4,5-tetrahydroxyoctadecane)	^{1}H and ^{13}C NMR, FAB-MS, IR	[85]
	Malvan, India	EtOH (90%). Extract fractionated. *n*-hexane fraction chromatographed on SiO_2 and flash SiO_2	Ceramide (Erythro-sphinga-4,8-dienine-*N*-palmitate)	^{1}H and ^{13}C NMR, ESI-MS, GC-MS, IR	[86]
	Mediterranean Sea, Egypt	$CHCl_3$/MeOH (2:1, *v*/*v*). Glycolipid separation using	Glycolipid-rich extracts (DGDG)	GC-FID, LC-MS/MS	[87]

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Scientific Name	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Methods for Compounds Identification	Ref.
		acetone on SiO_2 column			
	Mediterranean Sea, Egypt	MeOH/$CHCl_3$ (2:1, *v*/*v*). Sulfolipid isolation: diethylaminoethyl-cellulose column eluted with $CHCl_3$/MeOH (6:4, *v*/*v*) and NH_3	Sulfolipids (SQDG)	GC-MS, GC-FID, LC-MS/MS, IR	[75]
Ulva rigida	Cap Zebib and Ghar El Melh, Tunisia	CH_2Cl_2 and CH_2Cl_2/MeOH (1:1, *v*/*v*). Extracts fractionated on SiO_2 column and TLC with *n*-hexane/EtOAc/CH_2Cl_2/MeOH	FA	^1H and ^{13}C NMR, GC	[27]
		Macroalgae–Rhodophyta			
Chondria armata	Goa, West coast of India; Mumbai, India	MeOH and $CHCl_3$, Polar fractions: petroleum ether/EtOAc (1:1, *v*/*v*), MeOH/$CHCl_3$ (2:98, *v*/*v*), MeOH/$CHCl_3$ (5:95, *v*/*v*)	Neutral glycolipids [main compound MGDG(20:5/16:0)]	^1H and ^{13}C NMR, ESI-MS/MS	[88]
Chondrus crispus, Gracilaria vermiculophylla, Porphyra dioica	IMTA and Portuguese coast, Portugal	EtOAc in Soxhlet extractor	FA	GC-FID	[89]
Falkenbergia (heteromorphic sporophyte of *Asparagopsis taxiformis*)	Kollam coast, India	MeOH. Fractionation on SiO_2 column (petroleum ether/EtOAc and EtOAc/MeOH). Purification with TLC and RP HPLC	FA	GC-MS	[90]
Galaxaura cylindrica, Laurencia papillosa	Red Sea, Egypt	$CHCl_3$/MeOH (2:1, *v*/*v*). Glycolipid separation using acetone on SiO_2 columns	Glycolipid-rich extracts (DGDG)	LC-MS/MS	[87]
	Red Sea, Egypt	MeOH/$CHCl_3$ (2:1, *v*/*v*). Sulfolipid isolation: diethylaminoethyl-cellulose column ($CHCl_3$/MeOH (6:4, *v*/*v*) and NH_3)	Sulfolipids (SQDG)	GC-MS, GC-FID, LC-MS/MS, IR	[75]
Gigartina tenella	Sagami Bay, Kanagawa, Japan	Acetone. Extract partitioned with EtOAc/H_2O (3:1, *v*/*v*). Organic layer dissolved in EtOAc/MeOH/H_2O (100:20:5, *v*/*v*) and	Glycolipid (Sulfolipids)	^1H and ^{13}C NMR, HR-FAB-MS	[91]

Scientific Name	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Methods for Compounds Identification	Ref.
		chromatographed on SiO_2 column			
Gracilaria gracilis	Ganzirri lagoon and Margi channel, Eastern Sicily, Italy	$CHCl_3$, Et_2O in Soxhlet extractor	FA	GC-FID	[92]
Gracilariopsis longissima	Mar Piccolo of Taranto, Italy	$CHCl_3$/MeOH/H_2O (2:1:1, *v*/*v*)	FA	^1H and ^{13}C NMR, 1D and 2D NMR, GC-FID	[93]
Hypnea musciformis, Osmundaria obtusiloba, Porphyra acanthophora, Pterocladiella capillacea	Buzios, Rio de Janeiro, Brazil	Acetone insoluble material extracted with $CHCl_3$/MeOH (2:1 and 1:2, *v*/*v*). Extract partitioned on SiO_2 column ($CHCl_3$, acetone or MeOH)	Glycolipid-rich extracts (Sulfolipids, Glycosyldiacylglycerols)	HPTLC	[81]
Jania corniculata, Laurencia papillosa	Suez Canal, Egypt	EtOH (70%), CH_2Cl_2	FA	GC-MS	[94]
Laurencia okamurai	Nanji Island in the East China Sea, Zhejiang Province, China	EtOH (95%) extract partitioned with Et_2O and fractionated by SiO_2 (gradient system: petroleum ether – CH_2Cl_2 (10:0 → 1:9)), Sephadex column, and purification by semi-preparative C18 HPLC	FA ethyl esters [(9*Z*,12*Z*,15*Z*,18*Z*,21*Z*)-ethyl tetracosa-9,12,15,18,21-Pentaenoate, (10*Z*,13*Z*)-ethyl nonadeca-10,13-dienoate, (9*Z*,12*Z*)-ethyl nonadeca-9,12-dienoate, (*Z*)-ethyl octadec-13-enoate (4), and (*Z*)-ethyl hexadec-11-enoate]	^1H and ^{13}C NMR, 1D and 2D NMR, IR, HR-EI-MS	[95]
Laurencia spp.	Pulau Tioman, Pahang, Pulau Karah, Terengganu, Pulau Nyireh, Terengganu, Malaysia	MeOH. Extract partitioned with Et_2O and H_2O and fractionated by SiO_2 column (hexane/EtOAc)	Sesquiterpenes (Halogenated sesquiterpenes)	^1H and ^{13}C NMR, LREIMS, HREIMS	[96]
Osmundaria obtusiloba	Buzios, Rio de Janeiro, Brazil	Acetone insoluble material extracted with $CHCl_3$/MeOH (2:1 and 1:2, *v*/*v*). Extract	Glycolipids (Sulfoglycolipids)	^1H and ^{13}C NMR, ESI-MS/MS	[97]

