Marine Pharmacology in 2016–2017: Marine Compounds with Antibacterial, Antidiabetic, Antifungal, Anti-Inflammatory, Antiprotozoal, Antituberculosis and Antiviral Activities; Affecting the Immune and Nervous Systems, and Other Miscellaneous Mechanisms of Action

Alejandro M. S. Mayer 1,*, Aimee J. Guerrero 1, Abimael D. Rodriguez 2, Orazio Taglialatela-Scafati 3,*, Fumiaki Nakamura 4 and Nobuhiro Fusetani 5

Citation: Mayer, A.M.S.; Guerrero, A.J.; Rodríguez, A.D.; Taglialatela-Scafati, O.; Nakamura, F.; Fusetani, N. Marine Pharmacology in 2016–2017: Marine Compounds with Antibacterial, Antidiabetic, Antifungal, Anti-Inflammatory, Antiprotozoal, Antituberculosis and Antiviral Activities; Affecting the Immune and Nervous Systems, and Other Miscellaneous Mechanisms of Action. Mar. Drugs 2021, 19, 49. https://doi.org/10.3390/md19020049

Abstract: The review of the 2016–2017 marine pharmacology literature was prepared in a manner similar as the 10 prior reviews of this series. Preclinical marine pharmacology research during 2016–2017 assessed 313 marine compounds with novel pharmacology reported by a growing number of investigators from 54 countries. The peer-reviewed literature reported antibacterial, antifungal, antiprotozoal, antituberculosis, and antiviral activities for 123 marine natural products, 111 marine compounds with antidiabetic and anti-inflammatory activities as well as affecting the immune and nervous system, while in contrast 79 marine compounds displayed miscellaneous mechanisms of action which upon further investigation may contribute to several pharmacological classes. Therefore, in 2016–2017, the preclinical marine natural product pharmacology pipeline generated both novel pharmacology as well as potentially new lead compounds for the growing clinical marine pharmaceutical pipeline, and thus sustained with its contributions the global research for novel and effective therapeutic strategies for multiple disease categories.

Keywords: drug; marine; sea; chemical; natural product; pharmacology; pharmaceutical; review; toxicology; pipeline; preclinical

1. Introduction

The present review aims to consolidate the 2016–2017 preclinical marine pharmacology literature, with a format similar to our previous 10 reviews of this series which cover the period 1998–2015 [1–10]. All peer-reviewed articles were retrieved from the following databases: MarinLit, PubMed, Chemical Abstracts®, ISI Web of Knowledge, and Google Scholar. As in our previous reviews we have decided to limit the review to the bioactivity and/or pharmacology of structurally characterized marine chemicals, which we have classified using a modification of Schmitz’s chemical classification [11] into six major chemical classes, namely, polyketides, terpenes, peptides, alkaloids, shikimates, and sugars. The preclinical antibacterial, antifungal, antiprotozoal, antituberculosis, and antiviral pharmacology of marine chemicals is reported in Table 1, with the structures, shown in Figure 1. Marine compounds that showed immune and nervous systems activities,
as well as antidiabetic and anti-inflammatory effects are exhibited in Table 2, with their respective structures consolidated in Figure 2. Finally, marine compounds affecting a variety of cellular and molecular targets are noted in Table 3, and their structures presented in Figure 3.

Several publications during 2016–2017 reported on several marine extracts or structurally uncharacterized compounds, with potentially novel preclinical and/or clinical pharmacology: In vitro antibacterial and antibiotic potentiating activities of tropical Mauritian marine sponge extracts [12]; a sterol-rich fraction with significant synergistic anti-inflammatory activity isolated from the South Korean soft coral Dendronephthya gigantea [13]; two metabolites with anti-methicillin-resistant Staphylococcus aureus activity from an Indian marine sponge Clathria procea associated actinomycete S. pharmamarensis ICN40 with antimicrobial potential “after structure identification and clinical studies” are completed [14]; 49 of 251 bacterial isolates from sediments from several Red Sea harbor and lagoon environments with the potential to produce secondary metabolites with “antimicrobial activity” [15]; antibacterial activity in extracts from the marine bacterium Salinispora arenicola from the Gulf of California, Mexico [16]; activation by cyanobacterium Oscillatoria sp. lipopolysaccharide of rat microglia and murine B cells with concomitant Toll-like receptor 4 signaling in vitro [17,18]; and lipophilic fractions from the Icelandic marine sponge Halichondria santiens that decrease dendritic cells’ pro-inflammatory cytokine release [19].
**Table 1.** Marine pharmacology in 2016–2017: marine compounds with antibacterial, antifungal, antituberculosis, antiprotozoal and antiviral activities.

| Drug Class   | Compound/Organism | Chemistry | Pharmacologic Activity | IC<sub>50</sub> b<sup>1</sup> | MMOA b<sup>2</sup> | Country c | References |
|--------------|-------------------|-----------|------------------------|-----------------|------------------|------------|-------------|
| **Antibacterial** | ageloline A (1)/bacterium | Alkaloid f | C. trachomatis inhibition | 9.5 µM | Antioxidant activity | DEU [20] |
| **Antibacterial** | blasticidin S analog (2)/sponge | Alkaloid f | S. aureus inhibition | 6.2 µg/mL + | norA multidrug transporter inactivation | CAN, USA [21] |
| **Antibacterial** | dibromohemibastadin-1(3)/sponge | Peptide f | P. aeruginosa biofilm disruption | 10 µM + | Quorum sensing activity | DEU, FRA, GBR [22] |
| **Antibacterial** | ecteinamycin (4)/bacterium | Polyketide d | C. difficile inhibition | 0.059 µM + | K⁺ transport dysregulation | JPN, USA [23] |
| **Antibacterial** | 5-episuleptolide (5)/soft coral | Terpenoid e | A. baumannii biofilm formation inhibition | 20 µM + | PNAG gene expression inhibition | TWN [24] |
| **Antibacterial** | E. esculentus peptides (6,7)/sea urchin | Peptide f | Gram-positive and negative inhibition | 0.1–3.1 µM + | Heavy chains bioactive | NOR, SWE [25] |
| **Antibacterial** | granaticin and granatycin D (8,9)/bacterium | Polyketide d | B. subtilis and MR S. aureus inhibition | 1.6, 6.2 µg/mL + | Co-culture enhanced MIC | USA [26] |
| **Antibacterial** | keyicin (10)/bacterium | Polyketide d | B. subtilis and MR S. aureus inhibition | 2.5–9.9 µM + | Fatty acid metabolism modulation | USA [27] |
| **Antibacterial** | microcyanamides C and D (11, 12)/sponge | Peptide f | S. aureus inhibition | 6.2 µM + | Depolarize cytoplasmic membranes | DEU, IDN, IRN [28] |
| **Antibacterial** | mytticalin A5 (13)/mussel | Peptide f | Gram-positive and negative inhibition | 2–8 µM + | RNA synthesis inhibition | DEU, ITA [29] |
| **Antibacterial** | plakofuranolactone (14)/sponge | Polyketide d | Quorum quenching inhibition | 0.1 µM + | Specificity to QS systems | ITA [30] |
| **Antibacterial** | psammaplin A (15)/sponge | Peptide f | V. vulnificus in vivo growth inhibition | 50 µg/mouse ** | Associated in vitro and in vivo pathology suppressed | S. KOR [31] |
| **Antibacterial** | abyssomicin 2 (16)/bacterium | Polyketide d | B. thuringiensis and M. luteus inhibition | 3.6, 7.2 µg/mL + | Undetermined | CHN [32] |
| **Antibacterial** | actinomycins D, V, and X2 (17–19)/bacterium | Peptide f | MR S. aureus, B. subtilis and E. coli inhibition | 0.08–0.61 µM | Undetermined | CHN, EGY, SAU [33,34] |
| **Antibacterial** | aneurinifactin (20)/bacterium | Lipopeptide f | K. pneumoniae and S. aureus inhibition | 4.8 µg/mL + | Undetermined | IND [35] |
| **Antibacterial** | aspewentins D and H (21, 22)/fungus | Terpenoid e | P. aeruginosa and M. luteus inhibition | 4 µg/mL + | Undetermined | CHN [36] |
| **Antibacterial** | B. subtilis furanoiberopadon (23)/bacterium | Terpenoid e | V. vulnificus and parahaemolyticus inhibition | 3.12 µg/mL + | Undetermined | IND [37] |
| **Antibacterial** | bacillosporin A (24)/fungus | Polyketide d | B. subtilis inhibition | 0.12 µM + | Undetermined | BGD, CHN [38] |
| **Antibacterial** | bacilotetrin A (25)/bacterium | Peptide f | MR S. aureus inhibition | 8 µg/mL + | Undetermined | S. KOR [39] |
| **Antibacterial** | branycin B (26)/bacterium | Polyketide d | M. luteus and C. urealyticum inhibition | 1, 8 µg/mL + | Undetermined | ESP [40] |
| Drug Class   | Compound/Organism | Chemistry | Pharmacologic Activity | IC\textsubscript{50} | MMOA | Country | References |
|-------------|------------------|-----------|------------------------|----------------------|------|---------|------------|
| Antibacterial | brocazine G (27)/fungus | Alkaloid | \textit{S. aureus} inhibition | 0.25 µg/mL | + | Undetermined | CHN, DEU, HUN [41] |
| Antibacterial | cadiolides K and M (28, 29)/ascidian | Polyketide | MR \textit{S. aureus} inhibition | 1–2 µg/mL | + | Undetermined | S. KOR [42] |
| Antibacterial | cahuitamycin D (30)/bacterium | Peptide | \textit{A. baumannii} biofilm inhibition | 8.4 µM | | Undetermined | CRI, USA [43] |
| Antibacterial | chalconomycin (31)/bacterium | Polyketide | \textit{S. aureus} inhibition | 4 µg/mL | + | Undetermined | CHN [44,45] |
| Antibacterial | chermesins A and B (32, 33)/fungus | Terpenoid | \textit{M. luteus} inhibition | 8 µg/mL | + | Undetermined | CHN [46] |
| Antibacterial | chloro-preussomerins A and B (34, 35)/fungus | Polyketide | \textit{S. aureus} inhibition | 3.2, 6.2 µg/mL | + | Undetermined | CHN [47] |
| Antibacterial | collismycin C (36)/bacterium | Alkaloid | MR \textit{S. aureus} biofilm inhibition | 10 µg/mL | * | Undetermined | S. KOR [48] |
| Antibacterial | engyodontochones A and B (37, 38)/fungus | Polyketide | MR \textit{S. aureus} inhibition | 0.17, 0.24 µM | | Undetermined | CHN, DEU [49] |
| Antibacterial | hydromephyraquinones (39–43)/fungus | Polyketide | \textit{S. aureus} inhibition | 2–8 µg/mL | + | Undetermined | CHN, DEU [50] |
| Antibacterial | langcoquinone C (44)/sponge | Terpenoid | \textit{B. subtilis} inhibition | 6.2 µM | + | Undetermined | JPN, MMR, VNM [51] |
| Antibacterial | luffariellolide (45)/sponge | Terpenoid | \textit{S. enterica} inhibition | 4 µg/mL | * | Undetermined | S. KOR [52] |
| Antibacterial | manzamine alkaloids (46–48)/sponge | Alkaloid | Gram-positive and negative inhibition | 2–8 ng/mL | + | Undetermined | IDN, S. KOR [53] |
| Antibacterial | napyradiomycin A1 (49)/bacterium | Terpenoid | MR \textit{S. aureus} inhibition | 0.5–1 µg/mL | + | Undetermined | ESP [54] |
| Antibacterial | oxysporizoline (50)/fungus | Alkaloid | MR \textit{S. aureus} inhibition | 6.25 µg/mL | + | Undetermined | S. KOR [55] |
| Antibacterial | \textit{P. citrinum} 1-(2,6-dihydroxynaphthalen-1-one) (51)/fungus | Polyketide | \textit{S. aureus} inhibition | 6.95 µM | + | Undetermined | CHN [56] |
| Antibacterial | penicillstressols (52, 53)/fungus | Polyketide | MR \textit{S. aureus} inhibition | 0.5 µg/mL | + | Undetermined | CHN [57] |
| Antibacterial | pestalone (54)/fungus | Polyketide | MR \textit{S. aureus} inhibition | 6.25 µg/mL | + | Undetermined | CHN [58] |
| Antibacterial | pestalotionol (55)/fungus | Polyketide | \textit{B. subtilis} and \textit{S. aureus} inhibition | 2, 8 µg/mL | + | Undetermined | CHN, TWN [59] |
| Antibacterial | phomaethers A and C (56, 57)/fungus | Polyketide | \textit{E. coli} and \textit{S. aureus} inhibition | 0.15–1.25 µM | + | Undetermined | CHN [60] |
| Antibacterial | 4-methyl-3”-prenylcandidusin A (58)/fungus | Polyketide | MR \textit{S. aureus} and \textit{V. vulnificus} inhibition | 3.8, 7.8 µg/mL | + | Undetermined | CHN [61] |
### Table 1. Cont.

| Drug Class     | Compound/Organism                          | Chemistry       | Pharmacologic Activity                                      | IC₅₀ b¹ | MMOA b² | Country c | References |
|----------------|--------------------------------------------|-----------------|-------------------------------------------------------------|---------|---------|-----------|------------|
| Antibacterial  | *Pseudomonas* sp. rhamnolipid (59)/bacterium | Lipid e         | *B. cepacia* and *S. aureus* inhibition                      | 1.6–3.1 µg/mL e | Undetermined | GBR, ITA  | [62]       |
| Antibacterial  | smenospongine (60)/sponge                  | Terpenoid e     | *B. cepacia* and *S. aureus* inhibition                      | 3.1 µM e | Undetermined | CHN, USA  | [63]       |
| Antibacterial  | *S. cheonanensis* phthalate (61)/bacterium | Polyketide d    | *P. vulgaris* inhibition                                     | 4 µg/mL e | Undetermined | IND       | [64]       |
| Antibacterial  | sporalactam B (62)/bacterium               | Polyketide d    | MR *S. aureus* and *E. coli* inhibition                      | 0.4–1.8 µM ** | Undetermined | CAN, PHL  | [65]       |
| Antibacterial  | tetrocarcin A (63)/fungus                  | Polyketide d    | *B. subtilis* inhibition                                     | 0.03–0.125 µg/mL + | Undetermined | CHN       | [66,67]    |
| Antibacterial  | tricepyridinium (64)/sponge                | Alkaloid f      | *B. subtilis* and *S. aureus* inhibition                      | 0.78–1.56 µg/mL + | Undetermined | JPN       | [68]       |
| Antibacterial  | trochelane (65)/soft coral                 | Terpenoid e     | *A. baumannii* and *S. aureus* inhibition                    | 4–4.2 µM * | Undetermined | EGY, IDN, SAU | [69]       |
| Antibacterial  | tulongicin (66)/bacterium                  | Alkaloid f      | *S. aureus* inhibition                                       | 1.2 µg/mL + | Undetermined | ITA, NZL, USA | [70]       |
| Antibacterial  | vineomycin A₁ (67)/bacterium               | Polyketide d    | *S. aureus* inhibition                                       | 4 µg/mL + | Undetermined | CHN       | [71]       |
| Antifungal     | amphidinol 3 (68)/dinoflagellate           | Polyketide d    | Pore formation requires cholesterol or ergosterol           | 2.0 µM * | Toroidal pore 2.6-4.0 nM | JPN, PHL | [72,73] |
| Antifungal     | avarol (69)/sponge                         | Terpenoid e     | *C. albicans* inhibition                                     | 6–8 µg/mL + | Undetermined | SRB       | [74]       |
| Antifungal     | dihydromaltophilin (70)/bacterium          | Polyketide d    | *C. albicans* inhibition                                     | 3 µM | Undetermined | AUS, MEX | [75]       |
| Antifungal     | hippolide j (71a, 71b)/sponge              | Terpenoid e     | *C. albicans* inhibition                                     | 0.1 µg/mL + | Undetermined | CHN, GBR | [76]       |
| Antifungal     | ilicicolin H (72)/fungus                   | Polyketide d    | *C. albicans* inhibition                                     | <0.25 µg/mL + | Undetermined | DEU, DKK, ESP | [77] |
| Antifungal     | iturin F₁ and F₂ (73, 74)/bacterium        | Peptide f       | *A. flavus* and *P. geoselflum* inhibition                  | 3.1 µg/mL + | Undetermined | JPN, S. KOR | [78]       |
| Antifungal     | *P. meleagrinum* macrolides (75, 76)/fungus | Polyketide d    | *C. albicans* inhibition                                     | 1–2 µg/mL ** | Undetermined | JPN       | [79]       |
| Antifungal     | plakinic acid M (77)/sponge                | Polyketide d    | *C. gattii* inhibition                                       | 2.4 µM ** | Undetermined | USA       | [80]       |
| Antifungal     | poecillastroside D (78)/sponge             | Terpenoid e     | *A. fumigatus* inhibition                                     | 6 µg/mL ** | Undetermined | ESP, FRA, IRL, OMN, SWE | [81] |
| Antifungal     | rocheicoside A (79)/bacterium              | Alkaloid f      | *C. albicans* inhibition                                     | 4 µg/mL + | Undetermined | TUR       | [82]       |
| Antimalarial   | diacarperoxide A (80)/sponge               | Terpenoid e     | *P. falciparum* D6 and W2 strain inhibition                 | 1.9–2.0 µM | Undetermined | CHN, USA | [83]       |
| Antimalarial   | dudawalamide A and D (81, 82)/cyanobacterium | Peptide f       | *P. falciparum* W2 strain inhibition                        | 3.5 µM | Undetermined | JOR, PAN, USA | [84]    |
| Drug Class       | Compound/Organism a          | Chemistry | Pharmacologic Activity | IC<sub>50</sub> b1 | MMOA b2  | Country c | References |
|------------------|------------------------------|-----------|------------------------|---------------------|----------|-----------|------------|
| Antimalarial     | eudistidine A (83)/soft coral | Alkaloid f | P. falciparum D6 and W2 strain inhibition | 1.1–1.4 µM | Undetermined | CAN, USA  | [85]       |
| Antimalarial     | naseseazine C (84)/bacterium | Alkaloid f | P. falciparum 3D7 inhibition | 3.5 µM | Undetermined | AUS       | [86]       |
| Antimalarial     | P. opacum β-carboline (85)/ascidian | Alkaloid f | P. falciparum FcB1 inhibition | 3.8 µM | Undetermined | FRA, NZL  | [87]       |
| Antimalarial     | ptilomycalin F (86)/sponge   | Alkaloid f | P. falciparum 3D7 strain inhibition | 0.23 µM | Undetermined | BEL, FRA, CHE, NLD | [88] |
| Antimalarial     | pustulosaisonitrile-1 (88)/nudibranch | Terpenoid e | P. falciparum 3D7 strain inhibition | 1.08 µM | Undetermined | AUS, USA  | [89]       |
| Antileishmanial  | A. Niger fatty acids (89, 90)/sponge | Lipid e | L. infantum inhibition | 0.17, 0.34 mg/mL TopIB inhibition | Undetermined | ESP, USA  | [90]       |
| Antileishmanial  | dudawalamide D (82)/cyanobacterium | Peptide f | L. donovani inhibition | 2.6 µM | Undetermined | JOR, PAN, USA | [84] |
| Antileishmanial  | Gorgonia sp. sterol (91)/sponge | Terpenoid e | L. infantum inhibition | >10 µM * | Undetermined | ESP, PAN  | [91]       |
| Antileishmanial  | icrinin-1 and 2 (92, 93)/sponge | Terpenoid e | L. donovani inhibition | 28–31 µM | Undetermined | CHE, DEU, ITA, TUR | [92] |
| Antitrypanosomal | janadolide (94)/cyanobacterium | Peptide f | T. b. brucei inhibition | 0.047 µM | Undetermined | JPN       | [93]       |
| Antitrypanosomal | malformin A1 (95)/fungus | Peptide f | T. congolense inhibition | 0.015 µg/mL | Undetermined | JPN, PHL  | [94]       |
| Antitrypanosomal | rhodozepinone (96)/bacterium | Alkaloid f | T. b. brucei inhibition | 16.3 µg/mL | Undetermined | DEU, EGY  | [95]       |
| Antituberculosis | melophlin A (97)/sponge | Alkaloid f | M. smegmatis inhibition | 0.8 µg/mL * | BCG1083 & BCG1212c proteins targeted | IDN, JPN  | [96]       |
| Antituberculosis | methoxypuupehenol (98)/sponge | Terpenoid e | Dormant M. tuberculosis inhibition | 0.5 µg/mL * | Bactericidal activity | USA | [97] |
| Antituberculosis | gliotoxin (99)/fungus | Alkaloid f | M. tuberculosis inhibition | 0.03 µM * | Undetermined | CHN       | [98]       |
| Antituberculosis | proximicin B (100)/bacterium | Peptide f | M. bovis Pasteur 1173P2 inhibition | 6.25 µg/mL * | Undetermined | AUS, CHN, EGY, NGA | [99] |
| Antituberculosis | smenothiozole A (101)/sponge | Peptide f | M. tuberculosis H37Rv inhibition | 4.1 µg/mL * | Undetermined | POL, USA  | [100]      |
| Antituberculosis | sporalactam B (62)/bacterium | Polyketide d | M. tuberculosis inhibition | 0.06 µM ** | Undetermined | CAN, PHL  | [101]      |
| Antituberculosis | talarmide A (102)/fungus | Alkaloid f | Mycobacterial PknG inhibition | 55 µM | Undetermined | CHN       | [102]      |
| Antituberculosis | viomellein (103)/fungus | Polyketide d | Dormant M. bovis BCG inhibition | 1.56 µg/mL * | Undetermined | IDN, JPN  | [103]      |
| Antiviral        | hymenialdisine (104)/sponge | Alkaloid f | HIV-1 inhibition | >3.1 µM * | Reverse transcriptase inhibition | DEU, SAU, USA | [104] |
| Antiviral        | metachromin A (105)/sponge | Terpenoid e | HBV inhibition | 0.8 µM | Viral promoter inhibition | JPN, NLD  | [105] |
| Antiviral        | perdinin (106)/coral | Terpenoid e | HTLV-1 infected T cell inhibition | 0.7-5.4 µM | NF-kB inhibition | JPN       | [106]      |
| Drug Class | Compound/Organism | Chemistry | Pharmacologic Activity | IC₅₀ b¹ | MMOA b² | Country c | References |
|------------|-------------------|-----------|------------------------|--------|---------|-----------|------------|
| Antiviral  | spiromastilactone D (107)/fungus | Polyketide d | H1N1 influenza A virus inhibition | 6.0 µM | HA-sialic acid receptor binding inhibition | CHN, USA | [106] |
| Antiviral  | xiamycin D (108)/bacterium | Terpenoid e | PEDV virus inhibition | 0.93 µM | Virion structural proteins inhibition | S. KOR | [107] |
| Antiviral  | zoanthone A (109)/sea anemone | Terpenoid e | DENV-2 virus inhibition | 19.6 µM | RNA pocket tunnel binding | TWN | [108] |
| Antiviral  | A. polyclada aromatic sulfate (110)/crinoid | Polyketide d | HCV NS3 helicase inhibition | 5 µM | Undetermined | JPN | [109] |
| Antiviral  | alotaketal C (111)/sponge | Terpenoid e | HIV expression activation | 1 µM * | Undetermined | CAN | [110] |
| Antiviral  | aspergilipepptide D (112)/fungus | Peptide f | HSV-1 inhibition | 9.5 µM | Undetermined | CHN | [111] |
| Antiviral  | aspergillus H and I (113, 114)/fungus | Polyketide d | HSV-1 inhibition | 4.7, 6.2 µM | Undetermined | CHN | [112] |
| Antiviral  | astetoxin E (115)/fungus | Polyketide d | H1N1 and H3N2 influenza virus inhibition | 3.5, 6.2 µM | Undetermined | CHN | [113] |
| Antiviral  | S. verrucosa cyclopentenone (116)/soft coral | Polyketide d | HIV infection inhibition | 5.8 µM | Undetermined | CHN, USA | [114] |
| Antiviral  | eutypellazine E (117)/fungus | Alkaloid f | HIV-1 inhibition | 3.2 µM | Undetermined | CHN, DEU | [115] |
| Antiviral  | ω-hydroxyemodin (118)/fungus | Polyketide d | HCV NS3 protease inhibition | 10.7 µM | Undetermined | EGY, SAU | [116] |
| Antiviral  | malformin C (119)/fungus | Peptide f | HIV infection inhibition | 1.4 µM | Undetermined | CHN | [117] |
| Antiviral  | manzamine A (120)/sponge | Alkaloid f | HSV-1 inhibition | 1 µM * | Undetermined | USA | [118] |
| Antiviral  | perdinin (106)/zoanthid | Terpenoid e | Anti-dengue virus 2 inhibition | 4.5 µM | Undetermined | TWN | [119] |
| Antiviral  | stachybonoid A (121)/fungus | Terpenoid e | Dengue virus prM protein expression inhibition | 25 µM | Undetermined | CHN | [120] |
| Antiviral  | subergorgols T and U (122, 123)/soft coral | Terpenoid e | H1N1 influenza A virus inhibition | 35–37 µM | Undetermined | CHN, NLD | [121] |