Scientific Name	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Methods for Compounds Identification	Ref.
		partitioned ($CHCl_3$/MeOH/0.75% KCl (8:4:3, *v*/*v*)). Fractionation on SiO_2 column ($CHCl_3$, acetone and MeOH). MeOH fraction purified on SiO_2 column ($CHCl_3$/MeOH, 90:10, *v*/*v*)			
Palmaria palmata, Grateloupia turuturu	Batz-sur-Mer, France	CH_2Cl_2/MeOH (2:1, *v*/*v*), MeOH/H_2O (1:1, *v*/*v*)	Polar lipids	^1H and ^{13}C NMR	[98]
Pyropia orbicularis	Maitencillo, Chile	MeOH, acetone, CH_2Cl_2, *n*-hexane. Soxhlet extractor. *n*-hexane extract fractionated on SiO_2 column (2, 10, 20, 30 and 100% acetone)	Phospholipids (main compounds PC-O, PE, PS, PI, SM, GlCer), Glycolipids (MGDG), Triacylglycerol, DAG	LC-ESI-MS/MS	[99]
Sphaerococcus coronopifolius	Atlantic coast of Morocco	MeOH/CH_2Cl_2. Extract separated on SiO_2 column (hexane, gradients of hexane/CH_2Cl_2 and CH_2Cl_2/acetone, and MeOH)	Bromoditerpenes (Sphaerolabdadiene-3,14-diol (1), Sphaerococcenol)	^1H and ^{13}C NMR, HRMS, EIMS, CIMS, FTIR, UV	[100]
		Macroalgae–Ochrophyta			
Dictyota cervicornis, Dictyota menstrualis	Buzios, Rio de Janeiro, Brazil	Acetone insoluble material extracted with $CHCl_3$/MeOH (2:1 and 1:2, *v*/*v*). Extract partitioned on SiO_2 column ($CHCl_3$, acetone or MeOH)	Glycolipid-rich extracts (Sulfoglycolipids, Glycosyldiacylglycerols)	HPTLC	[81]
Dictyota fasciola, Taonia atomaria	Mediterranean Sea, Egypt	$CHCl_3$/MeOH (2:1, *v*/*v*). Glycolipid separation using acetone on SiO_2 column	Glycolipid-rich extracts (DGDG)	GC-FID, LC-MS/MS	[87]
	Mediterranean Sea, Egypt	MeOH/$CHCl_3$ (2:1, *v*/*v*). Sulfolipid isolation: diethylaminoethyl-cellulose column ($CHCl_3$/MeOH (6:4, *v*/*v*) and NH_3)	Glycolipids (Sulfolipids)	GC-MS, GC-FID, LC-MS/MS, IR	[75]
Fucus evanescens	West coast of Ungava Bay, Canada	EtOAc (99%), CH_2Cl_2. EtOAc algal extract acetylated and organic layer purified by flash chromatography (0% → 50% EtOAc in hexane and flushed with 100% EtOAc and 5% MeOH in 95% EtOAc)	Glycolipid-rich extracts	^1H and ^{13}C NMR	[101]

Scientific Name	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Methods for Compounds Identification	Ref.
Himanthalia elongata	Las Palmas, Spain	Pressurized liquid extraction Hexane, EtOH, H_2O	Sterol (Fucosterol), FA	GC-MS, HPLC-DAD	[102]
Laminaria cichorioides	Khasan region of the Primorskii Territory, in the Troitsa Gulf (the Sea of Japan), Russia	EtOH (96%). Lipophilic fraction extracted with $CHCl_3$. Fractionation of lipid classes on SiO_2 column	Glycolipids (MGDG, DGDG, SQDG), Free FA, PUFA		[77]
Sargassum dentifolium	Suez Canal,	EtOH (70%), CH_2Cl_2	FA	GC-MS	[94]

Scientific Name	Antimicrobial Activity	Tested Microorganisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (IZ, in mm) or Other	Ref.
Macroalgae–Chlorophyta						
Caulerpa racemosa	Antiviral	Viruses: Cox B3, HSV	Cytopathic effect (CPE) reduction assay, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) method	Acyclovir (HSV), Ribavirin (Cox B3)	IC_{50}/CC_{50} (μg/mL)/SI Cox B3: 31.3/500/16 HSV: 7.9/250	[79]
Caulerpa racemosa, Caulerpa lentillifera	Antibacterial	G(+):MRSA (MTCC 381123) G(-): *E. coli* K1 (MTCC 710859)	Disk diffusion method, crude extracts ($CHCl_3$ and MeOH)	Penicillin-streptomycin	PI: 97.7% (*C. racemosa*)	[80]
Caulerpa racemosa, Ulva fasciata	Antiviral	Viruses: HSV-1-ACVs, HSV-1-ACVr	Titer reduction			[81]
Caulerpa spp., *Chlorodesmis fastigiata, Halimeda* spp., *Penicillus capitatus, Penicillus dumentosus, Penicillus pyriformis, Rhipocephalus phoenix, Udotea argentea, Udotea cyathiformis, Udotea flabellum, Udotea petiolata*	Antibacterial, Antifungal	G(-):*Serratia marinoruba, Vibrio splendida, V. harveyi, V. leiognathi, Vibrio* sp. Undescribed bacteria: VJP Cal8101, VJP Cal8102, VJP Cal8103 Fungi: *Leptosphaeria* sp. *Lulworthia* sp., *Alternaria* sp., *Dreschleria haloides, Lindra thallasiae*, Undescribed fungi: VJP Cal8104, VJP Cal8105	Plate assay-disk method		IZ (mm) > 2	[82]
Chaetomorpha linum	Antibacterial	G(+): *Pseudomonas* sp., *Staphylococcus* sp., *Streptococcus agalactiae*, *Enterococcus* sp. G(-): *Vibrio alginolyticus, V. harveyi, V. mediterranei, V. ordalii, V. parahaemolyticus, V. salmonicida, V. vulnificus*	Disk diffusion method		IZ (mm) *V. ordalii*: 8–12 *V. vulnificus*: 8–12	[83]
Chaetoceros muelleri			Supercritical fluid extraction, EtOH (99.5%)	Triacylglycerol, DAG, MAG, sterols (cholesterol), FA	HPLC-ELSD, GC-FID	[107]
Chlorococcum HS-101	Japan		MeOH extract, partitioned with hexane. SiO_2 column ($MeOH/CHCl_3$ gradient).	FA	^1H and ^{13}C NMR, GC-MS	[108]