a Organism, Kingdom Animalia: ascidian (Phylum Chordata); gorgonian, coral, crinoids, sea anemone, zoanthid (Phylum Cnidaria); sea urchin (Phylum Echinodermata), nudibranch (Phylum Mollusca), sponge (Phylum Porifera); Kingdom Monera: bacterium, cyanobacterium (Phylum Cyanobacteria); Kingdom Fungi: fungus; Kingdom Protista: dinoflagellates; b¹ IC₅₀: concentration of a compound required for 50% inhibition in vitro; *: estimated IC₅₀; **: in vivo study; b² MMOA: molecular mechanism of action; c Country: AUS: Australia; BEL: Belgium; BGD: Bangladesh; CAN: Canada; CHE: Switzerland; CHN: China; CRI: Costa Rica; DEU: Germany; DNK: Denmark; EGY: Egypt; ESP: Spain; FRA: France; GBR: United Kingdom; HUN: Hungary; IDN: Indonesia; IND: India; IRL: Ireland; IRN: Iran; ITA: Italy; JOR: Jordan; JPN: Japan; MEX: Mexico; MMR: Myanmar; NGA: Nigeria; NLD: The Netherlands; NOR: Norway; NZL: New Zealand; OMN: Oman; PAN: Panama; PHL: Philippines; POL: Poland; SAU: Saudi Arabia; S. KOR: South Korea; SAU: Saudi Arabia; SRB: Serbia; SWE: Sweden; TWN: Taiwan; TUR: Turkey; VNM: Vietnam; Chemistry: d Polyketide; e Terpene; f Nitrogen-containing compound; Abbreviations: AHL: acylated homoserine lactones; DENV-2: dengue virus type 2; HA: hemagglutinin; HBV: hepatitis B virus; HCV: hepatitis C virus; HSV: herpes simplex virus; MR: methicillin-resistant; PEDV: porcine epidemic diarrhea virus; PknG: mycobacterial protein kinase G; PNAG: polysaccharide poly-β-(1,6)-N-acetylglucosamine; TopIB: topoisomerase IB.
2. Marine Compounds with Antibacterial, Antifungal, Antiprotozoal, Antituberculosis, and Antiviral Activities

Table 1 presents 2016–2017 preclinical pharmacological research on the antibacterial, antifungal, antiprotozoal, antituberculosis, and antiviral activities of marine natural products (1–123) shown in Figure 1.
Figure 1. Cont.
Figure 1. Cont.
Figure 1. Cont.
Figure 1. Cont.
Figure 1. Cont.
Figure 1. Cont.
Figure 1. Cont.
Figure 1. Cont.
2.1. Antibacterial Activity

During 2016–2017, 51 studies reported on antibacterial bioactivity in marine natural products (1–67) isolated from ascidians, bacteria, fungi, mussels, sea urchins, soft corals, and sponges, global research that contributed new preclinical pharmacology that may contribute to the ongoing search of novel therapeutics for multi-drug resistant bacterial infections.

As shown in Table 1, and Figure 1, eleven publications reported on the mode of action of marine-derived antibacterial compounds. Cheng and colleagues reported a new chlorinated quinolone, ageloline A (1) isolated from a Streptomyces sp. derived from the Mediterranean sponge Agelas oroides that inhibited growth of Chlamydia trachomatis inclusions resulting from a mechanism that “might be related to its antioxidant potential” [20]. Davison and colleagues discovered a new analog of the peptidyl nucleoside antibiotic blasticidin S (2) produced by the actinomycete Streptomyces griseochromogenes that demonstrated increased potency against both Gram-positive and Gram-negative bacteria, with the NorA multidrug transporter being a key factor involved in membrane permeability that “facilitates cellular entry of peptidyl nucleosides” [21]. Le Norcy and colleagues described the activity of dibromohemibastadin-1 (3), derived from natural bastadins discovered in the marine sponge Ianthella basta, and which prevented and disrupted Gram negative bacterial biofilms without toxicity by a mechanism that involved “regulation in the quorum sensing” which is a process considered important for “biofilm formation and organization” [22]. Wyche and colleagues demonstrated in a series of in vitro and in vivo studies that the polyether antibiotic ecteinaminycin (4) isolated from a marine-derived bacterium Actinomadura sp., showed significant activity against the toxigenic strains of Clostridium difficile and proposed that the mechanism of action leading to detoxification and cell death likely involved “potassium transport dysregulation” [23]. Tseng and colleagues identified 5-episinuleptolide (5) isolated from the soft coral Sinularia leptoclados as an inhibitor of biofilm-associated Gram-negative bacterium Acinetobacter baumannii infections,
shown to be of high incidence in immunocompromised individuals, by a mechanism that correlated with a decreased production of the extracellular polysaccharide poly-β-(1,6)-N-acetylglucosamine [24]. Solstand and colleagues described two new antimicrobial peptides eecentrocin 1 and eestrongylocin 2 (6, 7) from the haemocytes of the edible sea urchin *Echinus esculentus* with potent antimicrobial activity against both Gram-positive and Gram-negative bacteria, concluding that “a genomic approach to discover homologues in other echinoderms for the discovery of novel antimicrobial peptides could be a beneficial venture” [25]. Sung and colleagues observed the increased production of the antibiotics granaticin and granatomyacin D (8, 9) from marine-derived *Streptomyces* PTY08712 isolated from the tunicate *Styela canopus* when co-cultured with several human bacterial pathogens, concluding that “utilization of co-culture experiments . . . may enhance metabolite production and further our understanding of . . . microbial interactions” [26]. Adnani and colleagues reported the isolation of new antibiotic anthracycline keyicin (10) from a co-culture of marine bacteria *Rhodococcus* sp. and *Micromonospora* sp. derived from the ascidian *Ecteinascidia turbinata*, which was found to be selective for Gram-positive bacteria by a unique mechanism that “does not involve nucleic acid damage” [27]. Mokhlesi and colleagues discovered two new peptides microcionamides C and D (11, 12) from the marine sponge *Clathria basilana* which inhibited Gram-positive bacterial growth with a mechanism that suggested “dissipation of the bacterial membrane potential”, which is an electrical gradient across the bacterial cytoplasmatic membrane that is required for both ATP generation and active transport processes [28]. Leoni and colleagues reported that the novel peptide myticalin A5 (13) isolated from the mussel *Mytilus galloprovincialis* had antimicrobial activity against both Gram-positive and Gram-negative bacteria by a mode of action that appeared to involve inhibition of RNA synthesis but “remains to be elucidated” [29]. Costantino and colleagues isolated a new γ-lactone plakofuranolactone (14) from the extract of the marine sponge *Plakortis cf. liia* that inhibited the bacterial Lasl/R quorum sensing system, a “mechanism of cell-cell communication and gene regulation in bacteria” [30]. Lee and colleagues studied the activity of psammaplin A (15), a marine natural product isolated from sponges, on Gram-negative bacterium *Vibrio vulnificus* infections noting that it suppressed cytotoxicity in vitro and prolonged both the survival and pathology of *V. vulnificus*-infected mice [31].

As shown in Table 1 and Figure 1, 51 marine natural products (16–67), some of them novel, were reported to exhibit antibacterial activity with MICs < 10 µg/mL or 10 µM against several Gram-positive and Gram-negative bacterial strains, although their respective mechanisms of action remained undefined: A polycyclic macrolactone abyssomicin 2 (16) isolated from a South China Sea *Streptomyces koyangensis* CSIO 5802 [32]; three bioactive actinomycins (17–19) isolated from a marine-derived *Streptomyces* sp. [33,34]; a new lipopeptide aneurinifactin (20) produced by the Indian marine *Aneurinibacillus aneurinilyticus* SBP-11 [35]; two new 20-nor-isopimarane diterpenoids aspewenins D and H (21, 22), isolated from a South China Sea marine fungus *Aspergillus wentii* SD-310 [36]; a polyketide furanoterpenoid (23) isolated from the Indian brown seaweed-associated heterotrophic bacterium *Bacillus subtilis* MTCC 10405 [37]; a chromone polyketide derivative bacillispore A (24) isolated from a Chinese mangrove-derived marine fungus *Penicillium aculeatum* (No.9EB) [38]; a new cyclic-lipotetrapeptide bacilotetron A (25) isolated from a Korean marine sediment-derived bacterium *Bacillus subtilis* strain 109GCG20 [39]; a new polyketide branimonycin B (26) isolated from a Cantabrian Sea abyssal (3000 m) actinobacterium *Pseudonocardia carboxydivorans* M-227 [40]; a novel disulfide diketopiperazine alkaloid breocazine G (27) was characterized from a mangrove-derived endophytic fungus *Penicillium brocae* MA-231 [41]; two new polyphenyl butenolides cadiolides K and M (28, 29) identified from the Korean marine tunicate *Pseudodistoma antinboja* [42]; a novel peptide cahuitamycin D (30) isolated from the Costa Rican marine-sediment derived bacterium *Streptomyces gandocaensis* [43]; a known macrolide chalcomycin (31) isolated from a Chinese marine-sediment derived bacterium *Streptomyces* sp. HK-2006-1 [44,45]; two novel spiromeroterpenoids chermesins A and B (32, 33) isolated from the Chinese marine red
alga *Pterocladiella tenuis*-derived endophytic fungus *Penicillium chermesinum* EN-480 [46]; two novel chloro-preussomerins A and B (34, 35) isolated from the Chinese mangrove endophytic fungus *Lasiodipodia theobromae* ZJ-HG1 [47]; a bipyridine collismycin C (36) isolated from the Micronesian marine red alga-derived bacterium *Streptomyces* sp. MC025 [48]; two new polyketides engyodontochoanes A and B (37, 38) isolated from the Croatian marine sponge *Cacospongia scalaris*-derived fungus *Engyodontium album* LF069 [49]; five new polyhydroxylated hydroanthraquinone derivatives (39–43) isolated from the Chinese marine red alga *Laurencia okamuraei*-derived fungus *Talaromyces islandicus* EN-501 [50]; a novel sesquiterpene hydroxyquinine langcoquinone C (44) isolated from a Vietnamese marine sponge *Spongia* sp. [51]; the sesterterpene luffariellolide (45) isolated from the Philippine marine sponge *Suberea* sp. [52]; three new manzamine alkaloids (46–48) isolated from an Indonesian marine sponge *Acanthostrongylus* [53]; a naphtoquine terpenoid napyradiomycin A1 (49) isolated from the Sao Tome and Principe marine ascidian-derived actinomycete *Streptomyces* sp. strain CA-271078 [54]; a new polycyclic quinazoline alkaloïd oxysporizoline (50) isolated form a Korean marine mudflat-derived fungus *Fusarium oxysporum* [55]; a 1-(2,6-dihydroxyphenyl)butan-1-one (51) obtained from the South China Sea mangrove-derived endophytic fungus *Penicillium citrinum* HL-5126 [56]; two novel polyketides penicillistressol and isopenicillistressol (52, 53) isolated from the Chinese marine sediment-derived fungus *Penicillium* sp. BB1122 [57]; a dechlorinated benzophenone polyketide pestalolone (54) isolated from the South China Sea soft coral-derived fungus *Pseudolatriopsis* sp. [58]; a known phenol pestaltionol (55) isolated from a Taiwanese marine hydrothermal vent sediment-derived *Penicillium* sp. Y-5-2 [59]; two new diphenyl ether derivatives phomaethers A and C (56, 57) isolated from the South China Sea gorgonian-derived fungus *Phoma* sp. [60]; a polyketide 4-methyl-3”-prenylcandidusin A (58) isolated from the Malaysian marine coral *Galaxea fascicularis*-derived fungus *Aspergillus trittici* SP2-8-1 [61]; a mono-rhamnolipid (59) isolated from Ross Sea (Antarctica) sediments-derived fungus *Pseudomonas* sp. BTN1 [62]; the sesquiterpene smenospongine (60) isolated from the South China Sea “purple-colored encrusting” marine sponge *Dysidea* sp. [63]; a methyl butyl propyl phthalate (61) isolated from Indian mangrove sediments-derived fungus *Streptomyces cheonanensis* VUK-A [64]; a new macrolide sporalactam B (62) isolated from Northeastern Pacific Canadian marine sediment-derived *Micromonospora* sp. RJA4480 [65]; a glycosidic spirotetronate polyketide tetrocarcin A (63) isolated from a Chinese marine sediment-derived *Micromonospora* sp. 5-297 [66]; a novel pyridinium polyketide tricepyridinium (64) was isolated from *Escherichia coli* EPI300 clone pDC113 transfected with metagenomic DNA prepared from the Japanese marine sponge *Discodermia calyx* [68]; a new tetracyclic biscembrane trocheliane (65) isolated from the Red Sea soft coral *Sarcophytion trochelohorum* [69]; a new indole alkaloid tulongicin (66) isolated from a Paluan deep-water marine sponge *Topsentia* sp. [70]; and a polyketide vineomyцин A1 (67) isolated from the culture broth of a Taiwanese Strait marine sediment-derived actinomycete *Streptomyces* sp. A6H [71].

Furthermore, during 2016–2017, several other marine natural products, some of them novel, reported antimicrobial activity in MICs or IC₅₀ values ranging from 10 to 50 µg/mL, or 10–50 µM, respectively, and thus because of their lower antibacterial potency were excluded from Table 1 and Figure 1: an alkaloid halichonadiamine from the Okinawan sponge *Halichondria* sp. (MIC = 10 µg/disk) [122]; a sesquiterpene alismol from a Red Sea soft coral *Lobophytum* sp. (MIC = 15 µg/mL) [123]; a new unicellane diterpene eu-nicellol A from the Arctic soft coral *Gersemia fruticosa* (MIC = 28–48 µg/mL) [124]; a new cembrane diterpene16-hydroxyecbrom-1,3,7,11-tetraene (MIC = 25 µg/mL) from the Malaysian soft coral *Sarcophytion* sp. [125]; a new bisindole alkaloid hyrindic D (MIC = 16 µg/mL) isolated from the Okinawan marine sponge *Hyrtios* sp. [126]; a briarane diterpenoid dichotelide O (MIC = 2 µg/mL) isolated from the South China Sea gorgonian *Dichotella gemmacea* [127]; two new sesquiterpene aminoquinones langcoquinones A and B isolated from the Vietnamese sponge *Spongia* sp. (MIC = 12.5 µM) [128]; a new lobane diterpenoid 5’-prenyl-α-elemenone (MIC = 20 µg/mL) from a Malaysian soft coral *Sinularia* sp. [129]; a new diterpene scaffold darwinoilide (MIC = 32.2 µM) from the Antarctic sponge...
Dendrilla membranosa [130]; echinochrome A and spinochrome C (MIC = 22.5 µM) from sea urchins D. savignyi, T. gratilla, E. mathaei and T. pileolus from Madagascar [131], the meroterpenoid verruculide B2 (MIC = 32 µg/mL) from the fermentation broth of Penicillium sp. SCS-KFD09 isolated from the Chinese marine worm Sipunculus nudus [132]; a bioactive sterol (MIC = 20 µg/mL) from a Red Sea soft coral S. terspilli [133]; a new norditerpene citrovirin (MIC = 12.4 µg/mL) isolated from a marine algiicolous fungus Trichoderma citroviride [134]; two new bisabolene sesquiterpenes asperchondols A and B (MIC = 25 µM) isolated from the marine sponge Chondrilla nucula [135]; long-chain peptaibol peptides (MIC = 25 µg/mL) by a French marine blue mussel-derived strain of Trichoderma longibrachiatum [136]; a polyketide antibiotic haliangicin (MIC > 32 µg/mL) and its analogues isolated from the marine myxobacterium Halangium ochraceum SMP-2 [137]; two curvatin macrolides (MIC = 20 µg/mL) isolated from the broth of a cultured marine actinomycete Pseudonocardia sp. HS7 [138]; a new halimane-type diterpenoid micromonohalimane B (MIC = 40 µg/mL) isolated from a Micromonospora sp. cultivated from the marine ascidian S. brakenhielmi [139]; a azaphilonidal derivative penicilazaphilone C (MIC = 15.6 µg/mL) isolated from the marine fungus strain Penicillium sclerotiorum M-22 [140]; a new 2′-acetoxy-7-chlorocitreorosein anthraquinone (MIC = 10 µM) from a South China Sea endophytic marine fungus Penicillium citrinum HL-5126 [141]; a new antibacterial macrolide borrelidin C (MIC = 6 µM) from a saltarn-derived holophilic Nocardiosis sp. [142]; a new antichlamydial dimeric indole derivative (IC50 = 46.6–96.4 µM) isolated from the South China Sea sponge-derived actinomycyte Rubrobacter radiotolerans [143]; the anthraquinone emodin (MIC = 32 µg/mL) isolated from a culture of the endophytic fungus Eurotium chevalieri KUFA 0006 [144]; new thiodiketopiperazines eutypellazines P-R (MIC = 16–32 µM) isolated from a deep sea fungus Euptyelia sp. [145]; a new lipophilic cyclic hexapeptide thermoactinoamide A (MIC = 35 µM) isolated from the Icelandic thermophilic bacterium Thermoactinomyces vulgaris [146] and a new neo-actinomycin A (MIC = 16 µg/mL) isolated from a Chinese marine-derived Streptomyces sp. IMB094 [147].

2.2. Antifungal Activity

Eleven studies during 2016–2017 reported on the antifungal activity of several marine natural products (68–79) isolated from marine bacteria, dinoflagellates, fungi and sponges, a slight increase from our last review [10], and previous reviews of this marine pharmacology series.

As shown in Table 1 and Figure 1, two reports investigated an antifungal marine compound with a novel mechanism of action. Espiritu investigated the polydroyxy polyene antifungal amphidinol 3 (68) isolated from cultures of the marine dinoflagellate Amphidinium klebsii [72], observing that membrane integrity loss by direct interaction with membrane lipids showed “an absolute dependence on the presence of sterols”. Furthermore, Iwamoto and colleagues, using atomic force microscopy, determined that amphidinol 3 formed “different types of sterol-aided polymorphic channels in a concentration dependent manner” [73].

As shown in Table 1 and Figure 1, ten marine natural products (69–79) showed antifungal activity with MICs that were either less than 10 µg/mL, 10 µM, or 10 µg/disk but no mechanism of action studies were reported in the papers: a sesquiterpene avarol (69) isolated from the Mediterranean sponge Dysidea avara [74]; a polycyclic tetramacrolactam dihydromaltophilin (70) isolated from a marine Conus miles-derived Streptomyces sp. CMB-CS038 [75]; a pair of enantiomeric sesterterpenoids (+) hippolide J (71a, 71b) isolated from the South China Sea sponge Hippospongia lachne [76]; a hybrid polyketide ilicicolin H (72) isolated from the Danish marine-derived fungus Stilbella fenestrata [77]; new cyclic lipopeptides iturin F1 and iturin F2 (73, 74) from the Korean saltern-derived marine Bacillus sp. KCB148006 [78]; two macrolide polyketides PF1163A (75) and -B (76) isolated from a Japanese unidentified marine alga-derived fungus Penicillium meleagrinum var. viridi-flavum [79]; a terpene plakinic acid M (77) isolated from the Bahamian sponge association Plakortis halichondrioides-Xestospongia deweerdtae [80]; a new steroidal saponin poecillastro-
and (antimalarial, antileishmanial and antitrypanosomal) 1,2,3,4-tetrahydro-
Streptomyces Australian marine-sediment derived 81, 82 A and D (ptilomycalin F (potently inhibited chloroquine-sensitive P. falciparum activity against chloroquine-sensitive P. falciparum) isolated from the tropical Micronesian sponge Halichondria sp. [148]; several new bromopyrrole alkaloids (apparent IC$_{50}$ = 20 µM) isolated from the South China sea sponge Agelas sp. [149]; and a novel polyketide kalkipyrone B (IC$_{50}$ = 13.4 µM) isolated from American Samoan cyanobacterium Leptolyngbya sp. [150].

2.3. Antiprotozoal and Antituberculosis Activity

As shown in Table 1, and as reported in the 1998–2015 marine pharmacology reviews of this series [1–10], 22 studies contributed novel findings in 2016–2017 on the antiprotozoal (antimalarial, antileishmanial and antitrypanosomal) and antituberculosis pharmacology of structurally characterized marine natural products (80–103).

Malaria, a global disease caused by protozoan genus Plasmodium (P. falciparum, P. ovale, P. vivax and P. malariae), currently affects over 2 billion people worldwide. Further contributing to the global antimalarial drugs research, 8 marine molecules (80–88) isolated from bacteria, molluscs, sponges, soft corals, and ascidians were shown to possess antimalarial activity during 2016–2017. As shown in Table 1 and Figure 1, potent (IC$_{50}$ < 2 µM) to moderate (IC$_{50}$ > 2–10 µM) antimalarial activity was reported for several marine natural products (80–88) although the mechanism of action for these compounds remained underestimated at the time of publication: a norterpene cyclic peroxide diacarperoxide A (80) isolated from the South China Sea sponge Diacarnus megaspinorhabdosa shown to be a potent inhibitor of both P. falciparum W2 and D6 clones [83]; cyclic depsipeptides dudawalamides A and D (81, 82) from the Papua New Guinean cyanobacterium Moorea producens with moderate antimalarial activity against chloroquine-resistant P. falciparum strain W2 [84]; the alkaloid eudistidine A (83) isolated from Paluan marine ascidian Eudistoma sp. that potently inhibited chloroquine-sensitive P. falciparum strain D6 and chloroquine-resistant strain W2 [85]; a novel dimeric diketopiperazine nasaseazcine C (84) isolated from an Australian marine-sediment derived Streptomyces sp. that exhibited moderate inhibitory activity against chloroquine-sensitive P. falciparum strain 3D7 [86]; a new N-hydroxylated 1,2,3,4-tetrahydro-β-carboline alkaloid analogue of the known 7-bromohomoterpamine (85) isolated from the New Zealand ascidian Pseudodistoma opacum with moderate activity against P. falciparum chloroquine-resistant strain FcB1 [87]; a new guandine alkaloid ptilmycin F (86) and known fromiamycin (87) from the Madagascar marine sponge Monanchora unguiculata which demonstrated potent activity against P. falciparum strain 3D7 [88], and a new isocyanoditerpene pustulosaisonitrile-1 (88) from the Australian nudibranch Phyllidiella pustulosa which showed potent activity against P. falciparum strain 3D7 [89].

As shown in Table 1 and Figure 1, 9 marine compounds (83, 89–96) isolated from bacteria, fungi, sponges were reported to possess bioactivity towards the so-called neglected protozoal diseases: Leishmaniasis, caused by the genus Leishmania (L.), amebiasis, trichomoniasis, as well as African sleeping sickness (caused by Trypanosoma (T.) rhodesiense and T. brucei gambiense) and American sleeping sickness or Chagas disease (caused by T. cruzi).

Only one report described two antitrypanosomal marine chemicals as well as their mechanisms of action. Carballéira and colleagues examined the mode of action of novel very long-chain α-methoxylated fatty acids (89, 90), isolated from the Caribbean sponge Asteropus niger, and demonstrated that they were toxic towards L. infantum amastigotes and free living promastigotes by inhibition of Leishmania topoisomerase 1B enzyme considered...
“an important therapeutic target against L. infantum” [90]. In addition, seven marine natural products (82, 91–96) exhibited antileishmanial and antiprotozoal activity, although their mechanisms of action remained undetermined: The cyclic depsipeptide dudawalamide D (82) from the Papua New Guinean cyanobacterium Moera producens with potent against L. donovani. [84]; a new oxysterol (91), isolated from a Panamanian octocoral Gorgonia sp. that moderately reduced the multiplication of L. infantum promastigotes thus suggesting “antileishmanial efficacy against intracellular amastigotes” [91]; two linear furanosteroids icerin-1 and -2 (92, 93) from the Turkish sponge Ircinia oros with moderate activity against L. donovani, suggesting the compounds “bifuran terminus … positively influences the in vitro antiprotozoal activity” [92]; a new cyclic polyketide-peptide hybrid janadolide (94) from the Japanese marine cyanobacterium Okennia sp. which demonstrated very potent activity against T. brucei brucei, thus revealing potential for development as “new antitrypanosomal drugs” [93]; the cyclic pentapeptide malformin A1 (95) isolated from the Philippine marine seagrass-derived fungus Aspergillus tubengensis IFM 63452 highly active towards the parasit T. congolense and recommended as “an antiprotozoal agent” [94]; a novel azepino-diindole alkaloid rhodozepinone (96) isolated from a Red Sea marine sponge-derived bacteria Rhodococcus sp. UA13 s with moderate activity against T. brucei brucei TC221 and perhaps a “promising future contribution to drug discovery” [95].

The emergence of drug-resistant Mycobacterium tuberculosis has continued to stimulate an ongoing global search for novel therapeutic leads with novel mechanisms of action, and, as shown in Table 1 and Figure 1, during 2016–2017, 8 novel marine natural products (62, 97–103), isolated from bacteria, sponges and fungi, generated promising pharmacological activity and thus contributed to the search for novel antituberculosis agents. Arai and colleagues identified the alkaloid melpholin A (97) isolated from the Indonesian marine sponge Melphulus sp. that demonstrated strong inhibitory activity against dormant M. smegmatis by targeting the “BCG1083 protein of putative exopolyphosphatase and the BCG1321c protein of diadenosine 5′,5′-P1,P4-tetraphosphate phosphorylase” [96]. Rodrigues Felix and colleagues isolated the polyketide 15-α-methoxypuupehenol (98) from the marine sponge Petrosia sp. that demonstrated potent antibacterial activity against dormant M. tuberculosis, highlighting a mode of action in which bacterial killing “is observed only for dormant but not metabolically active bacteria” [97].

As shown in Table 1 and Figure 1, additional six marine natural products (99–103) exhibited antituberculosis activity, although their mechanisms of action remained undetermined: the alkaloid gliotoxin (99) derived from a deep-sea fungus Aspergillus sp. SCSIO Ind09F01 that strongly inhibited “at very low μM level” M. tuberculosis in vitro [98]; the polyketide proximicin B (100) isolated from the South China Sea sediments-derived Verrucosispora sp. MS100047 which demonstrated “a good anti-BCG activity” [99]; the hybrid peptide/polyketide smenothiazole A (101) isolated from a sponge consortium of Puerto Rican marine sponge Plakortis symbiotica-Xestospongia deweerdtiae and identified as a “new lead compound with high activity” against M. tuberculosis H37Rv [100]; a new macrolide spiralaclam B (62) isolated from Northeastern Pacific Canadian marine sediments-derived Micromonospora sp. RA4480 reported to demonstrate “selective and potent inhibition of M. tuberculosis” [65]; an “unusual” alkaloid talaramide A (102) isolated from the mangrove endophytic fungus Talaromyces sp. HZ-YX1 that inhibited a mycobacterial protein kinase C required for localization of mycobacterial in macrophage [101], and a naphthoquinone dimer viomellein (103) produced by the Indonesian sponge-derived Aspergillus sp. that showed potent activity against dormant M. bovis BCG [102].

2.4. Antiviral Activity

As shown in Table 1 and Figure 1, 18 reports were published during 2016–2017 on the antiviral pharmacology of marine natural products (104–123) against dengue virus, human immunodeficiency virus type-1 (HIV-1), human T-cell leukemia virus type 1 (HTLV-1), human herpes simplex virus (HSV), influenza virus, hepatitis C virus, and porcine epidemic diarrhea virus.
As shown in Table 1, 6 reports described antiviral marine chemicals and their mechanisms of action. O’Rourke and colleagues communicated that the alkaloid hymenialdisine (104), isolated from the Red Sea sponge Stylissa carteri, inhibited HIV infection and while the retroviral reverse transcriptase was not inhibited, the investigators concluded that it could “serve as starting scaffold(s) for further investigation” [103]. Yamashita and colleagues discovered that the merosesquiterpene metachromarin A (105) isolated from the marine sponge Dactylospongia metachromia significantly inhibited the production of hepatitis B virus (HBV) by affecting the activities of the viral core promoter and reducing the hepatic nuclear factor α protein, a mechanism that may contribute to “ameliorating HBV-related disorders in the liver” [104]. Ishikawa and colleagues reported that the carotenoid peridin (106) isolated from the Japanese coral Isis hippuris inhibited the proliferation and survival of HTLV-1-infected T-cell lines by a mechanism that involved “suppression of NF-κB and Akt signaling” suggesting the compound was a “promising drug for HTLV-1-associated diseases” [105]. Niu and colleagues determined that the phenolic lactone spiromastilactone D (107) isolated from a South Atlantic deep-sea (2869 m) sediment-derived fungus Spiromastix sp. MCCC 3A00308 demonstrated “broad anti-influenza spectrum” by a mechanism that targeted viral attachment and entry by affecting “hemagglutinin protein-sialic acid receptor interaction” and viral genome replication by “targeting the viral RNP complex” [106]. Kim and colleagues investigated the indolosesquiterpenoid xiamycin D (108) isolated from the Korean saltern-derived halophilic actinomycete Streptomyces sp. strain HK18 and observed it displayed potent inhibition of porcine epidemic diarrhea virus by inhibiting genes encoding several essential structural proteins required for PEDV replication, thus demonstrating novel and “promising skeletons against PEDV-related viruses” [107]. Cheng and colleagues isolated a new edycone terpenoid zoanthone A (109) from a Taiwanese sea anemone Zoanthus spp. that demonstrated good activity against dengue virus 2 by a mechanism that inhibited viral replication by blocking the C-terminal RNA-dependent RNA polymerase domain of NS5, the “largest and the most conserved (non-structural) protein” of the virus [108].

An additional 15 marine natural products (106, 110–123), listed in Table 1 and shown in Figure 1, demonstrated antiviral activity, but the mechanism of action of these compounds remained undetermined at the time of publication. A new aromatic terpenoid (110) isolated from the Japanese marine crinoid Alloeocomatella polycladula which showed moderate activity against the hepatitis C virus (HCV) NS3 helicase [109]; a known sesterterpenoid alotaketal C (111) isolated from the Canadian marine sponge Phorbus sp. shown to activate latent HIV-1 provirus expression [110]; a new cyclic pentapeptide aspergillipeptide D (112) isolated from the South China Sea gorgonian Melitodes squamata-derived fungus Aspergillus sp. SCSIO 41502 with moderate activity against herpes virus simplex type 1 (HSV-1) [111]; new anthraquinones aspergillosins H and I (113, 114), isolated from a South China Sea deep sea sediment (2326 m)-derived fungus, Aspergillus versicolor SCSIO 41502, with moderate activity against HSV-1 [112]; a new polyketide asteltoxin E (115) isolated from a Chinese marine sponge Callyspongia sp.-derived fungus Aspergillus sp. SCSIO XWS02F40 with moderate activity against influenza virus subtype H1N1 and H3N2 [113]; a novel cyclopentenone derivative (116) was isolated from the South China Sea soft coral Sinularia verrucosa which was “moderately protective” against the cytopathic activity of in vitro HIV-1 infection [114]; a new thiodiketopiperazine-type alkaloid eutypellazine E (117) isolated form a South Atlantic deep sea (5610 m) sediment-derived fungus Eutypella sp. MCCC 3A00281 moderately inhibited in vitro HIV-1 infection [115]; a tricyclic anthraquinone ω-hydroxyemodin (118) isolated from the Red Sea brown alga Padina pavonica-derived fungus Fusarium equiseti moderately inhibited hepatitis C virus NS3/4A serine protease in vitro [116]; the known polyketide malformin C (119) isolated from the marine-derived fungus Aspergillus niger SCSIO JswF30 potently inhibited HIV-1 infection in vitro [117]; the known marine β-carboline alkaloid manzamine A (120) isolated from the Indo-Pacific sponge Acanthostrongylophora sp. potently inhibited HSV-1 replication and release in vitro, observing “that manzamine A had optimal structure features for anti-HSV-1 activity” [118]; the carotenoid peridin (106)
isolated from the Taiwanese zoanthid *Palythoa mutuki* moderately inhibited all serotypes of dengue virus in vitro [119]; a new meroterpenoid stachybonoid A (121) isolated from the Chinese marine crinoid *Himerometra magnipinna*-derived fungus *Stachybotrys chartarum* 952, which evidenced moderate activity against dengue virus replication and expression of prM protein [120], and two new pregnane-type steroids subergorgol T and U (122, 123) isolated from a South China Sea gorgonian coral *Subergorgia suberosa* that moderately inhibited influenza virus strain A/WSN/33 (H1N1) in vitro [121].