Scientific Name	Antimicrobial Activity	Tested Microorganisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (IZ, in mm) or Other	Ref.
		Yeast: *C. albicans*, *Candida famata, C. glabrata*				
Codium amplivesiculatum	Antibacterial	G(+): *S. aureus* (ATCC BAA-42, resistant to methicillin, penicillin, ampicillin/sulbactam, oxacillin, cefalotine) G(-): *V. parahaemolyticus* (17802)	Disk diffusion method		MIC (µg/mL)/IZ (mm) *S. aureus:* 125/15 *V. parahaemolyticus:* >250/8	[84]
Ulva fasciata	Antiviral	Virus: Semeliki Forest Virus (SFV)			20 mg/mouse/7 days by giving 50% protection	[85]
	Antiviral	Viruses: Japanese encephalitis virus (JEV), encephalomyocarditis (EMC) virus	96-well microtiter plates		CC_{50} (µg/mL)/EC_{50} (µg/mL)/TI JEV: 7.8/3.9/2.0	[86]
	Antifungal, Antiviral	Yeast: *C. albicans;* Fungus: *A. niger* Virus: HSV-1	Disk diffusion method; plaque reduction assay (antiviral)		MIC (µg/mL)/IZ (mm) *C. albicans:* 60/8, *A. niger*: 80/13 HSV-1: 9.37–15.62%	[87]
	Antibacterial, Antiviral	G(+):*B. subtilis* RRL B-94 G(-): *E. coli* NRRL B-3703 Virus: HSV-1	Disk diffusion method	Chloramphenicol (bacteria), Acyclovir (virus)	MIC (µg/mL)/IZ (mm) PI(%) *E. coli*: 60/13 *B. subtilis*: 40/16 HSV-1: 18.75–46.87%	[75]
Ulva rigida	Antibacterial	G(+): *S. agalactiae, S. aureus* (ATCC 25923), *S. aureus* (ATCC 6538), *E. faecalis* (ATCC 29212), *Micrococcus* sp. G(-): *Vibrio tapetis* (CECT4600), *V. anguillarum* (ATCC 12964T), *V. alginolyticus* (ATCC 17749T), *E. coli* O126-B16 (ATTC 14948), *E. coli* (ATCC 25922), *E. coli* (ATCC 8739), *Pseudomonas cepacia, P. fluorescens* (AH2), *P. aeruginosa* (ATCC 27853), *Aeromonas salmonicida* (LMG3780), *A. hydrophila* B3, *S. typhimurium* (C52) Yeast: *C. albicans* (ATCC10231)	Disk diffusion method and broth microdilution technique		IZ (mm) 6.3–16.3	[27]
		Macroalgae–Rhodophyta				
Chondria armata	Antibacterial, Antifungal	G(+): *S. aureus* G(-): *E. coli, P. aeruginosa, S. typhi, Salmonella flexneri, Klebsiella* sp., *V. cholerae* Yeast: *C. albicans, C. neoformans, Rhodotorula* sp. Fungi: *Aspergillus fumigatus, A. niger*	Disk diffusion method	Streptomycin, Nystatin	1 < IZ ≤ 4	[88]
Chondrus crispus, Gracilaria vermiculophylla, Porphyra dioica	Antibacterial, Antifungal	G(+): *Listeria innocua* (NCTC 11286), *B. cereus* (ATCC 11778), *E. faecalis* (LMG S 19456 5002), *Lactobacillus brevis* (LMG 6906), *S. aureus* (ATCC 6538), MRSA G(-): *E. coli* (ATCC 8739), *Salmonella enteritidis* (ATCC 3076), *P. aeruginosa* (ATTC 10145) Yeast: *Candida* spp. (CCUG 49242)	Disk diffusion method	Ampicillin (*L. innocua*), Cycloheximide (*Candida* spp.), Chloramphenicol	IZ (mm) *C. crispus:* 5 < IZ ≤ 20 *G. vermiculophylla:* 10 < IZ ≤ 15 *P. dioica:* 5 < IZ ≤ 12	[89]
			100%)). Fractionated by RP HPLC			
Synechocystis sp.		Las Palmas, Spain	Pressurized liquid extraction: hexane, EtOH, H_2O	FA, Sesquiterpenoids (Neophytadiene)	GC-MS, HPLC-DAD	[102]

Scientific Name	Antimicrobial Activity	Tested Microorganisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (IZ, in mm) or Other	Ref.
				(other microorganisms)		
Falkenbergia (heteromorphic sporophyte of *Asparagopsis taxiformis*)	Antibacterial	G(+): *S. epidermidis*, *S. aureus*, *B. subtilis* G(-): *V. vulnificus* (MTCC 1145), *V. parahaemolyticus* (MTCC 451), *V. harveyi* (MTCC 3438), *V. alginolyticus* (MTCC 4439), *V. alcaligenes* (MTCC 4442), *P. aeruginosa*, *K. pneumoniae*	Broth dilution method	Chloramphenicol, Nalidixic acid	IZ (mm)/MIC (μg)/MBC (μg) *S. epidermidis*: 21/1250/270 *S. aureus*: 21/750/170 *B. subtilis*: 23/750/180 *V. vulnificus*: 31/750/90 *V. parahaemolyticus:* 28/750/110 *V. harveyi*: 26/750/60 *V. alginolyticus*: 32/500/80 *V. alcaligenes*: 33/500/50 *P. aeruginosa*: 19/1250/420 *K. pneumoniae*: 15/1250/380	[90]
Galaxaura cylindrica, *Laurencia papillosa*	Antiviral	Virus: HSV-1	Plaque reduction assay	*Acyclovir*	Inhibition (%) *L. papillosa*: 9.37–31.25 *G. cylindrica*: 15.62–28.12	[87]
	Antibacterial, Antiviral	G(+): *B. subtilis NRRL B-94* G(-): *E. coli NRRL B-3703* Virus: (HSV-1)	Disk diffusion method	Chloramphenicol (bacteria), Acyclovir (virus)	MIC (μg/mL)/IZ (mm) PI(%) *L. papillosa* *E. coli*: -/8 *B. subtilis*: -/11 HSV-1: 40.62–59.37% *G. cylindrica* *E. coli*: 80/11 *B. subtilis*: 80/11 HSV-1: 45.87–59.37%	[75]
Gigartina tenella	Antiviral	HIV-reverse transcriptase type 1			IC_{50} 11.2 μM	[91]
Gracilaria gracilis	Antibacterial	G(+): *B. subtilis* G(-): *V. fischeri*, *V. cholerae*, *P. aeruginosa*, *Salmonella* sp., *A. hydrophila*	Disk diffusion method	Chloramphenicol	MIC: 5 μg/disk IZ (mm) *B. subtilis* 10.3–17.6 ($CHCl_3$)/10–15.6 (Et_2O)	[92]
Gracilariopsis longissima	Antibacterial, Antifungal	G(+): *S. agalactiae*, *Enterococcus* sp. G(-): *P. aeruginosa*, *V. salmonicida*, *V. fluvialis*, *V. vulnificus*, *V. cholerae* non-O1, *V. alginolyticus* Yeast: *C. albicans*, *C. famata*, *C. glabrata*	Disk diffusion method		IZ (mm) *V. alginolyticus*: 25 *V. fluvialis*: 8 *V. vulnificus*: 15 *V. cholerae* non-O-1:10	[93]
Hypnea musciformis, *Osmundaria obtusiloba*, *Porphyra acanthophora*, *Pterocladiella capillacea*	Antiviral	Virus: HSV-1-ACVs, HSV-1-ACVr	Titer reduction		PI(%)/VII *O. obtusiloba* ACVs-HSV-1: 82.2–99.5/0.75–2.35	[81]

Scientific Name	Antimicrobial Activity	Tested Microorganisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (IZ, in mm) or Other	Ref.
					HSV-1-ACVr: 99.7–99.9/2.5–4.5	
Jania corniculata, Laurencia papillosa	Antibacterial, Antifungal	G(+): *B. subtilis, Staphylococcus albus, E. faecalis* G(-): *E. coli* Yeast: *C. albicans* Fungus: *A. flavus*	Disk diffusion method		11 < IZ ≤ 15 No IZ (*A. flavus*)	[94]
Laurencia okamurai	Antifungal	Yeast: *C. neoformans* (32609), *C. glabrata* (537) Fungi: *Trichophyton rubrum* (Cmccftla), *A. fumigatus* (07544)	Broth dilution method	Amphotericin B, fluconazole, voriconazole, ketoconazole	MIC_{80} (µg/mL) *C. neoformans*: 8–64 *C. glabrata*: 4–64 *A. fumigatus*: >64 *T. rubrum*: 64	[95]
Laurencia spp.	Antibacterial	G(-): *Chromobacterium violaceum, P. mirabilis, P. vulgaris, Erwinia* sp., *V. parahaemolyticus, V. alginolyticus*	Disk diffusion method		MIC (µg/disk) *C. violaceum*: 10–40 *P. mirabilis*: 20–40 *P. vulgaris*: 20–40 *Erwinia* sp.: 10–30 *V. parahaemolyticus*: 20–40 *V. alginolyticus*: 20–30	[96]
Osmundaria obtusiloba	Antiviral	Virus: HSV-1, HSV-2	Titer reduction	Acyclovir	EC_{50} (µg/mL)/SI/PI(%) HSV-1: 42/1.7/75 HSV-2: 12/6/96	[97]
Palmaria palmata, Grateloupia turuturu	Antibacterial	G(-): *V. harveyi* ORM4	Broth microdilution method		0.2 < PI ≤ 7.9%	[98]
Pyropia orbicularis	Antibacterial	G(+): *S. aureus, B. cereus* G(-): *E. coli*	Disk diffusion method	Kanamycin	16 < IZ < 26	[99]
Sphaerococcus coronopifolius	Antibacterial, Antiplasmodial	G(+): *S. aureus* (ATCC # 6538) Parasitic protozoa: *P. falsciparum* (FCB1)	Antibacterial: Disk-diffusion, Antimalarial: inhibition of [^{3}H]-hypoxanthine uptake by *P. falsciparum* cultured in human blood		*S. aureus*-MIC: 0.104–0–146 µM *P. falciparum*-IC_{50}: 1 µM	[100]
			Macroalgae–Ochrophyta			
Dictyota cervicornis, Dictyota menstrualis	Antiviral	Virus: HSV-1-ACVs, HSV-1-ACVr	Titer reduction			[81]
Dictyota fasciola, Taonia atomaria	Antibacterial, Antifungal,	G(+): *B. subtilis* G(-): *E. coli*	Disk diffusion method		*D. fasciola:* Inhibition (%)	[87]

solvents. *aurencia* similar *pergillus* nds [92]. extracts from more polar solvents (EtOH, MeOH, and acetone). Less polar solvents isolated minor lipid classes (e.g., neutral and medium polar lipids) and showed lower amounts of soluble carbohydrates and total phenols than polar solvents. However, the diameter of the inhibition zones against *B. subtilis* were slightly lower in these extracts than in the extracts obtained with polar solvents (rich in soluble carbohydrates and phenolic compounds) [92]. These results suggest that although less polar solvents have lower yields, they contain compounds with interesting antibacterial features.

The lipids or lipid mixtures, their extracting solvent(s), and the methods used for their characterization in algae species are summarized in **Table 3**. The results of the antimicrobial assays with lipids and lipid-rich extracts from these algae are summarized in **Table 4**. Chemical structures of lipids isolated from algae are represented in **Figure 1**.

3.2. Marine Invertebrates

The chemotaxonomic diversity of marine invertebrates is responsible for the large number of novel compounds identified in their phyla. Tropical biodiversity-rich benthic communities have been the most explored, thus the most fruitful in the identification of new potential antimicrobial compounds [113][114][115]. However, less conventional environments such as the Arctic ocean or mesopelagic communities have been started to be surveyed [116][117].

Scientific Name	Antimicrobial Activity	Tested Microorganisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, MBC, Diameter of Inhibition Zone (IZ, in mm) or Other	Ref.
	Antiviral [116][119]	Fungi: *C. albicans, A. niger* Virus: HSV-1	(antibacterial); Plaque reduction assay (antiviral)		HSV-1: 50.00–81.25% *T. atomaria:* MIC (µm/mL)/IZ(mm) *B. subtilis*: 80/9, *E. coli:* 80/7, *C. albicans*: 80/10, *A. niger*: 60/12 Inhibition (%) HSV-1: 31.25–34.37%	[118]
	Antibacterial, Antiviral [120]	G(+):*B. subtilis NRRL B-94* G(-): *E. coli NRRL B-3703* Virus: HSV-1	Disk diffusion method (antibacterial); Plaque reduction assay (antiviral)	Chloramphenicol (bacteria), Acyclovir (virus)	MIC (µg/mL)/IZ (mm) PI(%) *D. fasciola E. coli*: -/8 *B. subtilis*: -/10 HSV-1: 46.87–70.12% *T. atomaria: E. coli*: 60/15 *B. subtilis*: 40/13 HSV-1: 43.75–56.25%	[83][119]
Fucus evanescens [124][125]	Antibacterial	G(+): *B. cereus, Clostridium difficile*, MRSA, *Propionibacterium acnes* (ATCC and clinical isolate), *S. pyogenes* G(-): *Acinetobacter baumannii, E. coli, Haemophilus influenzae, K. pneumoniae, Legionella pneumophila, P. aeruginosa*	Disk diffusion method		MIC_{100}: 50 µg/mL	[101]
Himanthalia elongata	Antibacterial	G(+): *S. aureus* ATCC 25923, G(-): *E. coli* ATCC 11775 Yeast: *C. albicans* ATCC 60193 Fungi: *A. niger* ATCC 16404	Broth microdilution method		MBC (mg/mL) *S. aureus:* 6.25 *E. coli:* 6.00 MFC (mg/mL) *C. albicans:* 8 *A. niger:* 12	[102]
Laminaria cichorioides	Antibacterial, Antifungal	G(+): *S. aureus* ATCC 21027 G(-): *E. coli* ATCC 15034 Yeast: *Safale* S04, *C. albicans* KMM 455 Fungi: *A. niger* KMM 4634, *F. oxysporum* KMM 4639	Disk diffusion method	Fucoxanthin, Nitrofungin	IZ (mm) *S. aureus*: 2–5 *E. coli*:1–6 *C. albicans*: 1–6 *A. niger*: 1–3 *F. oxysporum*: 1–4	[77]
Sargassum dentifolium	Antibacterial, Antifungal	G(+): *B. subtilis, S. albus, E. faecalis* G(-): *E. coli* Yeast: *C. albicans* Fungus: *A. flavus*	Disk diffusion method		11 < IZ (mm) ≤ 12 No IZ (*A. flavus*)	[94]
Sargassum fusiforme, Sargassum vulgare	Antibacterial	Multidrug resistant: *S. aureus, P. aeruginosa, Shigella flexneri,*	Agar well diffusion		9.33 < IZ (mm) ≤ 23.33 MIC: 50–100 mg/mL	[103]

[16][121] [122][123], [26] [14][128][126][129] [131][132] [113][115] [118][130]

bacteria, and eukaryotic organisms (pathogenic and non-pathogenic) [133][134].

Table 5 assembles the information regarding lipids from marine invertebrate species having antimicrobial activity. **Table 6** summarizes the information about the antimicrobial properties, the tested organisms, and the antimicrobial assays for each marine invertebrates' species listed in **Table 5**. **Figure 1** illustrates the chemical structure of the main lipid classes with antimicrobial properties from these natural sources.

Table 5. Marine invertebrate lipids or lipid-rich extracts with antimicrobial potential, their origin and extraction method.