3. Marine Compounds with Antidiabetic and Anti-Inflammatory Activity, and Affecting the Immune and Nervous System

Table 2 presents the 2016–2017 preclinical pharmacology of marine chemicals (124–234), which demonstrated either antidiabetic or anti-inflammatory activity, as well as affected the immune or nervous system, and whose structures are depicted in Figure 2.
Table 2. Marine pharmacology in 2016–2017: marine compounds with antidiabetic and anti-inflammatory activity; and affecting the immune and nervous system.

| Drug Class       | Compound/Organism | Chemistry       | Pharmacological Activity                      | IC50 b | MMOA c | Country d | References   |
|------------------|-------------------|-----------------|-----------------------------------------------|--------|--------|-----------|--------------|
| Antidiabetic     | agelasine G (124)/sponge | Alkaloid-terpenoid | PTP1B inhibition                             | 15 µM  | Akt insulin pathway increase | IDN, JAP    | [151]        |
| Antidiabetic     | BDDE (125)/alga    | Shikimate h      | Decrease glucose levels in vivo               | 10 mg/kg** | PTP1B expression inhibition | CHN         | [152]        |
| Antidiabetic     | dieckol (126)/alga | Shikimate h      | Decrease in glucose levels                    | 1 µg/g** | Akt insulin pathway increase | S. KOR      | [153]        |
| Antidiabetic     | gombasterol E (127)/sponge | Terpenoid f     | Enhanced glucose uptake in vitro              | 20 µM  | AMPK phosphorylation increase | S. KOR      | [154]        |
| Antidiabetic     | leptolide (128)/soft coral | Terpenoid f     | Murine glucose tolerance and insulin sensitivity increased | 0.1 mg/kg** | PKB phosphorylation | ESP         | [155]        |
| Antidiabetic     | nectriacids B and C (129, 130)/fungus | Polyketides d | α-glucosidase inhibition                      | 23.5, 42.3 µM | C-12 carboxyl esterification required | CHN         | [156]        |
| Antidiabetic     | penicilliumin B (131)/fungus | Terpenoid f     | Glomerular mesangial cells fibrogenic inhibition | 0.5 µM  | NADPH oxidase inhibition | CHN         | [157]        |
| Antidiabetic     | wailupemycin I (132)/bacterium | Polyketide d   | α-glucosidase inhibition                      | 8.3 µM | Competitive inhibition | CHN         | [158]        |
| Antidiabetic     | asperentin B (133)/fungus | Polyketide d   | PTP1B inhibition                              | 2 µM   | Undetermined | DEU         | [159]        |
| Antidiabetic     | lasiodiplactone A (134)/fungus | Polyketide d | Glomerular mesangial cells fibrogenic inhibition | 29.4 µM | Undetermined | CHN         | [160]        |
| Antidiabetic     | 7-hydroxy-de-O-methyllasiodiplodin (135)/bacterium | Polyketide d | α-glucosidase inhibition                      | 25.8 µM | Undetermined | CHN         | [161]        |
| Antidiabetic     | sescandelin B (136)/fungus | Polyketide d   | α-glucosidase inhibition                      | 17.2 µM | Undetermined | CHN         | [162]        |
| Anti-inflammatory| AMT-E (127)/alga    | Terpenoid f     | Murine colitis inhibition                     | 10 mg/kg** | Inhibition of TNF-α, IL-6 | ESP, MAR    | [163]        |
| Anti-inflammatory| Bacillus sp. diketopiperazines (138–140)/bacterium | Peptide e    | TGFBIp inhibition in vivo                     | 5 µM** | Septic responses inhibition | S. KOR      | [164,165]    |
| Anti-inflammatory| 6-bromoisatin (141)/mollusc | Alkaloid e    | Lung inflammation inhibition in vivo           | 0.05 mg/g** | Inhibition of TNF-α, IL-6 | AUS         | [166]        |
| Anti-inflammatory| ceylonamide A (142)/sponge | Terpenoid f   | Macrophage RANKL inhibition                   | 13 µM  | SAR completed | IDN, JPN, NLD | [167]        |
| Anti-inflammatory| citrinin H1 (143)/fungus | Polyketide e | Microglia NO and PGE2 release inhibition      | 8 µM   | NF-κB inhibition | S. KOR, VNM  | [168]        |
| Anti-inflammatory| nonenolide derivative (144)/alga | Polyketide e | BMDC cytokine release inhibition               | 7.6–10.9 µM | JNK, ERK, AP-1, NF-κB inhibition | S. KOR      | [169]        |
| Anti-inflammatory| cucumaroside A2-2 (145)/sea cucumber | Terpenoid f | Binding of macrophage P2X purinergic receptors | 0.02 µM  | Induction Ca2+ oscillations | RUS         | [170]        |
| Anti-inflammatory| curcularin derivative (146)/fungus | Polyketide e | Macrophage PGE2 and NO release inhibition       | 1.9–2.7 µM | NF-κB signaling inhibition | S. KOR      | [171]        |
| Anti-inflammatory| 9,11-dihydrogracilin A (147)/sponge | Terpenoid f   | PBMC proliferation inhibition                  | 3 µM  | IL-6 and IL-10 inhibition | ITA         | [172]        |
Table 2. Cont.

| Drug Class | Compound/Organism | Chemistry | Pharmacological Activity | IC₅₀ b | MMOA c | Country d | References |
|------------|------------------|-----------|--------------------------|--------|--------|-----------|------------|
| Anti-inflammatory | dysivillosin A (148)/sponge | Terpenoid f | Basophil β-hexosaminidase inhibition | 8.2 µM | IL-4 and LTB4 inhibition | CHN [173] |
| Anti-inflammatory | epinecidin-1 (149)/fish | Peptide g | Inhibition of MyD88 protein levels | 6 µg/mL * | Proteasome degradation required | TWN [174] |
| Anti-inflammatory | excavatolide B (150)/soft coral | Terpenoid f | Attenuation of rat arthritis [175] | 2.5, 5 mg/kg ** | Decreased MMP-2, MMP-9, CD11b in tissues | CHN, TWN [175] |
| Anti-inflammatory | fucoxanthin (151)/alga | Terpenoid f | Decreased mice paw edema, adipogenesis and ear inflammation | 4 mg/kg ** | Modulation of iNOS, PLA₂, COX-2, ACC, IL-6 and Nrf2 expression | JPN, S. KOR, MEX [176–179] |
| Anti-inflammatory | H. crispa peptide (152)/sea anemone | Peptide g | Macrophage histamine receptor inhibition | 10 µM * | Intracellular Ca²⁺ increase inhibition | RUS [180] |
| Anti-inflammatory | hipposponlachnin B (153)/sponge | Terpenoid f | Basophil β-hexosaminidase inhibition | 24 µM | IL-4 and LTB4 inhibition | CHN [181] |
| Anti-inflammatory | ogipeptins A-D (154–157)/bacterium | Peptide g | Macrophage TNF-α production inhibition | 1 µM * | Block LPS binding to CD14 | JPN [182] |
| Anti-inflammatory | oscarellin (158)/sponge | Alkaloid g | Macrophage TNF-α and IL-6 expression inhibition | >10 µM | JNK, ERK, AP-1, NF-κB inhibition | S. KOR, USA [183] |
| Anti-inflammatory | pseudane-VIII (159)/bacterium | Alkaloid g | Macrophage NO release inhibition | 6 µM * | iNOS and IL-1β inhibition | S. KOR [184] |
| Anti-inflammatory | acremeremophilane B (160)/fungus | Terpenoid f | Macrophage NO release inhibition | 8 µM | Undetermined | CHN, DEU [185] |
| Anti-inflammatory | actinoquinolines A and B (161, 162)/bacterium | Alkaloid g | COX-1 and -2 inhibition | 1.4–7.6 µM | Undetermined | EGY, USA [186] |
| Anti-inflammatory | anthenoxide O (163)/starfish | Terpenoid f | Macrophage SOX inhibition | >10 µM * | Undetermined | RUS, VNM [187] |
| Anti-inflammatory | aurasperone C (164)/fungus | Polyketide e | COX-2 inhibition | 4.2 µM | Undetermined | CHN [188] |
| Anti-inflammatory | briarenolides M and N (165–167)/soft coral | Terpenoid f | Macrophage iNOS expression inhibition | 10 µM * | Undetermined | TWN [189] |
| Anti-inflammatory | briarenolides ZII and ZVI (167, 168)/soft coral | Terpenoid f | Macrophage iNOS and COX-2 expression inhibition | 10 µM * | Undetermined | TWN [190] |
| Anti-inflammatory | dihydrobipolaroxin (169)/fungus | Terpenoid f | Macrophage NO release inhibition | >12.5 µM * | Undetermined | CHN [191] |
| Anti-inflammatory | echinulin (170)/fungus | Alkaloid g | Microglia NO release inhibition | 4.6 µM | Undetermined | CHN, S. KOR [192] |
| Anti-inflammatory | 5α-iodozoanthenamine (171)/zoanthid | Alkaloid g | Neutrophil SOX and elastase inhibition | >10 µM * | Undetermined | TWN [193] |
| Anti-inflammatory | klyfflaccisteroid J and K (172, 173)/soft coral | Terpenoid f | Neutrophil SOX and elastase inhibition | 1.5–5.8 µM | Undetermined | TWN [194,195] |
| Drug Class | Compound/Organism | Chemistry | Pharmacological Activity | IC<sub>50</sub> b | MMOA c | Country d | References |
|------------|------------------|-----------|--------------------------|------------------|---------|----------|------------|
| Anti-inflammatory | *L. varium* diterpenoid (174)/soft coral | Terpenoid | Neutrophil elastase inhibition | >10 µM * | Undetermined | EGY, SAU, TWN [196] |
| Anti-inflammatory | petasitosterones B and C (175, 176)/soft coral | Terpenoid | Neutrophil SOX and elastase inhibition | 2.7–4.4 µM | Undetermined | TWN [197] |
| Anti-inflammatory | *Pinnigorgia* sp. sterols (177, 178)/soft coral | Terpenoid | Macrophage COX-2 and iNOS expression inhibition | 10 µM * | Undetermined | TWN [198] |
| Anti-inflammatory | *Pinnigorgiol A* (179)/soft coral | Terpenoid | Neutrophil SOX and elastase inhibition | 4, 5 µM | Undetermined | TWN [199] |
| Anti-inflammatory | *Pinnigorgiol E* (180)/soft coral | Terpenoid | Neutrophil SOX and elastase inhibition | 1.6, 3.9 µM | Undetermined | TWN [200] |
| Anti-inflammatory | *Pinnisterols A and H* (181, 182)/soft coral | Terpenoid | Neutrophil SOX and elastase inhibition | 2.3–3.3 µM | Undetermined | TWN [201,202] |
| Anti-inflammatory | Plancipyrroside B (183)/starfish | Terpenoid | Macrophage iNOS expression inhibition | 5.9 µM | Undetermined | RUS, VNM [203] |
| Anti-inflammatory | Proolinckioside A (184)/starfish | Terpenoid | Macrophage SOX inhibition | 10 µM | Undetermined | IND, RUS [204] |
| Anti-inflammatory | Sarcophytonolide O (185)/soft coral | Terpenoid | Macrophage iNOS expression inhibition | 8 µM | Undetermined | CHN, USA [205] |
| Anti-inflammatory | Sinulariolide (198)/soft coral | Terpenoid | Neutrophil SOX and elastase inhibition | 0.9–8.5 µM | Undetermined | TWN [206] |
| Anti-inflammatory | *Sinularacols A and B* (186, 187)/soft coral | Terpenoid | Neutrophil SOX and elastase inhibition | 1.4–8 µM | Undetermined | CAN, SAU, TWN [207,208] |
| Anti-inflammatory | Sinubrasolides A and D (188, 189)/soft coral | Terpenoid | Macrophage TNF-α and IL-6 release inhibition | 1.4–4.2 µM | Undetermined | IND, PAN, USA [209] |
| Immune system | Cucumarioside A₂-2 (145)/sea cucumber | Terpenoid | Increase in spleen white pulp and macrophage activation | 3 mg/kg ** | Increased B cell PCNA and M1 macrophages | RUS, TWN [210,211] |
| Immune system | Gracilins A, H and L (193–195)/sea cucumber | Terpenoid | CD147 receptor modulation and T-cell IL-2 release inhibition | 1 µM * | Hypersensitivity and NFATc inhibition | ESP, GBR [212,213] |
| Immune system | Shinorine and porphyra-334 (196, 197)/algae | Peptide | NF-κB stimulation | 50 µg/mL * | Tryptophan metabolism modulation | AUT [214] |
| Immune system | Sinulariolide (198)/soft coral | Terpenoid | Dendritic cell maturation suppression | 25 µg/mL * | IL-6, IL-12 and NO inhibition | TWN [215] |
| Immune system | CDMW-3 (199)/fungus | Peptide | PCA inhibition in vivo | 20 mg/kg ** | Mast cell histamine and cytokine release inhibition | CHN [216] |
| Immune system | Chrysamide C (200)/fungus | Alkaloid | IL-17 inhibition | >1 µM * | Undetermined | CHN [217] |
| Drug Class         | Compound/Organism * | Chemistry | Pharmacological Activity                          | IC₅₀ b | MMOA c | Country d | References |
|--------------------|---------------------|-----------|---------------------------------------------------|--------|--------|-----------|------------|
| Immune system      | cocosolide (201)/cyanobacterium | Polyketide d | IL-2 inhibition                                  | 2.5 µM * | Undetermined | CHN, USA  | [218]     |
| Immune system      | myxillin A (202)/sponge      | Alkaloid g | IL-12p40 release inhibition                       | 10 µg/mL * | Undetermined | DNK, ISL  | [219]     |
|Immune system      | pectinioside A (203)/starfish | Terpenoid f | Increase OVA-specific IgG1 in vivo                | 25 µg *  | Undetermined | JPN       | [220]     |
| Immune system      | peniphenone (204)/fungus     | Polyketide d | Lymphocyte immune suppression                     | 8.1–9.3 µg/mL | Undetermined | CHN       | [221]     |
| Immune system      | USF-19A (205)/bacterium     | Peptide g  | Splenocyte IL-5 release inhibition                | 0.57 µM  | Undetermined | CHN       | [222]     |
| Nervous system     | APETx4 (206)/sea anemone    | Peptide g  | Kv10.1 potassium channel inhibition               | 1.1 µM   | Binds channel in closed state | BEL, DEU  | [223]     |
| Nervous system     | astaxanthin (207)/sponge    | Terpenoid f | Penitrem A toxicity reversal                      | 20 µM *  | AMPA and NMDA receptors involved | EGY, USA  | [224]     |
| Nervous system     | crambescidin 816 (208)/sponge| Alkaloid g | Cortical neurons cytosolic Ca²⁺ increase          | 10 µM *  | Non-competitive inhibition | ESP, CUB, FRA, MEX | [225] |
| Nervous system     | C. generis O-conotoxin (209) | Peptide g  | A9α10 nACh receptor inhibition                    | 16.2 nM  | AUS, CHN   | [226]     |
| Nervous system     | C. princeps PiVIIA peptide (210)/cone snail | Peptide g  | Neuronal Ca²⁺ current increase                    | 3 µM *   | Potentiates two types Ca²⁺ channels | CUB, MEX  | [227]     |
| Nervous system     | conorphin T (211)/cone snail | Peptide g  | KOR agonist                                       | 9.8 µM   | In vivo colorectal receptor inhibition | AUS      | [228]     |
| Nervous system     | 11-dehydrosinulariolide (212)/soft coral | Terpenoid f | Amelioration PD and spinal cord injury attenuation | 5 µg/rat ** | DJ-1 expression upregulation and microglia activation | TUN      | [229,230] |
| Nervous system     | discorhabdin G (213)/sponge  | Alkaloid g | Eel and human AChE inhibition                     | 1.3 µM   | DEU, ITA, SVN | [231]     |
| Nervous system     | fucoxanthin (151)/alga       | Terpenoid f | BACE1 inhibition                                   | 5.3 µM   | Mixed inhibition | GBR, S. KOR | [232]     |
| Nervous system     | fucoxanthin (151)/alga       | Terpenoid f | Reversal BDNF expression                           | 50 mg/kg ** | Reversed AChE activity | CHN      | [233]     |
| Nervous system     | fucoxanthin (151)/alga       | Terpenoid f | Neuroprotection after TBI-induced brain injury     | 100 mg/kg ** | Nrf2-ARE pathway modulation | CHN      | [234]     |
| Nervous system     | 5-hydroxycyclopenicillone (214)/fungus | Polyketide d | H₂O₂-induced neuronal death protection            | 30 µM *  | CHN, USA   | [235]     |
| Nervous system     | maitotoxin (215)/alga        | Polyketide d | Activation of NSCC                                 | 10 pM *  | MEX       | [236]     |
| Nervous system     | makaluvamine J (216)/sponge  | Alkaloid g | Reduction of mitochondrial damage                  | 0.1–1 µM * | ESP, FJl, GBR | [237]     |
| Nervous system     | MEC-1 (217)/sponge           | Polyketide d | AChE inhibition                                    | 20.9 µM  | EGY       | [238]     |
| Nervous system     | mellpaladine A (218)/ascidian| Alkaloid g | In vivo behavior modulation                        | 8 nM/mouse ** | Serotonin receptor affinity | JPN      | [239]     |
| Nervous system     | Ms 9a-1 peptide (219)/sea anemone | Peptide g  | Decrease in nociceptive and inflammatory response in vivo | 0.3 mg/kg ** | TRPA1 modulation | NOR, RUS  | [240]     |
| Nervous system     | phlorofucofuroeckol-A (220)/alga | Polyketide d | Glutamate-induced neurotoxicity inhibition        | 10 µM *  | Intracellular and mitochondrial ROS inhibition | S. KOR   | [241]     |
| Drug Class       | Compound/Organism | Chemistry                        | Pharmacological Activity               | IC₅₀  | Country  | References |
|------------------|-------------------|----------------------------------|----------------------------------------|------|----------|------------|
| Nervous system   | piloquinone (221)/bacterium | Polyketide<sup>d</sup> | MAO-B inhibition                        | 1.2 μM | Reversible competitive inhibition | S. KOR, USA [242] |
| Nervous system   | pseudopterosin A (222)/soft coral | Terpenoid<sup>f</sup> | Synaptic transmission alteration        | 1 μM  | Extensive brain distribution | USA [243] |
| Nervous system   | squalamine (223)/shark | Terpenoid<sup>f</sup> | Reduction of α-synuclein aggregation in vivo | 50 μM | α-synuclein displaced from lipid membranes | ESP, GBR, ITA, NLD, USA [244] |
| Nervous system   | stryphnusin (224)/sponge | Alkaloid<sup>g</sup> | Eel AChR inhibition                     | 232 μM | Reversible competitive inhibition | HRV, NOR, SVN, SWE [245] |
| Nervous system   | xyloketal B (225)/fungus | Polyketide<sup>d</sup> | Cerebral infarction modulation         | 50 mg/kg | Decreased ROS and cytokines | CAN, CHN, USA [246] |
| Nervous system   | araplysillin X (226)/fungus | Alkaloid<sup>g</sup> | BACE1 inhibition                        | 31.4 μM | Undetermined | NZL, USA [247] |
| Nervous system   | caracolamide A (227)/cytobacterium | Alkaloid<sup>g</sup> | Ca²⁺ channel modulation                 | 10 pM  | Undetermined | BRA, JOR, PAN, USA, [248] |
| Nervous system   | conoramide-Sr3 (228)/snail | Peptide<sup>g</sup> | Blocks voltage-gated K⁺ channel        | 2.7 μM | Shaker channel specific | MEX [249] |
| Nervous system   | contryphan-Bt (229)/cone snail | Peptide<sup>g</sup> | Stiff-tail syndrome in vivo          | 5 ng/mouse | Undetermined | CHN [250] |
| Nervous system   | dehydroaustin (230)/fungus | Meroterpenoid<sup>f</sup> | AChE inhibition                       | 0.4 μM | Undetermined | CHN [251] |
| Nervous system   | hymenadin (231)/spoon | Alkaloid<sup>g</sup> | K<sub>1.3</sub> - K<sub>1.6</sub> + channel inhibition | 2.5–7.6 μM | Reversible competitive inhibition | HRV, NOR, SVN, SWE [245] |
| Nervous system   | psammnaplysen A (232)/spoon | Alkaloid<sup>g</sup> | Binding to RNA-binding protein HNRNPK | 86.2 μM | Undetermined | USA [253] |
| Nervous system   | terreulactone C (233)/fungus | Meroterpenoid<sup>f</sup> | AChE inhibition                       | 28 nM  | Undetermined | CHN [254] |
| Nervous system   | terreulactone D (234)/turd snail | Peptide<sup>g</sup> | A9α10 nAChR inhibition                | 10.2 μM | Undetermined | AUS, KAS, MEX, PHL, USA [255] |

<sup>a</sup> Organism: *Kingdom Animalia*: shrimp (Phylum Arthropoda); ascidian, fish (Phylum Chordata); coral, sea anemone and zoanthid (Phylum Cnidaria); sea cucumber, starfish (Phylum Echinodermata); cone snail, turrid snail (Phylum Mollusca); sponge (Phylum Porifera); *Kingdom Fungi*: fungus; *Kingdom Plantae*: alga; diatoms; *Kingdom Monera*: bacterium; <sup>b</sup> IC₅₀: concentration of a compound required for 50% inhibition; <sup>c</sup> MMOA: molecular mechanism of action; <sup>d</sup> Country: AUS: Australia; AUT: Austria; BEL: Belgium; BRA: Brazil; CAN: Canada; CHN: China; CUB: Cuba; DEU: Germany; DNK: Denmark; EGY: Egypt; ESP: Spain; FJI: Fiji; FRA: France; GBR: United Kingdom; HRV: Croatia; IDN: Indonesia; IND: India; IRL: Ireland; ITA: Italy; JOR: Jordan; JPN: Japan; KAS: Kazakhstan; MAR: Morocco; MEX: Mexico; NZL: New Zealand; NLD: Netherlands; NOR: Norway; PAN: Panama; PHL: Philippines; RUS: Russian Federation; SAU: Saudi Arabia; S. KOR: South Korea; SVN: Slovenia; SWE: Sweden; TWN: Taiwan; VNM: Vietnam; Chemistry: * Polyketide; * Terpene; * Nitrogen-containing compound; <sup>f</sup> Shikimate. Abbreviations: ACC: acetyl-CoA carboxylase; Ach: acetylcholine; AChE: acetylcholinesterase; Akt: also known as protein kinase B is a serine/threonine protein kinase; AMPA: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; AMPK: AMP-activated protein kinase; AMT-E: 11-hydroxy-1'-O-methylamantadione; AP-1: activator protein-1; BACE1: beta secretase aspartic protease; BDDE: Bis (2,3-dibromo-4,5-dihydroxybenzyl) ether; BK: voltage-gated potassium channels; BMDC: bone marrow-derived dendritic cells; CD14: cluster of differentiation 14; COX: cyclooxygenase; DHHP: α- diphenyl-ß-pircylylhydrazyl; DJ-1: protein encoded by the PARK7 gene; ERK: extracellular signal-regulated kinase; HNRNPK: heterogenous nuclear ribonucleoprotein K; IL: interleukin; iNOS: inducible nitric oxide synthase; JNK: c-Jun NH<sub>2</sub>-terminal kinase; LPS: Lipopolysaccharide; MAO-B: monoamine oxidase B; MyD88: myeloid differentiation primary response protein 88; NMDA: N-methyl-D-aspartate receptor; NO: nitric oxide; PTP1B: tyrosine protein phosphatase 1B; RANKL: receptor activator of nuclear factor-κB ligand; ROS: reactive oxygen species; SOX: superoxide; SQDC: sulfoquinovosyl diacylglycerols; TGFβ; transforming growth factor β; TNF-α: tumor necrosis factor-α; TRPA1: transient receptor potential ankyrin-repeat 1 receptor; TRPC1: transient receptor potential canonical type 1.
Figure 2. Cont.
Figure 2. Cont.
Figure 2. Cont.
Figure 2. Cont.
Figure 2. Cont.
Figure 2. Cont.
Figure 2. Cont.
Mar. Drugs 2021, 19, 35 of 71

Figure 2. Marine pharmacology in 2016–2017: marine compounds with antidiabetic and anti-inflammatory activity; and affecting the immune and nervous system.