Scientific Name	Phylum (Class)	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Compound Identification Methods	Ref.
Acanthodendrilla sp.	Porifera (Demospongiae)	Gokasho Bay, Tokyo, Japan	MeOH. Aqueous residue extracted with Et_2O and *n*-BuOH. Organic extract fractionated by SiO_2 ($MeOH/CHCl_3$), purified by ODS column and C18 RP HPLC	Steroid sulfates	^1H and ^{13}C NMR	[135]

Scientific Name	Phylum (Class)	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Compound Identification Methods	Ref.
Sargassum vulgare	Porifera (Demospongiae)	Kundingarengkeke Island, Indonesia	EtOH, acetone and MeOH. Crude extract partitioned between aqueous MeOH and hexane, EtOAc, and BuOH. Hexane extract fractionated on normal-phase SiO_2 column (*n*-hexane/EtOAc, 7:3, *v*/*v*). Purification by semi-preparative HPLC	Sesterterpenes (Luffariellolide derivatives, Acantholides)	^{1}H and ^{13}C NMR, ESI-MS, HR-EI-MS	[136]
Agelas oroides	Porifera (Demospongiae)	Gökçeada, Northern Aegean Sea, Turkey	MeOH, MeOH/$CHCl_3$ (1:1, *v*/*v*) and $CHCl_3$. Extract dissolved in MeOH/H_2O (9:1, *v*/*v*) partitioned against *n*-hexane. *n*-hexane, CH_3Cl and MeOH extracts fractionated on SiO_2 (EtOAc (0 → 100%) in hexane). Sephadex LH20 and C18 flash column	FA	^{1}H and ^{13}C NMR, 1D and 2D NMR, GC-MS, ESI-MS	[137]
Caminus sphaeroconia	Porifera (Demospongiae)	Dominica	MeOH extracts chromatographed on Sepahdex LH 20 (MeOH and EtOAc/MeOH/H_2O 20:5:2). Purification by gradient on SiO_2 (CH_2Cl_2 to CH_2Cl_2/MeOH 9:1, *v*/*v*)	Glycolipid (Caminoside)	^{1}H and ^{13}C NMR, ESI-MS	[123]
		Dominica	MeOH extract purified by Sephadex LH-20 (MeOH). Sephadex LH-20 (EtOAc/MeOH/H_2O (20:5:2, *v*/*v*))	Glycolipid (Caminoside)	^{1}H and ^{13}C NMR, ESI-MS	[138]
Dysidea arenaria	Porifera (Demospongiae)	Hainan Island, South China Sea, China	$CHCl_3$-soluble portion was repartitioned between petroleum ether and 90% MeOH. MeOH extract on flash SiO_2 column (ether/EtOAc gradient)	Sesquiterpenoid (Sesquiterpenoid hydroquinone)	^{1}H and ^{13}C-NMR, ESI-MS	[139]
Dysidea sp.	Porifera (Demospongiae)	Lakshadweep Islands, Kerala, India	EtOAc and MeOH. EtOAc extract chromatographed on Sephadex LH20 (MeOH/$CHCl_3$, 1:1, *v*/*v*),	Sesterterpenes (Sesterterpene sulfates)	^{1}H and ^{13}C NMR, HR-FAB-MS	[140]

Scientific Name	Phylum (Class)	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Compound Identification Methods	Ref.
			SiO_2 (2% EtOAc petroleum ether)			
Erylus lendenfeldi	Porifera (Demospongiae)	Gulf of Eilat, Red Sea	MeOH/$CHCl_3$, RP on a C18 column (decreasing percentage of H_2O in MeOH)	Steroidal glycoside (Eryloside)	^1H and ^{13}C NMR, UV, IR	[141]
Erylus placenta	Porifera (Demospongiae)	Hachijo Island, Japan	*n*-PrOH/H_2O (3:1, *v*/*v*). Extracts partitioned between H_2O and $CHCl_3$. H_2O layer partitioned between *n*-BuOH and H_2O. BuOH fraction separated by C18 flash (*n*-PrOH/H_2O (1:9, 3:7, 5:5, and 8:2, *v*/*v*) and $CHCl_3$/MeOH/H_2O(6:4:1, *v*/*v*))	Steroidal glycoside (Sokodosides)	^1H and ^{13}C NMR, GC-FID, UV	[142]
Eurypongia sp.	Porifera (Demospongiae)	Light House Reef, Koror, Palau	MeOH. Extracts fractionated by HP20SS column (acetone/H_2O)	Steroid sulfates (Eurysterols)	^1H and ^{13}C NMR, ESI-MS, UV, IR	[143]
Fasciospongia sp.	Porifera (Demospongiae)	Cape Leeuwin, Western Australia	EtOH extract partitioned into *n*-BuOH and H_2O soluble fractions. *n*-BuOH fraction subsequently defatted by sequential trituration in *n*-hexane and CH_2Cl_2 soluble fractions. CH_2Cl_2 fractions subjected to SPE or HLPC	Meroterpene (Meroterpene sulfate fascioquinol)	^1H and ^{13}C NMR, HR-ESI-MS, UV	[144]
Halichondria sp.	Porifera (Demospongiae)	Unten Port, Okinawa, Japan	Methanolic extract partitioned between H_2O and EtOAc. EtOAc soluble material subjected to SiO_2 column ($CHCl_3$/MeOH, (95:5, *v*/*v*) and petroleum ether/Et_2O (9:1, *v*/*v*))	Sesquiterpenoids (Halichonadins)	^1H and ^{13}C NMR, EI-MS, IR	[145]
	Porifera (Demospongiae)		MeOH extract partitioned between H_2O and EtOAc. EtOAc-soluble material subjected to SiO_2 column (*n*-hexane/EtOAc, 1:1 → MeOH). MeOH fraction subjected to SiO_2 column ($CHCl_3$/MeOH, 95:5 → 7:3). $CHCl_3$/MeOH (7:3) fraction separated on SiO_2 column (EtOAc/MeOH, 5:1 → MeOH)	Sesquiterpenoid (Halichonadins)	^1H and ^{13}C NMR, ESI-MS, HR-ESI-MS, IR	[146]

Abbreviations: CC: cytotoxic concentration; EC: effective concentration; HSV: herpes simplex virus; IC: inhibitory concentration; IZ: inhibition zone; MIC: minimum inhibitory concentration; MBC: minimum bactericidal concentration; MFC: minimum fungicidal concentration; MRSA: methycillin-resistant *Staphylococcus aureus*; PI: percentage of inhibition; SI: selectivity index; TI: therapeutic index; VII: viral inhibition index.

Scientific Name	Phylum (Class)	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Compound Identification Methods	Ref.
Haliclona simulans	Porifera (Demospongiae)	Kilkieran Bay, Galway, Ireland	Acetone and MeOH extracts subjected to HP20 chromatography (100% H_2O → 100% MeOH). Fractionated on flash forward system. SiO_2 column (100% hexane → 100% EtOAc)	Steroids (24-vinyl-cholest-9-ene-3β,24-diol, 20-methyl-pregn-6-en-3β-ol,5α,8α-epidioxy, 24-methylenecholesterol)	^1H- and ^{13}C NMR, GC-MS	[147]
Jaspis stellifera	Porifera (Demospongiae)	Ishigaki Island, Okinawa, Japan	MeOH. EtOAc soluble material subjected to SiO_2 column ($CHCl_3$/MeOH, 9:1 and hexane/EtOAc, 3:7, *v*/*v*). EtOAc-soluble material subjected to SiO_2 columns and C18 HPLC	Nortriterpenoids (Jaspiferals)	^1H and ^{13}C NMR, EI-MS, UV, IR	[148]
Luffariella geometrica	Porifera (Demospongiae)	Great Australian Bight, Australia	CH_2Cl_2. Sequential fractionation to obtain pure compounds	Sesterterpenes (Luffarins)	^1H and ^{13}C NMR, EI-MS, UV, IR	[149]
Luffariella variabilis	Porifera (Demospongiae)	Western Carolines, Palau	CH_2Cl_2, purified by chromatography	Sesterterpenoids (Manoalide)	^1H and ^{13}C NMR, UV, IR	[150]
		Western Carolines, Palau	CH_2Cl_2, purified by chromatography	Sesterterpenoids (Manoalides)	^1H and ^{13}C NMR, UV, IR	[151]
Melophlus sarasinorum	Porifera (Demospongiae)	Makassar, Sulawesi Island, Indonesia	Acetone and MeOH. Extract partitioned between EtOAc and H_2O. Aqueous extract on HP20 (MeOH, H_2O). MeOH eluate on C18 (MeOH and H_2O, gradient elution)	Steroidal glycosides (Sarasinoside)	^1H and ^{13}C NMR, HR-ESI-MS, LC-MS, UV	[152]
Oceanapia sp.	Porifera (Demospongiae)	Kamagi Bay, Sada Peninsula, Japan	MeOH extracts partitioned between ether and H_2O. Organic phase partitioned between *n*-hexane and MeOH/H_2O (9:1, *v*/*v*). Aqueous MeOH fraction subjected to C18. Purification on SiO_2 column ($CHCl_3$, $CHCl_3$/MeOH (9:1), $CHCl_3$/MeOH/H_2O (6:4:1), and MeOH)	Acetylenic acid	^1H and ^{13}C NMR, FAB-MS, UV, IR	[153]
Paragrantia cf. *waguensis*	Porifera (Calcarea)	Onna village, Okinawa, Japan	MeOH extract partitioned between H_2O and EtOAc.	Acetylenic acid	^1H and ^{13}C NMR, ESI-	[154]

Scientific Name	Phylum (Class)	Collection Site	Extracting Solvent(s)/Method	Isolated Lipids or Lipid Classes	Compound Identification Methods	Ref.
			EtOAc extract subjected to Sephadex LH20 (CH_2Cl_2/MeOH, 1:1, *v*/*v*). Fraction separation on RP HPLC		MS, UV, IR	
Petrosia weinbergi	Porifera (Demospongiae)	Acklin Island, Bahamas	MeOH/$CHCl_3$ (1:1, *v*/*v*). Aqueous suspension extracted with EtOAc, EtOAc/*n*-BuOH (1:1), and *n*-BuOH. Active extracts fractionated by C18 HPLC	Steroid sulfates (Weinbersterol disulfates)	^{1}H and ^{13}C NMR, FAB-MS, IR	[155]
Poecillastra wondoensis, Rhabdastrella wondoensis (two-sponge association)	Porifera (Demospongiae)	Cheju Island, South Korea	MeOH (70%). Extract partitioned with Et_2O and H_2O. Aqueous phase extracted with *n*-BuOH, subjected to C18 flash chromatography and Sephadex LH-20. Purification on C18 HPLC	Steroidal glycosides (Wondosterols)	^{1}H and ^{13}C NMR, FAB-MS, UV, IR	[156]
Pseudoceratina purpurea	Porifera (Demospongiae)	Kaunakakai Harbor, O'ahu island, Hawaii, USA	EtOH and methylene chloride. Combined extracts partitioned (hexane, methylene chloride and BuOH) Isolation: SiO_2 flash column (hexane). Purification: Sephadex LH-20	Bromotyramine homoserine-derived (Mololipids)	^{1}H and ^{13}C NMR, HR-FAB-MS, UV, IR	[157]
Axinyssa digitata	Porifera (Demospongiae)	Tunisia	Acetone extract partitioned between H_2O and Et_2O. Aqueous residue re-extracted with *n*-BuOH and chromatographed on Sephadex LH-20 column (MeOH) and C18 HPLC	Steroid sulfates (Halistanol sulfates)	^{1}H and ^{13}C NMR, FAB-MS	[158]
Siliquariaspongia sp.	Porifera (Demospongiae)	Motualevu reef, Fiji	H_2O and MeOH/CH_2Cl_2 (1:1, *v*/*v*). *n*-BuOH-soluble material from the aqueous extract and $CHCl_3$-soluble material from the organic extract chromatographed on Sephadex LH-20 (MeOH/H_2O, 3:1, *v*/*v*). Purification by RP HPLC	Brominated long-chain acids (Motualevic acids)	^{1}H- and ^{13}C-NMR, LC-MS, HR-ESI-MS, FT-IR	[159]

Table 6. Antimicrobial activity of lipids or lipid-rich extracts from marine invertebrates.

Scientific Name	Activity	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, Diameter of Inhibition Zone (IZ) or Other	Ref.
Acanthodendrilla sp.	Antifungal	Yeast: *S. cerevisiae* (A364A, STX338-2C, 14028g, GT160-45C)	Disk diffusion method		IZ (mm): 7–11	[135]
	Antibacterial Antifungal	G(+): *S. aureus, B. subtilis* G(-): *E. coli,*	Disk diffusion method		IZ (mm) *S. aureus*: 7–11 *B. subtilis*: 7–12	[136]

Scientific Name	Activity	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, Diameter of Inhibition Zone (IZ) or Other	Ref.
corallinophagum		Yeast: *C. albicans* Fungi: *Cladosporium herbarum*			*E. coli*: 7–12 *C. albicans*: 9–10 *C. herbarum*: 10–20	
Agelas oroides	Antibacterial, Antiplasmodial	Acid-fast bacterium: *M. tuberculosis* Parasitic protozoa: *P. falciparum*, *Trypanosoma brucei rhodesiense*, *T. cruzi*, *L. donovani* G(-): *E. coli*	[^{3}H]-hypoxanthine incorporation assay, 96-well microtiter plates, inhibition of enzymatic activity	Artemisinin, Benznidazole, Melarsoprol, Miltefosine, Podophyllotoxin, Triclosan	IC_{50} (µg/mL) Antibacterial *M. tuberculosis:* 9.4–>50 *E. coli*: 0.07–>50 Antiprotozoal: 0.35–>30	[137]
	Antibacterial	G(+): MRSA, *Enterococcus* (VRE) G(-): *E. coli*	in vitro inhibition		MIC (µg/mL) MRSA: 12 VRE: 12 *E. coli*: > 100	[123]
Caminus sphaeroconia	Antibacterial	G(+): MRSA, *Enterococcus* (VRE) G(-): *Xanthomonas maltophilia* Plant pathogen: *Pythium ultimum*	Disk diffusion method		MIC (µg/disk) MRSA: 6.3–>100 VRE: 3.1–>100 *X. maltophilia:* 25–>100 *P. ultimum*: 25–>100	[138]
Dysidea arenaria	Antiviral	Virus: HIV-1		PFA	IC_{50} (µM) 16.4–239.7	[139]
Dysidea sp.	Antibacterial	G(+): *S. aureus, B. subtilis, M. luteus* G(-): *P. vulgaris, S. typhimurium, E. coli*	Broth macrodilution method	Linezolid	MIC (µg/mL) 0.117–>15	[140]
Erylus lendenfeldi	Antifungal	Yeast: *C. albicans*			MIC (µg/mL) 15.6	[141]
Erylus placenta	Antifungal	G(+): *S. aureus* G(-): *E. coli* Fungus: *Mortierella ramanniana* Yeasts: *S. cerevisiae* (cdc28, act1-1, erg6)	Disk diffusion method		IZ (mm) *M. ramanniana*: 11–12 *S. cerevisiae*: 8–18	[142]
Euryspongia sp.	Antifungal	Yeasts: *C. albicans* (ATCC 32354, wild-type) (ATCC 90873, amphotericin B-resistant)	Liquid antifungal assay	Amphotericin B	MIC (µg/mL): 15.6–62.5	[143]
Fasciospongia sp.	Antibacterial	G(+): *S. aureus* (ATCC 25923,	96-well microtiter plate	Penicillin, Fluconazole	IC_{50} (µM) *S. aureus*: 0.95–2.5	[144]