3.1. Antidiabetic Activity

As shown in Table 2 and Figure 2, twelve publications reported on the mode of action of marine-derived antidiabetic compounds (124–132) during 2016–2017. Yamazaki and colleagues contributed to the pharmacology of diabetes by noting that the diterpene marine alkaloid agelasine G (124) isolated from the Japanese marine sponge *Agelas nakamurai* selectively inhibited protein tyrosine phosphatase B (PTP1B) and enhanced insulin-stimulated phosphorylation of serine/threonine protein kinase B or Akt in vitro, noting that further studies may “provide a candidate for anti-diabetes therapeutic agents” [151]. Xu and colleagues observed that a novel bromophenol bis (2,3-dibromo-4,5-dihydroxybenzyl) ether (BDDE) (125) isolated from the red alga *Odonthalia corymbifera*, increased glucose uptake in vitro, decreased the expression of protein tyrosine phosphatase 1B, activated the insulin signaling pathway and in mice “significantly decreased the blood glucose”, thus, suggesting
insulin signaling pathway and in mice “significantly decreased the blood glucose”, thus, suggesting BDDE might be a “treatment of type-2 diabetes” [152]. Kim and colleagues reported that the marine algal polyphenol dieckol (126), isolated from the marine brown alga *Ecklonia cava* attenuated blood glucose levels in the zebrafish model of hyperglycemia, an in vivo paradigm used to study chronic diseases, such as diabetes, by a mechanism that stimulated the protein kinase B (Akt) pathway, thus demonstrating the “anti-diabetic effect” of this compound [153]. Woo and colleagues showed that the novel polyoxygenated steroid gombasterol E (127) isolated from the Korean marine sponge *Clathria gomboawuensis* moderately enhanced both glucose uptake in adipocytes and phosphorylation of AMP-activated protein kinase and acetyl-CoA carboxylase in mouse skeletal myoblasts [154]. Villa-Pérez and colleagues reported that the furanocembranolide diterpenoid leptolide (128) isolated from soft coral *Leptogorgia alba* improved insulin sensitivity by increasing intracellular insulin signaling in both liver and skeletal muscle tissues of a diet-induced obese mice model, a “preclinical model of insulin resistance”, concluding that “furanocembranolides as a new therapeutic class to treat Type 2 diabetes” [155]. Cui and colleagues demonstrated that two new polyketides nectriacids B and C (129, 130) isolated from a South China Sea mangrove *Sonneratia ovata*-derived endophytic fungus *Nectria* sp. HN001 moderately inhibited α-glucosidase, a significant finding because this enzyme prevents “breaking down complex carbohydrates for absorption” [156]. Lin and colleagues discovered a new sesquiterpene penicilliumin B (131) isolated from South China Sea deep sea (1300 m) sediment-derived *Penicillium* strain F00120 that potently inhibited kidney fibrogenic action of high glucose in vitro through oxidative stress disruption, thus, suggesting this compound had potential for “therapy of diabetic nephropathy” [157]. Chen and colleagues studied a polyketide wailupemycin I (132) isolated from a Chinese marine alga *Enteromorpha prolifera*-derived *Streptomyces* sp. OUCMDZ-3434 that moderately inhibited α-glucosidase by competitive inhibition of the enzyme [158].

Moreover, four marine natural products (133–136) listed in Table 2 and shown Figure 2, demonstrated antidiabetic activity during 2016–2017, but the mechanism of action of these compounds remained undetermined at the time of publication: a new polyketide asperentin B (133) isolated from a deep (2769 m) Mediterranean Sea sediment-derived *Aspergillus sydowi* which “strongly” inhibited human protein tyrosine phosphatase 1B, an important “target for the treatment of type 2 diabetes” [159]; a novel lactone lasiodiplactone (134) isolated from a South China Sea mangrove *Acanthus ilicifolius*-derived endophytic fungus *Nectria* sp. *H. nigricans* moderately inhibited α-glucosidase, “which was much better than acarbose” [162].

### 3.2. Anti-Inflammatory Activity

As shown in Table 2 and Figure 2, there was a remarkable increase in anti-inflammatory pharmacology of marine compounds (127, 138–192) during 2016–2017. The molecular mechanism of action of anti-inflammatory marine natural products (127, 138–159) was assessed in both in vitro and in vivo preclinical pharmacological studies in twenty one papers, which used several in vitro and in vivo models of inflammation. Zbakh and colleagues evaluated the anti-inflammatory properties of the meroterpenoid 11-hydroxy-1′-O-methylamentadione (AMT-E) (127) isolated from the brown alga *Cystoseira usneoides* in a murine model of experimental colitis, observing that the levels of myeloperoxidase, cytokines and the expression of the pro-inflammatory genes nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) were reduced, concluding that AMG-W might be a candidate for “prevention/treatment of inflammatory bowel dis-
transcriptional factor(s) involved in inflammation-related disorders” [171]. Ciaglia and colleagues characterized the anti-inflammatory effects of the terpenoid excavatolide, which moderately inhibited LPS-induced RAW264.7 macrophages production of pro-inflammatory cytokines IL-12 p40 and IL-6 release from bone marrow-derived dendritic cells, as well as signal transduction by inhibiting phosphorylation of nuclear factor-κB (NF-κB), and thus, warranted further study to evaluate its potential as a “therapeutic agent for inflammation-associated maladies” [169]. Aminin and colleagues assessed the anti-inflammatory pharmacology of the triterpene glycoside 4-hydroxy-2,3-dimethyl-2-nonen-4-olide from an Antarctic Ross Sea sponge-derived fungus Dendrilla membranosa (146) derived from an Antarctic marine sponge Dysidea villosa (IL-1β) isolated from the Russian edible sea cucumber Epinephelus coioides (147) isolated from the orange-spotted grouper Epinephelus coioides (148) isolated from the South China Sea marine sponge Dysidea villosa that inhibited RBL-2H3 mast cell release of β-hexosaminidase, a marker of degranulation, as well as pro-inflammatory leukotriene B4 and IL-4 by suppressing the IgE/Syk signaling pathway, thus suggesting a “new chemotherapeutic scaffold targeting Syk-associated allergy” [173]. Su and colleagues extended the pharmacology of the known antimicrobial peptide epinecidin-1 (149) isolated from the orange-spotted grouper Epinephelus coioides by showing that its anti-inflammatory activity resulted from degradation of the Toll-like receptor signaling adaptor protein MyD88 in RAW 264.7 mouse macrophages and concomitant activation of the Smurf E3 ligase proteasome degradation pathway [174]. Lin and colleagues continued the evaluation of the terpenoid excavatolide (150) isolated from...
the Taiwanese gorgonia coral *Briareum excavatum*, observing that it inhibited LPS-induced osteoclast-like cell formation and tartrate-resistant acid phosphatase (TRAP) expression, in vitro, while also significantly reducing paw oedema and TRAP-positive multinucleated cell formation in two rat models of experimental arthritis [175]. Several studies extended the anti-inflammatory mechanisms of the marine carotenoid fucoxanthin (151) isolated from the edible brown alga *Undaria pinnatifida*: Choe and colleagues reported that fucoxanthin inhibited paw edema in an experimental in vivo model of inflammation by reducing activation of iNOS, COX-2 and NF-κB [176]; Grassa-López and colleagues observed that fucoxanthin ameliorated lipogenesis, decreased insulin resistance as well as biomarkers of both inflammation and cardiovascular disfunction in an experimental rat obesity model [177]; Sugiu and colleagues determined that in vitro fucoxanthin suppressed PLA₂ and COX-2 expression in a rat basophilic leukemia-2H3 cells, while in vivo inhibiting PLA₂, COX-2 and hyaluronidase in several ICR mouse ear models of inflammation [178]; Taiga and colleagues observed that concentration-dependent cytoprotection or apoptosis in RAW264.7 macrophage cells by the carotenoids fucoxanthinol and fucoxanthin resulted from activation of the Nrf2-ARE signaling pathway [179]. Sintsova and colleagues characterized a novel Kunitz-type peptide (152) isolated from the sea anemone *Heteractis crispa* that significantly decreased intracellular Ca²⁺ in histamine-treated murine bone marrow-derived macrophages thus suggesting the involvement of “H₁-type histamine receptor blockage” in the anti-inflammatory mechanism of action of this peptide [180]. Hong and colleagues determined that the diterpenoid hippopsononachnin B (153) isolated from the South China Sea marine sponge *Hippospongia lachne* decreased production of β-hexosaminidase, a degranulation biomarker and pro-inflammatory mediators IL-4 and LTB4 by RBL-2H3 cells, suggesting a possible therapeutic use for “the treatment of allergy” [181]. Kozuma and colleagues isolated new cyclic peptides ogipeptins A-D (154–157) from the culture broth of the Japanese marine Gram-negative bacterium *Pseudoalteromonas* sp. SANK 71903 that blocked the binding of LPS to the cluster of differentiation 14 (CD14) in vitro and decreased TNF-α release by human U937 monocyctic cells, concluding that these peptides could be developed for use “as anti-LPS drugs against LPS-associated diseases” [182]. Kwon and colleagues reported a new anthranilic acid derivative oscarellin (158) isolated from a Philippine sponge *Oscarella stillans* that strongly inhibited LPS-induced TNF-α and IL-6 production in murine macrophage RAW 264.7 macrophages by a mechanism “associated with inactivation of c-Jun NH₂-terminal kinase (JNK), extracellular signal-regulated kinase (ERK), activator protein-1 (AP-1), and NF-κB and activation of activating transcription factor-3 (ATF-3)” [183]. Kim and colleagues observed that the novel alkaloid pseudane-VII (159) isolated from the marine bacterium *Pseudoalteromonas* sp. M2 modulated release of pro-inflammatory mediators (NO, IL-1β and IL-6) by LPS-treated RAW 264.7 murine macrophage cell line in vitro via inhibition of “MAPK phosphorylation and NF-κB translocation”, while in vivo treatment with this compound suppressed production of IL-1β and iNOS expression, suggesting “pseudane VII has potential as treatment for inflammatory responses and diseases” [184].

In contrast, for marine compounds (160–192) shown in Table 2 and Figure 2, only the anti-inflammatory activity (IC₅₀) was reported, no molecular mechanism of action was reported at the time of publication: A new eremophilane-sesquiterpene acrememophilane B (160) isolated from a South Atlantic deep sea (2869 m)-sediment derived fungus *Acremonium* sp. [185]; two new quinoline alkaloids actinoquinolines A and B (161, 162) isolated from a Californian marine-derived *Streptomyces* sp. strain CNP975 [186]; a new polyhydroxysteroidal glycoside anthenoside O (163) isolated from the tropical South China Sea starfish *Anthenea aspera* [187]; a new polyketide aurasperone C (164), isolated from a South China Sea brown alga *Sargassum* sp.-derived *Aspergillus niger* SCSIO Jscw6F30 [188]; two new 9-hydroxybriarane diterpenoids briarenolides ZII and ZVI (167, 168) isolated from the Taiwanese gorgonian coral *Briareum* sp. [190]; a known eremophilane sesquiterpene dihydrobipolaroxin (169) isolated from a South China Sea deep (2439 m) marine sediment-derived *Aspergillus* sp. SCSIOW2 [191]; a known alkaloid echinulin (170) iso-
lated from an Antarctic Ross Sea “unidentified” marine organism-derived Aspergillus sp. SF-5976 [192]; a novel halogenated 5α-iodozoanthamine (171) isolated from the colorful Taiwanese zoanthid Zoanthus kuroshio [193]; two novel steroids klyfaccisteroid J and K (172, 173) isolated from the Taiwanese soft coral Klyxum flaccidum [194,195]; a known lobane diterpenoid (174) isolated from a Taiwanese soft coral Lobophytum varium [196]; two new bioactive steroids petasistosterones B and C (175, 176) isolated from the Taiwanese soft coral Umbellulifera petasites [197]; two new sterols (177, 178) [198], and novel 9,11-secoesters pinnigorgiol A (179) [199], pinnigorgiol E (180) [200], pinnisterol A (181) [201] and pinnisterol H (182) [202] isolated from the Taiwanese gorgonian coral Pinnigorgia sp.; a new pyrrole oligoglycoside plancipyrrside B (183) isolated from an extract of the Vietnamese starfish Acanthaster planci [203]; a novel steroidal glycoside protolinckioside A (184) isolated from an Arabian sea starfish Protoreaster lincki [204]; a known terpenoid sarcophytonolide O (185) isolated from the Chinese soft coral Lobophytum crassum [205]; two novel norembra-noids sinulerectols A and B (186, 187) isolated from South China Sea soft coral Sinularia erecta [206]; a known terpenoid sinubrasolide A (188) and the steroid sinubrasone D (189) isolated from the Taiwanese “cultivation pool” soft coral Sinularia brassica [207,208]; and the novel diterpenes uprolides N, O and P (190–192) isolated from the Panamanian octocoral Eunicea succinea [209].

3.3. Marine Compounds with Activity on the Immune System

In 2016–2017, the preclinical pharmacology of marine compounds that were reported to affect the immune system is shown in Table 2 and Figure 2. The molecular mechanism of action of marine natural products that affected the immune system (145, 193–199) was described in seven papers which used several in vitro and in vivo models. Pilsyagin and colleagues reported that the triterpene glycoside cucumarioside A 

\[
A_2-2 (145)
\]

isolated from the Far Eastern sea cucumber Cucumaria japonica caused changes in mouse spleen morphology, proliferative activity “predominantly in B-cells” and macrophage activation in mouse spleen, concomitant with increase in IL-1β, iNOs, ROS and NO production [210,211]. Sánchez and colleagues investigated three terpenoids gracillin A, H and L (193–195) isolated from the marine sponge Spongiaola gracillis that inhibited human T lymphocyte IL-2 production, as well as CD147 expression by reducing calcineurin phosphatase activity, thus concluding that gracilins are a “valuable option for synthetic drug development” [212,213]. Kicha and colleagues determined the immunomodulatory effects of the mycosporine-like amino acids (MAA) shiorine and porphyra-334 (196, 197) isolated from the red alga Porphyra sp. and reported they both induced NF-κB activity and moderated tryptophan metabolism in human myelomonocytic cell line THP-1, thus recommending “a more detailed risk-benefit assessment” before MAA are used “in daily care products” [214]. Chung and colleagues studied the embrane-type diterpenoid sinulariolide (198), isolated from the Taiwanese cultured soft coral Sinularia flexibilis and observed suppression of LPS-phenotypic maturation, cytokine and NO production and co-stimulatory molecule expression of murine bone marrow-derived dendritic cells, as well as signaling pathways, concluding “that sinulariolide may be utilized in the treatment of autoimmune andinflammatory disorders” [215]. Gao and colleagues determined significant effects of several peptides (199) isolated from Indian Ocean deep (1654 m) sediment-derived actinomycete Williamsia sp. MCCC 1A11233 on both IgE-sensitized RBL-2H3 mast cell histamine and proinflammatory cytokine release, and a murine model of passive cutaneous anaphylaxis, thus observing that “the three compounds have the potential to prevent or treat IgE-sensitized allergic disorders” [216].

In contrast, for the marine compounds (200–205) listed in Table 2 and depicted in Figure 2, only the immune bioactivity (IC\(_{50}\)) was reported, but no molecular mechanism of action had been described by the time of publication: A novel dimeric nitrophenyl trans-epoxymamide chrysamide C (200) produced by a Indian Ocean deep (3386 m) sediment-derived fungus Penicillium chrysogenum SCsIO41001 [217]; a new dimeric macrolide xylopyranoside coscosolide (201) isolated from the Guamanian marine cyanobacterium Symploca
sp. [218]; a new N-acyl dopamine glycoside myxillin A (202) isolated from the Icelandic hydrothermal vent-derived sponge *Mxillia incrustans* [219]; the known steroidal saponin pectinoside A (203) isolated from the starfish *Patiria pectinifera* [220]; a new benzophenone polyketide peniphenone (204) obtained from the mangrove *Sonneratia apetala* endophytic fungus *Penicillium* sp. ZJ-SY2 [221]; and a known analog of the antimycin-type depsipeptide somalimycin, named USF-19A (205) isolated from the South China Sea deep (3536 m) sediment-derived *Streptomyces somaliensis* SCSIO ZH66 [222].

### 3.4. Marine Compounds Affecting the Nervous System

As shown in Table 2 and Figure 2, in 2016–2017, the preclinical nervous system pharmacology of marine compounds (206–225) reported several mechanisms of action involving potassium (K⁺) channels, nicotinic acetylcholine, calcium (Ca²⁺) and serotonin receptors, as well as in vivo models of antinociception and neuroprotection.

Five marine compounds were shown to bind K⁺ channels (206, 207), calcium channels (208), nicotinic acetylcholine receptors (nACHR) (209) and serotonin receptor 5-HT7 (218). Moreels and colleagues electrophysiologically demonstrated that the novel peptide APETx4 (206) isolated from the marine sea anemone *Anthopleura elegantissima* inhibited the K⁺ channel Kᵥ10.1 by keeping it in a closed state and thus, because the Kᵥ10.1 is overexpressed in a human tumors, APETx4 could become a “scaffold for design and synthesis of more potent and safer anticancer drugs” [223]. Goda and colleagues conducted detailed studies that determined that the marine xanthophyll carotenoid astaxanthin (207) reversed the toxicity of the calcium-dependent Maxi-K (BK) K⁺ channel antagonist food mycotoxin penitrem A (PA) “by restoring normal levels of the targeted neurotransmitters” both in Schwann cells CRL-2765 in vitro and in both the nematode *Caenorhabditis elegans* and rat in vivo models thus concluding astaxanthin might be useful “for in vivo prevention of PA-induced brain toxicity” [224]. Mendez and colleagues investigated the marine guanidine alkaloid crambescidin 816 (208) produced by the Mediterranean sponge *Crambe crambe* and known to block voltage dependent L-type Ca²⁺ channels, and observed that cytotoxicity was concomitant with an increase of cytosolic Ca²⁺ in a primary culture of cortical neurons by a mechanism that “was mediated by both NMDA and AMPA glutamate receptor subtypes” activation [225]. Jiang and colleagues discovered a novel O-conotoxin GeXXVIIA linear peptide (209) from the venom of the South China sea cone snail *Conus generalis* that potently inhibited the human α9α10 nicotinic acetylcholine receptor (nACH), a nACH receptor expressed in both the nervous system, as well as in other non-neuronal cells, by a non-competitive and voltage-independent mechanism. The data suggest that this new inhibitor “would facilitate unraveling the functions of this nACHR subtype” [226]. Uchimasu and colleagues reported a novel guanidine alkaloid mellpaladine A (218) isolated from a Palauan Didemnidae tunicate that modulated mice behavioral profiles after an intracerebroventricular injection with particular selectivity for the serotonin receptor 5-HT₇, thus, supporting the notion that “marine alkaloids are unique . . . source of neuroactive compounds” [239].

Two additional studies extended the pharmacology of conopeptides (210–211). Bernáldez and colleagues discovered a novel 25-mer peptide member of the γ-conotoxin family PiVIIIA (210) in the venom of the Mexican marine snail *Conus princeps* that increased Ca²⁺ currents in dorsal root ganglion neurons without affecting the Na⁺, K⁺ or acid sensing ionic channel currents, further studies being proposed to “define its potential use as a positive modulator of neuronal activity” [227]. Brust and colleagues identified a previously uncharacterized nine amino acid conorphin-T (211) from a *Conus textile* venom peptide library with selectivity for κ-opioid receptors (KOR) that led to the development of several novel KOR agonists, which potently inhibited splanchic colonic nociceptors, thus, becoming promising leads “for the development of irritable bowel syndrome treatments” [228].

One study contributed to nociceptive pharmacology. Logashina and colleagues reported that the novel peptide Ms 9a-I (219), isolated from the venom of the sea anemone *Metridium senile*, produced significant analgesic and anti-inflammatory effects in a marine
thermal hyperalgesia model by a mechanism that potentiated the response of transient receptor potential ankyrin-repeat 1 receptor (TRPA1) and was followed by loss of TRPA1-expressing neurons [240].

The neuroprotective activity of marine compounds (151, 212, 214, 216, 220, 223, 225) was reported in ten studies. Three studies reported on the neuroprotective pharmacology of the marine carotenoid fucoxanthin (151) isolated from several brown algae: Undaria pinnatifida, Ecklonia stolonifera and Sargassum horneri: Jung and colleagues studied β-site amyloid precursor protein cleaving enzyme 1 (BACE-1), which is strongly correlated with Alzheimer’s disease, and observed that fucoxanthin inhibited BACE1 activity exhibiting mixed-type inhibition in vitro, while molecular docking simulations showed that two fucoxanthin hydroxyl groups interacted with two BACE1 residues (Gly11 and Ala127), mechanistic studies that suggest fucoxanthin “may be a good template for anti-AD drugs” [232]. Lin and colleagues demonstrated that in mice fucoxanthin reversed scopolamine-induced cognitive impairments by inhibiting brain acetylcholinesterase by a non-competitive mechanism, as well as increasing choline acetyltransferase activity and brain-derived neurotrophic factor (BDNF) expression in hippocampus and cortex. The studies appear to anticipate fucoxanthin’s “therapeutic efficacy for the treatment of AD by acting on multiple targets” [233]. Zhang and colleagues discovered that fucoxanthin provided neuroprotection in an experimental murine model of traumatic brain injury (TBI), “a major public health problem” by alleviating TBI-induced secondary brain injury, cerebral edema and lesions, while also demonstrating that it attenuated TBI-induced apoptosis and oxidative stress “at least partly” via regulation of the nuclear factor erythroid 2-related factor (Nrf2)-antioxidant-response element (ARE) and Nrf2-autophagy pathways, thus, making fucoxanthin “an attractive therapeutic agent in the treatment of TBI in the future” [234]. Two studies were reported by the same research group describing the neuroprotective and anti-inflammatory effects of the cembranolide analog 11-dehydrosinulariolide (11-de) (212) isolated from the soft coral Sinularia flexibilis: Feng and colleagues observed that 11-de increased the expression of BDNF in a neuroblastoma cell line in vitro and had a protective effect in both an in vivo zebrafish and rat Parkinson’s disease model, results that the investigators hoped would “help treat patients diagnosed with Parkinson’s disease” [229]. Chen and colleagues reported that 11-de improved the functional recovery in a rat thoracic spinal cord contusion injury experimental model with an antiapoptotic and anti-inflammatory mechanism that attenuated iNOS and TNF-α, thus, proposing “this compound may be a promising therapeutic agent for spinal cord injury” [230]. Fang and colleagues showed that a new cyclopentenone 5-hydroxycyclopenicillione (214) isolated from a culture of the marine sponge Hymeniacidon perleve-derived fungus Trichoderma sp. HPQJ-34 acted as a moderate free radical scavenger, and had anti-Aβ fibrillization and neuroprotective properties, concluding that this compound “might be of interest to neuropharmacology research and anti-AD drug discovery programs” [235]. Alonso and colleagues evaluated the pyrroloiminoquinone makaluvamine J (216), isolated from a Fijian marine sponge Zyzzya sp. and showed that it “provided full neuroprotection”, as it potently reduced mitochondrial damage by reactive oxygen species, as well as improved endogenous glutathione and catalase in mouse and human neuronal models, thus, potentially contributing to “antioxidant therapies in neurodegenerative diseases” [237]. Kim and colleagues found that the phlorotannin phlorofucofuroeckol (220) isolated from the brown seaweed Ecklonia cava, increased cell viability in glutamate-treated rat adrenal phaeochromocytoma PC12 cells by inhibiting apoptotic cell death as well as mitochondrial reactive oxygen species generation, results, which taken together, suggest PFF may be developed as “a neuroprotective agent in ischemic stroke” [241]. Perni and colleagues discovered that the aminosterol squalamine (223) isolated from the dogfish shark Squalus acanthias displaced the “intrinsically disordered” protein α-synuclein, associated with Parkinson’s disease, from lipid vesicles and membranes by competitively binding at the surfaces, as well as suppressed muscle paralysis in a nematode worm Caenorhabditis elegans strain overexpressing α-synuclein, suggesting squalamine “could be a means for a therapeutic intervention in
Parkinson’s disease” [244]. Pan and colleagues extended the pharmacology of xyloketal B (225) isolated from the mangrove fungus Xylaria sp. by investigating effects of xyloketal in an adult mice stroke model, observing that pre- and post-treatment treatment reduced both brain infarct volume and the generation of ROS and pro-inflammatory cytokines by suppression of ROS/TLR4/NF-κB inflammatory signaling pathway, thus providing evidence for “potential application of xyloketal B in stroke therapy” [246].

As shown in Table 2, five marine compounds were shown to modulate other molecular targets, i.e., the acetylcholinesterases (213, 217, 224), endogenous transient receptor potential canonical type 1 channel (TRPC1) (215), human monoamine oxidase B enzyme (221), and prolonged synaptic transmission (222). Botic Lee and colleagues discovered that the brominated alkaloid discorhabdin G (213) isolated from the Antarctic Latrunculia biformis sponge inhibited electric eel and human acetylcholinesterases by a reversible and competitive mechanism, observations that could potentially lead to new Alzheimer’s disease “cholinesterase inhibitors based on the scaffold of discorhabdins” [231]. Adelhammed and colleagues reported the isolation and structure elucidation of a new phytoceramide MEC-1-4 (217) from the Egyptian Red Sea sponge Mycale euplectellioides that moderately inhibited acetylcholinesterase by interacting with the enzyme "via hydrogen bonding, hydrophobic contacts and hydrophilic-hydrophobic interactions”, thus suggesting MEC-1-4 might become a “valuable lead compound for AD management” [238]. Moodie and colleagues evaluated the known brominated phenethylamine derivative stryphnusin (224) isolated from the Norwegian sponge Stryphus fortis that moderately inhibited electric eel acetylcholinesterase by a reversible competitive mechanism and with no effect on muscle function or neuromuscular transmission thus contributing to novel and promising approaches for “symptomatic treatment of AD” [245]. Flores and colleagues investigated the marine polyether toxin maitotoxin (215) produced by the dinoflagellate Gambierdiscus toxicus that is responsible for ciguatera fish poisoning, demonstrating that its mechanism of action involves activation of the non-voltage-gated cation TRPC1 in X. laevis oocytes and thus proposing this toxin as a “useful tool for further studies of TRPC1 channels” [236]. Lee and colleagues reported that the polyketide piloquinone (221) isolated from a Californian marine sediment-derived Streptomyces sp. CNQ-027 potently inhibited recombinant human monoamine oxidase B enzyme considered a “target in AD and Parkinson’s disease”, by a competitive and reversible mechanism which highlighted the importance of the “ester functionality in the ring system for bioactivity”, thus possibly becoming “a new potential lead compound for the development of MAO inhibitors” [242]. Caplan and colleagues extended the pharmacology of the marine diterpene glycoside pseudopterosin A (222) isolated from the Bahamanian gorgonian soft coral Pseudopterogorgia elisabethae by demonstrating it prolonged synaptic transmission in an experimental oxidative stress model, as well as extensively distributed in murine brain, findings that suggested a “potential as a novel neuromodulatory agent” [243].

Finally, and as shown in Table 2, several marine compounds (226–234) affected the nervous system, but their detailed molecular mechanisms of action remained undetermined at the time of publication: a novel Indonesian Aplysinellidae sponge-derived bromotyrosine araplysillin X (226) that inhibited the aspartic protease BACE1 involved in AD [247]; a novel Panamanian marine cyanobacterium cf. Symploca sp.-derived terpene caracolamide A (227) with in vitro calcium influx and calcium channel oscillation modulatory activity [248]; a Mexican marine cone snail Conus spurius peptide conorfamide-Sr3 (228) shown to block Shaker subtype voltage-gated potassium channels [249]; a new conopeptide contrypnan-Bt (229) isolated from the South China Sea cone snail Conus betulinus shown to be neurotoxic to mice [250]; acetylcholinesterase inhibitory activity in two know meroterpenoids, dehydraouastin (230) isolated from the Chinese mangrove endophytic fungus Aspergillus sp. 16-Sc [251], and terreuleactone C (233) isolated from the South China Sea mangrove-derived endophytic fungus Penicillium sp. SK5W11 [254]; a known alkaloid hymenidin (231), originally isolated from the Caribbean marine sponge Agelas citrina that inhibited voltage-gated potassium channels [252]; a neuroprotective and known bromotyrosine alkaloid...
psammaplysene A (232) originally isolated from the marine sponge Psammaplysilla sp. [253]; and inhibition of α9α10 nicotinic acetylcholine receptor by turripeptide (234) isolated from the Philippine marine gastropod Unedogemmula bisaya venom [255].

4. Marine Compounds with Miscellaneous Mechanisms of Action

Further 2016–2017 preclinical pharmacology for marine compounds (49, 51) as well as that of 79 compounds (235–313) with miscellaneous mechanisms of action is shown in Table 3, with their corresponding structures, presented in Figure 3. Given that, at the time of publication, a comprehensive pharmacological characterization of these compounds remained unavailable, their assignment to a particular drug class will probably require further investigation into their molecular mechanism of action.

Table 3 presents not only the pharmacological activity (an IC₅₀), but also the molecular mechanism of action of the following marine natural compounds: Fungus Acremonium sp. (F9A015) polyketide acredinone C (235) [256]; algal terpenoid astaxanthin (207) [257]; sponge Axinysa sp. bisabolene sesquiterpene (236) [258]; sponge Carteariospongia sp. scleranthene sesterterpenoid (237) [259]; fungus Aspergillus unguii NKH-007 depsidone 7-chlorofoliolipastatin (238) [260]; sponge Acanthostrogylophora ingens halogenated alkaloid chloromethylhalicyclamine B (239) [261]; cyanobacterium Leptolyngbya sp. depsipeptide coibamide A (240) [262]; sponge Theona aff. zwinhoai cyclic peptide cyclolovelactonellamide A (241) [263]; bacterium SNA-024 N⁶,N⁶-dimethyladenosine (242) [264]; gorgonian Briareum excavaillum briarane-type diterpenes excavatolide B (150) [265]; brown algae Undaria pinnatifida, Ecklonia stolonifera and/or Sargassum horneri marine carotenoid fucoxanthin (51) [266]; sponge Phorbas sp. diterpenoid gagnun D (243) [267]; bacterium Bacillus sp. strain SCO-147 (-)–4-hydroxyxattabacin (244) [268]; cyanobacteria Lyngbya majuscula and Tolypothrix sp. γ-pyrone kalkipyrone (245) [269]; sponge Stylissacarteri sp. alkaloid latonduine A (246) [270]; sponge Negombata sp. alkaloid latrunulin A (247) [271]; bacterium Streptomyces sp. polyketide nahuoc acid A (248) [272]; bacterium Streptomyces sp. YP127 napyradiomycin A1 (49) [273]; sponge Leucetta microphairs alkaloid leucetamine B-related synthetic analogue polyandrocarpamine A (249) [274]; sponge Cacospongia sp. terpenoid scalaradial (250) [275]; fungus Stachybotrys sp. KCB13F013 meroterpenoid stachybotrins (251) [276]; soft coral Clarianaria sp. terpenoid stolonidiol (252) [277]; cyanobacterium Lyngbya sp. peptide tasmamide F (253) [278]; sponge Theona sp. cyclic peptide theonellamide A (254) [279]; fungus Penicillium sp. HL-85-ALS5-R004 polyketide tolquonin (255) [280]; fungus Penicillium janthinellum alkaloid N-M-trichomerdamide B (256) [281]; gorgonian-derived fungus Aspergillus versicolor cyclopeptides versicotide D-F (257–259) [282]; sponges Incria and Spongilla spp. furanoterpenes (7E, 12E, 20Z, 18S)-variabilin (260) [283]; and fungus Xylaria sp. terpenoid xyloketol B (259) [284].

Also presented in Table 3 is the pharmacological activity (IC₅₀ for enzyme or receptor inhibition) of marine-derived compounds (261–313), although their respective mechanisms of action remained undetermined and will require further investigation: sponge Aaptos aaptos alkaloid 9-methoxyaaptamine (261) [285]; mangrove-derived fungus Ascomycota sp. SK2YWS-L polyketide ascomidine A (262) [286]; mudflat-derived fungus Aspergillus niger polyketide auraasperone B (263) [287]; alga-derived fungi Penicillium thomii and Penicillium lividum meroterpenoid austalide H acid ethyl ester (264) [288]; fungus Biscogniauxia mediterranea peptide bincogniauxone (265) [289]; fungus Aspergillus usus sesterterpenoid cerebroside D (266) [290]; sponge Spongilla ceylonensis dieterpene ceylonin A (267) [291]; sponge-derived fungus Stachybotrys chartarum sesquiterpene chartarene D (268) [292]; sponge-associated fungus Talaromyces stipitatus KUFA 0207 anthraquinone citreoroisin (269) [293]; fungus Aspergillus sp. SC81O3 polyketide cordyol (270) [294]; fungus Chaetomium cristatum dioxopiperazine alkaloid cristazine (271) [295]; sponge- associated fungus Emeriellla variceloid polyketides diasteltoxins A-C (272–274) [296]; sponge Latrunculia sp. pyrroloiminoquinone alkaloid discorhabdin L (275) [297]; sponge Dysidea sp. polybrominated diphenyl ether 3,4,5-tribromo-2-(2′,4′- dibromophenoxy)-phenol (276) [298]; sponge Dysidea sp. tetracyclic meroterpene dysiherbol A (277) [299]; sand dollar Scaphechinus mirabilis aminonaphtho-
quinone echinamine B (278) [300]; sponge derived fungus Stachylidium sp. tetrapeptide endolide B (279) [301]; mangrove-derived fungus Eurotium rubrum MA-150 (+)-europhenol A (280) [302]; sponge Fascaplysins sp. bis-indole alkaloid fascaplysin (281) [303]; nudi-branch foronula funebris tetrahydrosoquinolinequinone alkaloid fennecribin A (282) [304]; sponge Petrosia sp. depsipeptide halicyclamide A (283) [305]; sponge Halichondria cf. panicea polyacetylene isoprostosynol (284) [306]; cyanobacterium Leptolyngbya sp. macrolide polyketide leptomlyngbyolide B (285) [307]; ascidian Lissoclinum mandelai macrocyclic polykete- tide mandelalide C (286) [308]; sponge Hyrtios digitatus tetracyclic merosequistepnes 19- methoxy-9,15-ene-ppupehenol (287) [309]; sponge Monanchora pulchra cyclic guanidine alkaloid monochymoclin B (288) [310]; sponge Plakortis simplex polyketide motnoria- japonide A (289) [311]; sponge Mycale lissochela terpenoid mycalenitrile-15 (290) [312]; sponge Hyrtios sp. meroterpenoid nakijinol G (291) [313]; sponge Theonella swinhoei cyclic pentapeptide nazumazole D (292) [314]; fungus Aspergillus sp. LF660 benzocoumarin polyketide pannorin (293) [315]; fungus Alternaria sp. NH-F6 polyketides perylequinones (294, 295) [316]; sponge Petrosia alflani xestoquinone derivatives petroquinones A and B (296, 297) [317]; fungus Pseudorella glomerata isocoumarin derivatives peyroisocoumarins B and D (298, 299) [318]; fungus Phoma sp. NT0U4195 polyketide phomakete A (300) [319]; ascidian Sidnycum elegans phosphorylated polyketide phospacephelanin (301) [320]; soft coral Pseudopororergoria rigida sesquiterpenes (302, 303) [321]; sponge Spongia ceylonensis diterpene ent-13-norisocopalen-15-α-l-18-οic (304) [322]; bryozoan Schizomavella mamil- lata 5-alkylresorcinol derivations schizols A and B (305, 306) [323]; fungus Stachybotrys longispora FG216 isodolindoline derivatives FGFC6 and FGFC7 (307, 308) [324]; sponge Spongiam pertusa Esper sesquiterpene (309) [325]; sponge Psammocinia sp. furanosterterpene triconic acid sulawesin A (310) [326]; cyanobacterium Okania sp. cyclic depsipeptide urumamide (311) [327]; gorgonian-derived fungus Aspergillus versicolor LZD-14-1 alkaloid versiquinazoline B (312) [328]; and sponge Xestospongia testudinaria new bioactive steroidal ketone (313) [329].