Scientific Name	Activity	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, Diameter of Inhibition Zone (IZ) or Other	Ref.
		ATCC 9144), *B. subtilis* (ATCC 6051, ATCC 6633) G(-): *E. coli* (ATCC 11775), *P. aeruginosa* (ATCC 10145) Yeast: *C. albicans* (ATCC 90028)			*B. subtilis*: 0.3–7.0	
Halichondria sp.	Antibacterial Antifungal	G(+): *M. luteus, B. subtilis* G(-): *E. coli* Yeasts: *C. neoformans, C. albicans,* Fungi: *Paecilomyces variotii, A. niger, A. fumigatus*	Broth microdilution method		MIC (µg/mL) *M. luteus*: 0.52 *C. neoformans*: 0.0625 *C. albicans*: 2.09 *P. variotii*: 1.04 *A. niger*: 1.04 *A. fumigatus:* 1.04	[145]
	Antibacterial Antifungal	G(+): *M. luteus* Yeast: *C. neoformans* Fungi: *T. mentagrophytes*			MIC (µg/mL) *M. luteus*: 4 *T. mentagrophytes:* 8–16 *C. neoformans*: 16	[146]
Haliclona simulans	Anti-mycobacterial Antitrypanosomal	Acid-fast bacterium: *Mycobacterium marinum* Parasitic trypanosomatida: *T. brucei*	Broth microdilution method	Gentamycin	MIC (µM): *M. marinum*: 156.9–288.8 *T. b. brucei*: 4.58–21.56	[147]
Jaspis stellifera	Antibacterial Antifungal	G(+): *Sarcina lutea* Yeast: *C. neoformans* Fungi: *T. mentagrophytes*			MIC (µg/mL) *S. lutea*: 50 *C. neoformans*: 50 *T. mentagrophytes*: 12.5	[148]
Luffariella geometrica	Antibacterial	G(+): *S. aureus, Micrococcus* sp. Yeast: *S. cerevisiae*	Disk diffusion method		EC (µg/disk) *S. aureus*: 100 *Micrococcus* sp.: 100	[149]
Luffariella variabilis	Antibacterial	G(+): *Streptomyces pyogenes, S. aureus*			Active against *S. pyogenes, S. aureus*	[150]
	Antibacterial	G(+): *S. aureus, B. subtilis* G(-): *E. coli, P. aeruginosa* Yeast: *C. albicans*			Active against *S. aureus, B. subtilis*	[151]
Melophlus sarasinorum	Antibacterial Antifungal	G(+): *B. subtilis* (DSM2109) G(+): *E. coli* (DSM10290)	Disk diffusion method		IZ (mm) *B. subtilis*: 9	[152]

Scientific Name	Activity	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, Diameter of Inhibition Zone (IZ) or Other	Ref.
		Yeast: *S. cerevisiae*			*S. cerevisiae*: 10–13	
Oceanapia sp.	Antibacterial Antifungal	G(+): *B. subtilis, S. aureus* G(-): *E. coli, P. aeruginosa* Yeast: *S. cerevisiae, C. albicans* (GT160-45C, cdc5, act1-1, YAT2296c) Fungi: *Penicillium chrysogenum, Mortierella ramanniana*	Disk diffusion method		IZ (mm) *S. cerevisiae*: 6.5–10 *C. albicans*: 8 *E. coli*: 8.5–12.0 *P. aeruginosa:* 8.5–13.0 *B. subtilis*: 11.0 *S. aureus*: 9.5–13.5	[153]
Paragrantia cf. *waguensis*	Antibacterial	G(+): *S. aureus* (IAM 12084) G(-): *E. coli* (ATCC 12600)	Broth microdilution method	Rifampicin, Nalidixic acid	MIC (μg/mL) *S. aureus*: 64 *E. coli*: 128	[154]
Petrosia weinbergi	Antiviral	Viruses: Feline leukemia virus (FeLV), HIV			EC_{50} (μg/mL) FeLV: 4.0–5.2 HIV: 1.0	[155]
Poecillastra wondoensis, Rhabdastrella wondoensis (two-sponge association)	Antibacterial	G(-): *P. aeruginosa*, *E. coli*	Disk diffusion method		Active concentration 10 μg/disk	[156]
Pseudoceratina purpurea	Antiviral	Virus: HIV-1			EC_{50} (μM): 52.2	[157]
Axinyssa digitata	Antiviral	Viruses: HIV-1, HIV-2			EC_{50} (μg/mL) HIV-1: 3–6 HIV-2: Not referred	[158]
Siliquariaspongia sp.	Antibacterial	G(+): *S. aureus,* MRSA	Disk diffusion method, Microbroth dilution		MIC_{50} (μg/mL) *S. aureus*: 1.2–10.9 *S. aureus* (MRSA): 3.9–400	[159]
Siphonodictyon coralliphagum	Antibacterial	G(+): *S. aureus, B. subtilis*			Active against *S. aureus, B. subtilis*	[160]
Spheciospongia purpurea	Antifungal	Yeasts: *C. neoformans* (32609), *C. glabrata* (537) Fungi: *T. rubrum* (Cmccftla), *A. fumigatus* (07544),	Broth dilution	Amphotericin B, Fluconazole, Voriconazole, Ketoconazole	MIC_{80} (μg/mL) *C. neoformans*: 4–32 *C. glabrata*: 8–64 *A. fumigatus*: >64 *T. rubrum*: >64	[122]
Family *Spongiidae*	Antibacterial Antifungal	G(+): *B. subtilis, M. luteus, S. aureus*			MIC (μm/mL) *B. subtilis*: 33.3	[161]