Table 3. Marine pharmacology in 2016–2017: marine compounds with miscellaneous mechanisms of action.

| Compound/Organism     | Chemistry | Pharmacological Activity | IC₅₀ b | MMOA  c | Country  d  | References |
|-----------------------|-----------|--------------------------|-------|---------|-----------|------------|
| acredinone C (235)/fungus | Polyketide e | Osteoclast differentiation induction inhibition | 10 μM * | NFATc1 transcription inhibition | S. KOR [256] |
| astaxanthin (207)/shrimp | Terpenoid f | Hepatic stellate cell activation inhibition | 10 μM * | Decreased ROS and NOX2 expression reduction | USA [257] |
| Azinysia sp. bisabolene (236)/sponge | Terpenoid f | PTP1B inhibition | 1.9 μM | Akt phosphorylation | JPN [258] |
| Carteriospongia sp. terpenoid (237)/sponge | Terpenoid f | Apoptosis induction | 0.06 μg/mL * | Topoisomerase Iι and Hsp90 inhibition | EGY, SWE, TWN [259] |
| 7-chlorofolipastatin (238)/fungus | Polyketide o | Macrophage SOAT 1 inhibition | 6.8 μM | SOAT 1 and 2 inhibition in vitro | JPN [260] |
| chloromethylhalicyclamene B (239)/sponge | Alkaloid g | Protein kinase CK1ε inhibition | 6 μM | ATP-binding site docking | FRA, ITA, NLD [261] |
| coibamide A (240)/cyanobacterium | Peptide f | VEGFA secretion inhibition | <5 nM | Antiangiogenic properties | USA [262] |
| cyclothemonellazol A (241)/sponge | Peptide f | Chymotrypsin and elastase inhibition | 0.034–0.62 nM | Enzyme S2 substrate binding | BEL, ISR, NLD [263] |
| N²,N²-dimethyladenosine (242)/bacterium | Alkaloid g | AKT phosphorylation inhibition | 5 μM * | S473 site inhibition | USA [264] |
| excavatolide B (150)/soft coral | Terpenoid f | Modulation of atrial myocytes | 10 μM * | Ca²⁺ homeostasis modulation | TWN [265] |
| fucocyanin (51)/algae | Terpenoid f | Lung fibrosis attenuation | 10 mg/kg ** | Type 1 collagen expression decrease | S. KOR [266] |
| Compound/Organism a | Chemistry | Pharmacological Activity | IC<sub>50</sub> b | MMOA c | Country d | References |
|-------------------|-----------|--------------------------|------------------|-------|-----------|------------|
| gagunin D (243)/sponge | Terpenoid f | Melanin synthesis inhibition | 12.7 µM | Tyrosinase expression inhibition | S. KOR | [267] |
| (-)-4-hydroxysattabacin (244)/bacterium | Polyketide o | Melanin synthesis inhibition | 25 µg/mL * | Tyrosinase, TRP-1 and TRP-2 expression inhibition | S. KOR | [268] |
| kalkipyrone (245)/cyanobacterium | Polyketide o | Adipose tissue suppression | 5 mg/kg *** | Enhance LA plasma levels | JPN | [269] |
| latonduine A (246)/bacterium | Alkaloid g | CTFR inhibition | 62 nM | PARP isozymes inhibition | CAN, GBR | [270] |
| nahuic acid (248)/bacterium | Polyketide o | ECFC tube inhibition | 0.043 µM | Specific kinases inhibition | USA | [271] |
| napyradiomycin A1 (49)/bacterium | Terpenoid f | Angiogenesis inhibition | 10 µM | VE-cadherin inhibition | S. KOR | [272] |
| scalaradial (250)/sponge | Terpenoid f | TRPM2 ion channel inhibition | 0.2 µM | Lack of PLA<sub>2</sub> inhibition | JPN, NZL, USA | [273] |
| stachybotrysin (251)/fungus | Terpenoid f | Osteoclast differentiation inhibition | 5 µg/mL | MAPK kinase pathway inhibition | JPN, S. KOR | [274] |
| stolonidiol (252)/soft coral | Terpenoid f | PKC<sub>α</sub> membrane translocation | 5 µM * | Increased ChAT activity | USA | [275] |
| tasiamide F (253)/cyanobacterium | Peptide g | Cathepsin D and E inhibition | 23–57 nM | Docking studies completed | USA | [276] |
| theonellamide A (254)/sponge | Peptide g | Bilipid membrane disruption | 20 µM * | Binding to sterols | JPN | [277] |
| toluquinol (255)/fungus | Polyketide o | Lymphangiogenesis inhibition | 6.2 µM | Suppression of Akt and ERK<sub>1,2</sub> phosphorylation | BEL | [278] |
| N-Me-trichodermamide B (256)/fungus | Alkaloid g | H<sub>2</sub>O<sub>2</sub> oxidative damage inhibition | 5 µM * | Nrf2-signaling regulation | CHN | [279] |
| versicodides D–F (257–259)/fungus | Peptide g | Foam cell formation inhibition | 10 µM * | Cholesterol influx inhibition | CHN | [280] |
| variabilin (260)/sponge | Terpenoid f | PTP1B inhibition | 1.5 µM | TCPTP inhibition | IND, JPN | [281] |
| xylolilet B (225)/fungus | Terpenoid f | NAFLD attenuation | 5 mg/kg *** | SREBP-1c expression inhibition | CHN | [282] |
| 9-methoxyaaptamine (261)/sponge | Alkaloid g | PPRE activation | 0.039 µg/mL * | Undetermined | IDN, MYS | [283] |
| ascomindone A (262)/fungus | Polyketide o | DPPH radical scavenging inhibition | 18.1 µM | Undetermined | CHN | [284] |
| aurasperone B (263)/fungus | Polyketide o | DPPH radical scavenging inhibition | 0.01 µM | Undetermined | S. KOR | [285] |
| austalide H acid ethy ester (264)/fungus | Terpenoid f | Endo-1,3-β-D-glucanase inhibition | 0.2 µM | Undetermined | RUS | [286] |
| B. mediterranea cyclopentapeptide (265)/fungus | Peptide g | GSK-3β inhibition | 8.04 µM | Undetermined | CHN, DEU | [287] |
| cerebroside (266)/fungus | Polyketide o | Spermatzoa inhibition | 8 µM | Undetermined | RUS | [288] |
| ceylonin A (267)/sponge | Terpenoid f | Osteoclast inhibition | <50 µM * | Undetermined | NLD, JPN | [289] |
| chartarene D (268)/fungus | Terpenoid f | Tyrosine kinases inhibition | 0.1–0.8 µM | Undetermined | CHN, DEU | [290] |
| citrooscin (269)/fungus | Polyketide o | Anti-obesity activity | 0.17 µM | Undetermined | GBR, PRT, THAI | [291] |
### Table 3. Cont.

| Compound/Organism | Chemistry | Pharmacological Activity | IC<sub>50</sub> b | MMOA c | Country d | References |
|-------------------|-----------|--------------------------|------------------|--------|-----------|------------|
| cordyol C (270)/fungus | Polyketide o | Erythrocyte biomembrane protection | 4.9 µM | Undetermined | CHN | [294] |
| cristazine (271)/fungus | Alkaloid g | DHHP radical scavenging | 19 µM | Undetermined | S. KOR | [295] |
| diasteltoxins A–C (272–274)/fungus | Polyketide o | Thioredoxin reductase inhibition | 7.2–12.8 µM | Undetermined | CHN, DEU | [296] |
| discorhabdin L (275)/sponge | Alkaloid g | HIF-1α transcription inhibition | 0.73 µM | Undetermined | NZL, USA | [297] |
| Dysidea sp. diphenyl ether (276)/fungus | Polyketide e | Thioredoxin reductase inhibition | 7.2–12.8 µM | Undetermined | CHN, DEU | [296] |
| Dysidea sp. discorhabdin L (275)/sponge | Alkaloid g | NF-κB inhibition | 0.49 µM | Undetermined | AUS, CHN | [299] |
| Erythrocyte biomembrane protection | 4.9 µM | Undetermined | CHN | [294] |
| endolide B (279)/fungus | Peptide g | SR-B1 receptor activation | 1.78 µM | Undetermined | AUS, MYS | [309] |
| europhenol A (280)/fungus | Polyketide o | DHHP radical scavenging | 6.5 µM | Undetermined | RUS | [300] |
| fascaplysin (281)/sea urchin | Polyketide o | DHHP radical scavenging | 1.23 µg/mL | Undetermined | CHN, HUN | [302] |
| fennebricin A (282)/nudibranch | Alkaloid g | NF-κB inhibition | 1 µM * | Undetermined | CHN, HUN | [304] |
| halicylindramide A (283)/sponge | Peptide g | PXR receptor inhibition | 0.82 µM | Undetermined | IDN, JPN | [307] |
| halicylindramide A (283)/sponge | Peptide g | FXR receptor inhibition | 0.5 µM | Undetermined | AUS, S.KOR | [305] |
| isopetrosynol (284)/sponge | Polyketide o | PTP1B inhibition | 11.6 µM | Undetermined | JPN | [307] |
| mandelalide C (286)/ascidian | Polyketide o | Mitochondrial complex V inhibition | 3.4 µM | Undetermined | USA | [308] |
| monanchomycalin B (288)/sponge | Alkaloid g | TRPV1, 2 and 3 receptor inhibition | 2.8–6.0 µM | Undetermined | CHN, ITA, USA | [311] |
| monotriajaponide A (289)/sponge | Polyketide o | PPAR-α and -β activation | 12.5 µM * | Undetermined | CHN, USA | [311] |
| mycalenitrile-15 (290)/sponge | Terpenoid f | PTP1B inhibition | 8.6 µM | Undetermined | CHN, ITA | [312] |
| nakijinol G (291)/sponge | Terpenoid f | PTP1B inhibition | 4.8 µM | Undetermined | CHN | [313] |
| nazumazole D (292)/sponge | Peptide g | Chymotrypsin activity inhibition | 2 µM | Undetermined | JPN | [314] |
| panonoquinones (294, 295)/fungus | Polyketide o | BRD4 protein inhibition | 10 µM * | Undetermined | CHN | [316] |
| petroquinones A and B (296, 297)/sponge | Polyketide o | USP7 inhibition | 0.13–2.0 µM | Undetermined | IND, JPN, NLD | [317] |
| peyroisocoumarins B and D (298, 299)/fungus | Polyketide o | ARE expression induction | 10 µM * | Undetermined | CHN, DEU | [318] |
| phomaketide A (300)/fungus | Polyketide o | Angiogenesis inhibition | 8.1 µM | Undetermined | TWN | [319] |
| phospholeganin (301)/ascidian | Polyketide o | PTP1B inhibition | 11 µM | Undetermined | CHN, ITA | [320] |
| P. rigida sesquiterpenes (302, 303)/soft coral | Terpenoid f | CDC25 phosphatases | 12–3.4 µM | Undetermined | GRC, FRA | [321] |
| Compound/Organism | Chemistry | Pharmacological Activity | IC₅₀ b | MMOA c | Country d | References |
|------------------|-----------|--------------------------|--------|--------|-----------|------------|
| S. ceylonensis diterpene (304)/sponge | Terpene | USP7 inhibition | 8.2 µM | Undetermined | EGY, JPN | [322] |
| schizols A and B (305, 306)/bryozoan | Polyketide | ABTS cation radical inhibition | 6.2–7.6 µM | Undetermined | ESP | [323] |
| S. longispora isoidolinones (307, 308)/fungus | Alkaloid | Fibrinolytic activity | 25 µg/mL | Undetermined | CHN | [324] |
| S. pertusa quinone (309)/sponge | Terpene | CDK-2 inhibition | 4.8 µM | Undetermined | CHN | [325] |
| sulavesin A (310)/sponge | Terpene | USP7 inhibition | 2.8 µM | Undetermined | EGY, IDN, JPN, NLD | [326] |
| urumamide (311)/cyanobacterium | Peptide | Chymotrypsin inhibition | 33 µM | Undetermined | JPN | [327] |
| versiquinazoline B (312)/fungus | Alkaloid | Thioredoxin reductase inhibition | 12 µM | Undetermined | CHN, DEU | [328] |
| X. testudinaria steroidal ketone (313)/sponge | Terpene | PTP1B inhibition | 4.27 µM | Undetermined | CHN | [329] |

* Organism, Kingdom Animalia: shrimp (Phylum Arthropoda); bryozoan (Phylum Bryozoa); ascidian (Phylum Chordata), hydroids, soft corals (Phylum Cnidaria), sea urchin (Phylum Echinodermata), sponge (Phylum Porifera); Kingdom Monera: bacterium; Kingdom Fungi: fungus; Kingdom Plantae: alga; Abbreviations: ABTS: 2,2′-azinobis(3-ethylbenzothiazoline-6-sulphonic acid); Akt: protein kinase B; ARE: antioxidant response element; BRD4: bromodomain-containing protein 4; CDK: cyclin-dependent kinase; ChAT: choline acetyltansferase; CTRF: cystic fibrosis transmembrane conductance regulator; CLK: cdc2-like kinases; DDYRK: dual-specificity, tyrosine phosphorylation regulated kinase; DPPH: α, α-diphenyl-β-picrylhydrazyl; ECFC: endothelial colony-forming cell; ERK: extracellular signal-regulated kinase; FXR: farnesoid X receptor; GSK-3β: glycogen synthase kinase 3; Hsp90: heat shock protein 90; MAPK: mitogen-activated protein kinase; NAFLD: nonalcoholic fatty liver disease; NFA/Tc1: nuclear factor of activated T cells, cytoplasmic 1; NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells; NO: nitric oxide; NOX2: NADPH oxidase 2; Nrf2: nuclear factor-erythroid 2-related factor 2; PARP: poly-ADP ribose polymerase; PKC: protein kinase C; PPAR: peroxisome proliferator-activated receptor; PTP1B: protein tyrosine phosphatase 1B; PPRE: peroxisome proliferator activated receptor response element; ROS: reactive oxygen species; SERCA2A: SR Ca²⁺ ATPase 2A; SETD8: lysine histone methyltransferase 5A; SOAT: sterol O-acyltransferase; SREBP-1c: sterol regulatory element-binding protein-1c; TLR5: Toll-like receptor 5; TCPTP: T-cell protein tyrosine phosphatase; TRP: tyrosinase-related protein; TRPM2: melastatin-like transient receptor potential ion channel; USP7: ubiquitin-specific protease 7; VEGF: vascular endothelial growth factor.
Figure 3. Cont.
Figure 3. Cont.
Figure 3. Cont.

Theonellamide A (254)

toluquinol (255)

N-Me-trichodermamide B (256)

Versicotide D (257)

Versicotide E (258)

Versicotide F (259)

Variablin (260)

9-Methoxyaaptamine (261)
Figure 3. Cont.
Figure 3. Cont.
Figure 3. Cont.
Figure 3. Cont.
Figure 3. Cont.
5. Reviews on Marine Pharmacology and Pharmaceuticals

In 2016–2017 several reviews covered general and/or specific areas of marine preclinical pharmacology: (a) marine pharmacology and marine pharmaceuticals: new marine natural products and relevant biological activities published in 2016 and 2017 [330,331]; chemistry and biology of guanidine natural products [332,333]; biological properties of secondary metabolites from sea hares of Aplysia genus [334]; alkynyl-containing peptides of marine cyanobacteria and molluscs [335]; bioactive cyanobacterial secondary metabolites for health [336]; biological active metabolites from marine-derived myxobacteria [337]; antimicrobial metabolites from the marine bacteria genus Pseudomonas [338]; marine natural products from marine-derived Penicillium fungi [339]; biological activity of secondary metabolites from marine-algal-derived endophytic fungi [340]; pharmacological potential of fucosterol from marine algae [341]; pharmacological activities of Antarctic marine natural products [342]; bioactive acetylated triterpene glycosides from Holothuroidea in the past six decades [343]; terpenoids from octocorals of the genus Pachyclavularia [344]; bioactive marine natural products from sponges of the genus Hyrtios [345]; secondary metabolites from the marine sponge genus Phyllospongia [346]; discovery strategies of bioactive compounds synthetized by nonribosomal peptide synthetases and type-1 polyketide synthase derived from marine microbiomes [347]; developing natural product drugs: supply problems and how they have been overcome [348]; the global marine pharmaceutical pipeline in 2020: U.S. Food and Drug Administration-approved compounds and those in Phase I, II and III of clinical development http://marinepharmacology.midwestern.edu/clinPipeline.htm; (b) antimicrobial marine pharmacology: antimycobacterial metabolites from marine invertebrates [349]; antimicrobials from cnidarians [350]; (c) antiprotozoal and antimalarial marine pharmacology: natural products in drug discovery against neglected tropical diseases [351]; antymycobacterial natural products from marine Pseudopterogorgia elisabethae [352]; (d) immuno- and anti-inflammatory marine pharmacology: marine natural products inhibitors of neutrophil-associated inflammation [353]; (e) cardiovascular and antiadipic marine pharmacology: bioactive components from fish for dyslipidemia and cardiovascular risk reduction [354]; (f) nervous system marine pharmacology: marine natural products from sponges with neuroprotective activity [355]; a transcriptomic survey of ion channel-based conotoxin in the Chinese cone snail Conus betulinus [356]; dinoflagellate cyclic imine toxins as potent antagonists of nicotinic acetylcholine receptors [357]; inhibition of nociception
and pain transmission by analgesic conopeptides ion channel inhibition by targeting G protein-coupled receptors [358]; (g) miscellaneous molecular targets and uses: ichthyotoxicity evaluation of marine natural products [359]; pharmacological potential of non-ribosomal peptides from marine sponges and tunicates [360]; aeroplysinin-1 as a multi-targeted bioactive sponge-derived natural product [361]; therapeutic potential of the phycotoxin yessotoxin [362], and new modalities for challenging drug targets in pharmaceutical discovery [363].

6. Conclusions

This marine pharmacology 2016–2017 review is the eleventh contribution to the marine preclinical pharmacology pipeline review series that was initiated by Alejandro M. S. Mayer (AMSM) in 1998 [1–10], with the aim of providing a systematic overview of selected peer-reviewed preclinical marine pharmacological literature. The global preclinical marine pharmacology research highlighted in this review involved chemists and pharmacologists from 54 countries, a remarkable increase from our last review, namely: Australia, Austria, Bangladesh, Belgium, Brazil, Canada, China, Costa Rica, Croatia, Cuba, Denmark, Egypt, Fiji, France, Germany, Greece, Hungary, Iceland, India, Indonesia, Ireland, Israel, Italy, Japan, Jordan, Kazakhstan, Malaysia, Mexico, Morocco, Myanmar, the Netherlands, Nigeria, New Zealand, Norway, Oman, Panama, Papua New Guinea, Philippines, Poland, Portugal, Russian Federation, Saudi Arabia, Serbia, Slovenia, South Korea, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, United Kingdom, United States and Vietnam. Thus, during 2016–2017 the marine preclinical pharmaceutical pipeline continued to provide novel pharmacology and potential new leads for the marine clinical pharmaceutical pipeline. As shown at the marine preclinical and clinical pharmaceutical pipeline website: https://www.midwestern.edu/departments/marinepharmacology.xml there are currently 13 marine-derived pharmaceuticals approved by the U.S. Food and Drug Administration and 1 by Australia, and more than 23 marine-derived compounds in Phases I, II and III of global clinical pharmaceutical development.

Author Contributions: Marine pharmacology review conceptualization, A.M.S.M.; 2016–2017 literature analysis and investigation, A.M.S.M. and Aimee J. Guerrero (A.J.G.); writing—original draft preparation, A.M.S.M., A.J.G., Abimael Rodriguez (A.D.R.), Orazio Taglialetela-Scafati (O.T.-S.), Nobuhiro Fusetani (N.F.) and Fumiaki Nakamura (F.N.); writing—review and editing, A.M.S.M., A.J.G., A.D.R., O.T.-S., N.F. and F.N. All authors have read and agreed to the published version of the manuscript.