Scientific Name	Activity	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, Diameter of Inhibition Zone (IZ) or Other	Ref.
		G(-): *E. coli* Yeasts: *C. albicans, C. neoformans* Fungi: *A. niger*			*E. coli*: >33.3 *M. luteus*: 16.7–33.3 *S. aureus*: 33.3 *C. neoformans*: 8.35 *C. albicans*: 8.35 *A. niger*: 16.7	
Suberites domuncula	Antibacterial	Bacterium SB1 (strain isolated from *S. domuncula* with >98.0% similarity to the alpha-*Proteobacterium* (MBIC3368)	Disk diffusion method		IZ (mm): 4.5–6.8	[134]
Topsentia sp.	Antifungal	G(+):MRSA, Acid-fast bacterium: *M. intracellulare* Parasitic protozoa: *P. falciparum* (D6 and W2 clones), *L. donovani* Yeasts: *C. albicans, C. glabrata, Candida krusei, S. cerevisiae, C. neoformans* Fungus: *A. fumigatus*	Broth microdilution method	Beauvericin	FIC (μM) *C. albicans*: 0.2–1.8 *S. cerevisiae*: 0.08–1.34	[162]
Xestospongia sp.	Antibacterial	G(+): MRSA, *S. mutans, S. sobrinus*	Disk diffusion method		IZ (mm) MRSA: 12 *S. mutans:* 17 *S. sobrinus:* 14	[114]
Hyas araneus, Podopthalmus vigil, Lauridromia dehanni, Charybdis helleri, Portunus sanguinolentus, Portunus pelagicus	Antibacterial Antifungal	G(+): *S. aureus,* MRSA, *S. pyogenes* G(-): *E. coli*, *P. aeruginosa, S. typhi*, *S. flexneri*, *Klebsiella* sp., *V. cholerae*, *Acinetobacter* sp. Yeasts: *Rhodotorula* sp., *C. albicans*, *C. neoformans* Fungi: *A. fumigatus*, *A. niger*	Disk diffusion method	Penicillin, Ketoconazole	IZ (mm) *S. pyogenes*: 1 *S. typhi*: 1–3 *S. flexneri*: 1–6 *V. cholerae*: 1–4 *Acinetobacter* sp.: 1	[124]
Meganyctiphanes norvegica	Antibacterial	G(+): MRSA, MB5393, MSSA, ATCC 29213 G(-): *E. coli* (ATCC 25922), *K. pneumoniae* (ATCC 700603) Acid-fast bacterium: *M.*	Well plate, REMA method	Vancomycin hydrochloride, Aztreonam, Gentamycin sulfate	MIC (μg/mL) MRSA: 80–320 MSSA: 320 *M. tuberculosis*: 320	[117]

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Scientific Name	Activity	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, Diameter of Inhibition Zone (IZ) or Other	Ref.
		tuberculosis (H37Ra ATCC 25177)				
Aplidium sp.	Antibacterial Antiviral Antifungal	G(+): *B. subtilis* Fungi: *T. mentagrophytes* Virus: HSV-1	Disk diffusion method		IZ (mm) *B. subtilis/T. mentagrophytes:* 3–6 Antiviral activity at 2 µg/disk	[163]
Eunicea succinea	Antibacterial	G(+): *S. aureus* (ATCC 25923), *E. faecalis* (ATCC 29212) G(-): *P. aeruginosa* (ATCC 27853), *E. coli* (ATCC 25922)	Broth microdilution method		MIC (µmol/mL)/IC_{50} (µg/mL) *S. aureus:* 0.24/36 *E. faecalis*: 0.16/<10	[113]
Lobophytum crassum	Antibacterial	G(+): *S. epidermidis, B. subtilis, S. aureus* G(-): *P. aeruginosa*	Disk diffusion method	Ampicillin	IZ (mm) *S. epidermidis*: 9.5–16.5 *B. subtilis:* 8.5–18.0 *S. aureus*: 9.0–19.5 *P. aeruginosa*: 9.0–14.0	[164]
Antillogorgia elisabethae	Antibacterial	G(+): *S. pyogenes* (ATCC 19615), *S. aureus* (ATCC 25923), *E. faecalis* (ATCC 19433) G(-): *E. coli* (ATCC 25933), *P. aeruginosa* (ATCC 27853)	Disk diffusion method		MIC (µg/mL)/IZ (mm) *S. pyogenes*: 0.8–1.0/12–17 *S. aureus:* 2.0–2.3/8–11 *E. faecalis:* 3.2–3.8/8–9	[165]
Sinularia grandilobata, Sinularia sp.	Antibacterial Antifungal	G(+): *B. subtilis* (MTCC 441), *Bacillus pumilus* (NCIM 2327) G(-): *E. coli* (MTCC 443), *P. aeruginosa* (MTCC 1688) Yeast: *C. albicans* (MTCC 183) Fungi: *A. niger* (MTCC 1344), *Rhizopus oryzae* (MTCC 1987)	Disk diffusion method		IZ (mm) *B. subtilis*: 11–18 *B. pumilus*: 11–16 *E. coli*: 11–17 *P. aeruginosa*: 11–17 *C. albicans*: 8–17 *A. niger*: 10–16 *R. oryzae*: 10–15	[115]
Holothuria scabra	Antibacterial	G(+): *S. aureus* (ATCC 6538), *E. faecalis* G(-): *P. aeruginosa* (ATCC 8739), *V. damsela, E. coli*	Well-cut diffusion technique		AU *S. aureus*: 1.2–2.8 *E. faecalis*: 1.7–3.2 *P. aeruginosa*: 1.4–1.8	[166]

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Scientific Name	Activity	Tested (Micro)Organisms	Antimicrobial Testing Method/Evaluation	Reference Antimicrobial (Positive Control)	MIC, Diameter of Inhibition Zone (IZ) or Other	Ref.
					V. damsela: 1.6 *E. coli*: 1.2	
Dosidicus gigas	Antibacterial Antifungal	G(+): *B. cereus* (CCM 2010), *Clostridium perfringens* (CCM 4991), *Listeria monocytogenes* (CCM 4699), *S. aureus subs. aureus* (CCM 2461) G(-): *Haemophilus influenza* (CCM 4456), *K. pneumoniae* (CCM 2318), *S. enterica subs. enterica* (CCM 3807) Yeasts: *C. albicans* (CCM 8186), *C. glabrata* (CCM 8270), *C. tropicalis* (CCM 8223) Fungi: *Aspergillus clavatus, A. flavus, Aspergillus versicolor, Penicillium chrisogenum, Penicillium griseofulvum, Penicillium expansum*	Disk diffusion method		Inhibition (%) *B. cereus:* 39.4 *C. perfringens:* 45.5 *L. monocytogenes*: 60.7 *S. aureus subs. aureus*: 57.8 *H. influenza*: 54.5 *K. pneumoniae*: 39.4 *S. enterica subs. enterica*: 93.9 C. *albicans*: 66.7 *C. glabrata*: 42.4 *C. tropicalis*: 33.3 *A. clavatus*: 48.4 *A. flavus*: 42.4 *A. versicolor*: 42.4 *P. chrisogenum*: 39.4 *P. griseofulvum*: 42.4 *P. expansum*: 48.5	[120]
Saccostrea glomerata	Antibacterial Antifungal	G(+): *S. aureus* G(-): *P. aeruginosa*, *V. harveyi*, *A. hydrophila, P. aeruginosa*, *V. harveyi*, *V. parahaemolyticus* Yeast: *C. albicans* Fungi: *A. niger*, *A. flavus*, *Fusarium* sp. Virus: White spot syndrome virus (WSSV)	Disk diffusion method		IZ (mm) *P. aeruginosa*: 4.1–16.0 *V. harveyi*: 3.8–14.9 *A. hydrophila*: 5.1–14.5 *A. niger*: No activity–High activity *C. albicans:* No activity–High activity *Fusarium* sp: No activity–High activity Antiviral activity: PI < 91.85%	[167]

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Abbreviations: AU: activity unit for the clear zone; EC: effective concentration; FIC: fractional inhibitory concentration; IZ: inhibition zone; MIC: minimum inhibitory concentration; PI: percentage inhibition.

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