Funding: We acknowledge financial support from Midwestern University to AMSM; and NIH-SC1 Award (Grant 1SC1GM086271-01A1) of the University of Puerto Rico to ADR, and a grant from Regione Campania-POR Campania FESR 2014/2020 “Combattere la resistenza tumorale: piattaforma integrata multidisciplinare per un approccio tecnologico innovativo alle oncoterapie-Campania Oncoterapie” (Project N. B61G18000470007) to OTS. The content of this review is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Acknowledgments: We thank the contributions of Kelly Le, Pharm. D., Jefferson Trieu, Pharm. D., Linda Huang, Pharm. D from the Chicago College of Pharmacy, Midwestern University for 2016–2017 literature retrieval, and Colleen Bannon, Midwestern University Library, for Endnote database assistance. We particularly wish to acknowledge Mary Hall’s tireless and careful review of the pharmacology data presented in 940 peer-reviewed articles retrieved from the global marine preclinical pharmacology 2016–2017 literature. We are grateful for the secretarial assistance of Victoria Sears and Laura Phelps, Pharmacology Department, College of Graduate Studies.

Conflicts of Interest: The authors declare no conflict of interest.
19. Di, X.; Oskarsson, J.T.; Omarsdottir, S.; Freysdottir, J.; Hardardottir, I. Lipophilic fractions from the marine sponge Halichondria sitens decrease secretion of pro-inflammatory cytokines by dendritic cells and decrease their ability to induce a Th1 type response by allogeneic CD4+ T cells. *Pharm. Res.* 2017, 55, 2116–2122. [CrossRef]

20. Cheng, C.; Othman, E.M.; Reimer, A.; Grune, M.; Kozjak-Pavlovic, V.; Stopper, H.; Hentschel, U.; Abdelmohsen, U.R. Agelone A, a new antioxidant and antichlamydial guinolone from the marine sponge-derived bacterium *Streptomyces* sp. SBT345. *Tetrahedron Lett.* 2016, 57, 2786–2789. [CrossRef]

21. Davison, J.R.; Lohith, K.M.; Wang, X.; Bobyk, K.; Mandadapu, S.R.; Lee, S.L.; Cencic, R.; Nelson, J.; Simpkins, S.; Frank, K.M.; et al. A New Natural Product Analog of Bacinostatin S Reveals Cellular Uptake Facilitated by the NorA Multidrug Transporter. *Antimicrob. Agents Chemother.* 2017, 61. [CrossRef]

22. Le, N.T.; Niemann, H.; Proksch, P.; Tait, K.; Linossier, I.; Hellio, C.; Fay, F. Sponge-Inspired Dibromohemibastadin Prevents and Disrupts Bacterial Biofilms without Toxicity. *Mar. Drugs* 2017, 15. [CrossRef]

23. Wyche, T.P.; Alvarenga, R.F.R.; Piotrowski, J.S.; Duster, M.N.; Warrack, S.R.; Cornilascu, G.; De Wolfe, T.J.; Hou, Y.; Braun, D.R.; Ellis, G.A.; et al. Chemical Genomics, Structure Elucidation, and in Vivo Studies of the Marine-Derived Anticlotting Ecteinascidin. *ACS Chem. Biol.* 2017, 12, 222. [PubMed]

24. Tseng, S.P.; Hung, W.C.; Huang, C.Y.; Lin, Y.S.; Chan, M.Y.; Lu, P.L.; Lin, L.; Sheu, J.H. 5-Episinuleptolide Decreases the Expression of the Extracellular Matrix in Early Biofilm Formation of Multi-Drug Resistant *Acinetobacter baumanii*. *Mar. Drugs* 2016, 14, 143. [CrossRef] [PubMed]

25. Solstad, R.G.; Li, C.; Isaksson, J.; Johansen, J.; Svensson, J.; Stensvag, K.; Haug, T. Novel Antimicrobial Peptides EeCentrocins 1, 2 and EeStrongylocyn 2 from the Edible Sea Urchin Echinus esculentus Have 6-Br-Trp Post-Translational Modifications. *PloS ONE* 2016, 11, e0151820. [CrossRef]

26. Sung, A.A.; Gromek, S.M.; Balunas, M.J. Upregulation and Identification of Antibiotic Activity of a Marine-Derived *Streptomyces* sp. via Co-Cultures with Human Pathogens. *Mar. Drugs* 2017, 15, 250. [CrossRef]

27. Adnani, N.; Chevrette, M.G.; Adibhatla, S.N.; Zhang, F.; Yu, Q.; Braun, D.R.; Nelson, J.; Simpkins, S.W.; McDonald, B.R.; Myers, C.L.; et al. Co-culture of Marine Invertebrate-Associated Bacteria and Interdisciplinary Technologies Enable Biosynthesis and Discovery of a New Antibiotic, Keycin. *ACS Chem. Biol.* 2017, 12, 3093–3102. [CrossRef]

28. Mokhlesi, A.; Stuhldreier, F.; Wex, K.W.; Berscheid, A.; Hartmann, R.; Rehberg, N.; Sureechatchaiyan, P.; Chaidir, C.; Kassack, M.U.; Kalscheuer, R.; et al. Cyclic Cystine-Bridged Peptides from the Marine Sponge Clathria basilana Induce Apoptosis in Tumor Cells and Depolarize the Cytoplasmic Membrane. *J. Nat. Prod.* 2017, 80, 2941–2952. [CrossRef]

29. Leoni, G.; De, P.A.; Mardirossian, M.; Gambato, S.; Florian, F.; Venier, P.; Wilson, D.N.; Tossi, A.; Pallavicini, A.; Gerdol, M. Mythicalins: A Novel Multigene Family of Linear, Cationic Antimicrobial Peptides from Marine Mussels (*Mytilus* spp.). *Mar. Drugs* 2017, 15, 261. [CrossRef]

30. Costantino, V.; Della, S.G.; Saurav, K.; Teta, R.; Bar-Shalom, R.; Mangoni, A.; Steindler, L. Plakofuranolactone as a Quorum Quenching Agent from the Indonesian Sponge *Plakortis* cf. *lita*. *Mar. Drugs* 2017, 15, 59. [CrossRef]

31. Lee, B.C.; Lee, A.; Jung, J.H.; Choi, S.H.; Kim, T.S. In vitro and in vivo anti-Vibrio vulnificus activity of psammaplin A, a natural marine compound. *Mar. Med.* 2016, 14, 2691–2696. [CrossRef]

32. Song, Y.; Li, Q.; Qin, F.; Sun, C.; Liang, H.; Wei, X.; Wong, N.K.; Ye, L.; Zhang, Y.; Shao, M.; et al. Neobacteriosins A-C, polyacrolein macrolactones from the deep-sea derived *Streptomyces* koyangensis *SSC5082*. *Tetradrhedron* 2017, 73, 5366–5372. [CrossRef]

33. Zhang, X.; Ye, X.; Chai, W.; Lian, X.Y.; Zhang, Z. New Metabolites and Bioactive Actinomycins from Marine-Derived *Streptomyces* sp. ZZZ338. *Mar. Drugs* 2016, 14, 181. [CrossRef]

34. Wang, D.; Wang, C.; Gui, P.; Liu, H.; Khalaf, S.M.H.; Elsayed, E.A.; Wadaan, M.A.M.; Hozein, W.N.; Zhu, W. Identification, Bioactivity, and Productivity of Actinomycins from the Marine-Derived Streptomyces heliomycini. *Front. Microbiol.* 2017, 8, 1147. [CrossRef] [PubMed]

35. Balan, S.S.; Kumar, C.G.; Jayalakshmi, S. Aneurinificin, a new lipopeptide biosurfactant produced by a marine Aneurinibacillus aneuriniylacticus SSBP-11 isolated from Gulf of Mannar: Purification, characterization and its biological evaluation. *Microbiol. Res.* 2017, 194, 1–9. [CrossRef]

36. Li, X.D.; Li, X.M.; Li, X.; Xu, G.M.; Liu, Y.; Wang, B.G. Aspewentins D-H, 20-Nor-isopimarane Derivatives from the Deep Sea Sediment-Derived Fungus *Aspergillus wentii* strain SD-310. *J. Nat. Prod.* 2016, 79, 1347–1353. [CrossRef]

37. Chakraborty, K.; Thilakan, B.; Raola, V.K. Antimicrobial polyketide furanoterpenoids from seaweed-associated heterotrophic bacterium *Bacillus* subtilis MTCC 10403. *Phytochemistry* 2017, 142, 112–125. [CrossRef]

38. Huang, H.; Liu, T.; Wu, X.; Guo, J.; Lan, X.; Zhu, Q.; Zheng, X.; Zhang, K. A new antibacterial chromone derivative from mangrove-derived fungus *Penicillium digitatum* (No. 9EB). *Nat. Prod. Res.* 2017, 31, 2593–2598. [CrossRef]

39. Tareq, F.S.; Shin, H.J. Bacilotetetrins A and B, Anti-Staphylococcal Peptides with Spirocyclic Skeletons and One Bisthiodiketopiperazine Derivative from the Marine-Derived Endophytic Fungus *Penicillium brouce* MA-231. *Org. Lett.* 2016, 18, 5304–5307. [CrossRef]
42. Wang, W.; Kim, H.; Patil, R.S.; Giri, A.G.; Won, D.H.; Hahn, D.; Sung, Y.; Lee, J.; Choi, H.; Nam, S.J.; et al. Cadiolides J-M, antibacterial polyphenyl butenolides from the Korean tunicate Pseudodistoma antinooja. Biog. Med. Chem. Lett. 2017, 27, 574–577. [CrossRef] [PubMed]
43. Park, S.R.; Tripathi, A.; Wu, J.; Schultz, P.J.; Yim, I.; McQuade, T.J.; Yu, F.; Arengav, C.J.; Mensah, A.Y.; Tamayo-Castillo, G.; et al. Discovery of cahuitamycins as biofilm inhibitors derived from a convergent biosynthetic pathway. Nat. Commun. 2016, 7, 10710. [CrossRef] [PubMed]
44. Wang, C.X.; Ding, R.; Jiang, S.T.; Tang, J.S.; Hu, D.; Chen, G.D.; Lin, F.; Hong, K.; Yao, X.S.; Gao, H. Aldgamyccins J-O, 16-Member Macrolides with a Branched Octose Unit from Streptomyces sp. and Their Antibacterial Activities. J. Nat. Prod. 2016, 79, 2446–2454. [CrossRef] [PubMed]
45. Jiang, S.; Zhang, L.; Pei, X.; Deng, F.; Hu, D.; Chen, G.; Wang, C.; Hong, K.; Yao, X.; Gao, A.H. Chalcymycins from Marine-Derived Streptomyces sp. and Their Antimicrobial Activities. Mar. Drugs 2017, 15, 153. [CrossRef] [PubMed]
46. Liu, H.; Li, X.M.; Liu, Y.; Zhang, P.; Wang, J.N.; Wang, B.G. Chermesins A-D: Meroterpenoids with a Drimane-Type Spirosesquiterpenene Skeleton from the Marine Algal-Derived Endophytic Fungus Penicillium chermesinum EN-480. J. Nat. Prod. 2016, 79, 806–811. [CrossRef] [PubMed]
47. Chen, S.; Chen, D.; Cai, R.; Cui, H.; Long, Y.; Lu, Y.; Li, C.; She, Z. Cytotoxic and Antibacterial Preussomerins from the Mangrove Endophytic Fungus Lasiodiplodia theobromae ZJ-HQ1. J. Nat. Prod. 2016, 79, 2397–2402. [CrossRef]
48. Lee, J.H.; Kim, E.; Choi, H.; Lee, J. Collisymycin C from the Micronesian Marine Bacterium Streptomyces sp. MC025 Inhibits Staphylococcus aureus Biofilm Formation. Mar. Drugs 2017, 15, 387. [CrossRef]
49. Wu, B.; Wiese, J.; Wenzel-Storjohann, A.; Malien, S.; Schmaljohann, R.; Imhoff, J.F. Engyodontochones, Antibiotic Polyketides from the Marine Algal-Derived Endophytic Fungus Talaromyces islandicus EN-501. J. Nat. Prod. 2017, 80, 162–168. [CrossRef] [PubMed]
50. Li, H.L.; Li, X.M.; Liu, Y.; Zhang, P.; Wang, J.N.; Wang, B.G. Chermesins A-D: Meroterpenoids with a Drimane-Type Spirosesquiterpenene Skeleton from the Marine Algal-Derived Endophytic Fungus Talaromyces islandicus EN-501. J. Nat. Prod. 2017, 80, 162–168. [CrossRef] [PubMed]
51. Nguyen, H.M.; Ito, T.; Kurimoto, S.I.; Ogawa, M.; Win, N.N.; Hung, V.Q.; Nguyen, H.T.; Kubota, T.; Kobayashi, J.; Morita, H. New merosesquiterpenes from a Vietnamese marine sponge of Spongia sp. and their biological activities. Bioorg. Med. Chem. Lett. 2017, 27, 3043–3047. [CrossRef]
52. Lee, J.; Shin, A.; Lee, H. Isolation and synthesis of luffariellolide derivatives and evaluation of antibacterial activities against gram-negative bacteria. Bull. Korean Chem. Soc. 2017, 38, 804–807. [CrossRef]
53. Kim, C.K.; Riswanto, R.; Won, T.H.; Kim, H.; Elya, B.; Sim, C.J.; Oh, D.C.; Oh, K.B.; Shin, J. Manzamine Alkaloids from an Acanthostreptomyces sp. Sponge. J. Nat. Prod. 2017, 80, 1575–1583. [CrossRef] [PubMed]
54. Lacret, R.; Perez-Victoria, I.; Oves-Costales, D.; de la Cruz, M.; Domingo, E.; Martin, J.; Diaz, C.; Vicente, F.; Genilloud, O.; Reyes, F. MDN-0170, a New Napyradiomycin from the Marine Fungus Penicillium citrinum F. MDN-0170. J. Nat. Prod. 2016, 79, 806–811. [CrossRef] [PubMed]
55. Nenkep, V.; Yun, K.; Son, B.W. Oxysporizoline, an antibacterial polycyclic quinazoline alkaloid from the marine-mudflat-derived fungus Fusarium oxysporum. J. Antibiot. 2016, 69, 709–711. [CrossRef] [PubMed]
56. Zheng, C.J.; Huang, G.L.; Yu, X.; Song, X.M.; Yao, J.; Liu, H.; Wang, R.P.; Sun, X.P. A new benzopyrans derivatives from a mangrove-derived fungus Micromonospora sp. BB1122. Front. Microbiol. 2016, 7, 745–746. [CrossRef]
57. Wang, C.X.; Ding, R.; Jiang, S.T.; Tang, J.S.; Hu, D.; Chen, G.D.; Lin, F.; Hong, K.; Yao, X.S.; Gao, H. Aldgamyccins J-O, 16-Member Macrolides with a Branched Octose Unit from Streptomyces sp. and Their Antibacterial Activities. Mar. Drugs 2017, 15, 153. [CrossRef] [PubMed]
58. Shi, T.; Qi, J.; Shao, C.L.; Zhao, D.L.; Hou, X.M.; Wang, C.Y. Bioactive Diphenyl Ethers and Isocoumarin Derivatives from a Marine Algal-Derived Endophytic Fungus Penicillium citrinum EN-480. J. Nat. Prod. 2016, 79, 806–811. [CrossRef] [PubMed]
59. Pan, C.; Shi, Y.; Aucklo, B.N.; Hassan, S.S.U.; Akhter, N.; Wang, K.; Ye, Y.; Arthur Chen, C.T.; Tao, X.; Wu, B. Isolation and Antibiotic Screening of Fungi from a Hydrothermal Vent Site and Characterization of Secondary Metabolites from a Penicillium Isolate. Mar. Biotechnol. 2017, 19, 469–479. [CrossRef]
60. Shi, T.; Qi, J.; Shao, C.L.; Zhao, D.L.; Hou, X.M.; Wang, C.Y. Bioactive Diphenyl Ethers and Isocoumarin Derivatives from a Gorganian-Derived Fungus Phoma sp. (TA07-1). Mar. Drugs 2017, 15, 146. [CrossRef]
61. Wang, W.; Liao, Y.; Tang, C.; Huang, X.; Luo, Z.; Chen, J.; Cai, P. Cytotoxic and Antibacterial Compounds from the Coral-Derived Fungus Aspergillus tritici SP2-8-1. Mar. Drugs 2017, 15, 348. [CrossRef]
62. Tedesco, P.; Maida, I.; Palma, E.F.; Tortorella, E.; Subko, K.; Ezeofor, C.C.; Zhang, Y.; Li, H.; Magarvey, N.; et al. Antimicrobial Activity of Monomannolipids Produced by Bacterial Strains Isolated from the Ross Sea (Antarctica). Mar. Drugs 2016, 14, 83. [CrossRef] [PubMed]
63. Zhang, X.; Xu, H.Y.; Huang, A.M.; Wang, L.; Wang, Q.; Cao, P.Y.; Yang, P.M. Antibacterial Meroterpenoids from the South China Sea Sponge Dysidea sp. Chem. Pharm. Bull. 2016, 64, 1036–1042. [CrossRef] [PubMed]
64. Mangamuri, U.; Mouva, V.; Poda, S.; Naragani, K.; Munaganti, R.K.; Chitturi, B.; Yenamandra, V. Bioactive metabolites produced by Streptomyces Cheonanensis VUK-A from Coringa mangrove sediments: Isolation, structure elucidation and bioactivity. 3 Biotech. 2016, 6, 63. [CrossRef] [PubMed]
65. Williams, D.E.; Dalisay, D.S.; Chen, J.; Polischuck, E.A.; Patrick, B.O.; Narula, G.; Ko, M.; Av-Gay, Y.; Li, H.; Magarvey, N.; et al. Aminorifamycins and Sporalactams Produced in Culture by a Micromonospora sp. Isolated from a Northeastern-Pacific Marine Sediment Are Potent Antibiotics. Org. Lett. 2017, 19, 766–769. [CrossRef] [PubMed]
66. Tan, Y.; Hu, Y.; Wang, Q.; Zhou, H.; Wang, Y.; Gan, M. Tetrocarcins N and O, glycosidic spirotetronates from a marine-derived Micromonospora sp. identified by PCR-based screening. Sci. Adv. 2016, 6, 91773–91778. [CrossRef]
67. Gui, C.; Zhang, S.; Zhu, X.; Ding, W.; Huang, H.; Gu, Y.C.; Duan, Y.; Ju. J. Antimicrobial Spirotetronate Metabolites from Marine-Derived Micromonospora harpaii SCSIO GJ089. *J. Nat. Prod.* 2017, 80, 1594–1603. [CrossRef]

68. Okada, M.; Sugita, T.; Wong, C.P.; Wakimoto, T.; Abe, I. Identification of Pyridinium with Three Indole Moieties as an Antimicrobial Agent. *J. Nat. Prod.* 2017, 80, 1205–1209. [CrossRef]

69. Zubair, M.S.; Alarif, W.M.; Al-Footy, K.O.; Ph, M.; Ali, M.; Basai, S.A.; Al-Lihaibi, S.S.; Ayyad, S.E. New antimicrobial bisembrane hydrocarbon and cembranoid diterpenes from the soft coral Sarcophyton trochoeliophorum. * Turk. J. Chem.* 2016, 40, 385–392. [CrossRef]

70. Liu, H.B.; Lauro, G.; O’Connor, R.D.; Lohith, K.; Kelly, M.; Colin, P.; Bifulco, G.; Bewley, C.A. Tulongicin, an Antibacterial Tri-Indole Alkaloid from a Deep-Water *Topsetia* sp. Sponge. *J. Nat. Prod.* 2017, 80, 2556–2560. [CrossRef]

71. Hu, Z.; Qin, L.; Wang, Q.; Ding, W.; Chen, Z.; Ma, Z. Angucycline antibiotics and its derivatives from marine-derived actinomycete *Streptomyces* sp. A6H. *Nat. Prod. Res.* 2016, 30, 2551–2558. [CrossRef]

72. Espiritu, R.A. Membrane permeabilizing action of amphidinol 3 and theonellamide A in raft-forming lipid mixtures. *Z. Naturforsch. C* 2017, 72, 43–48. [CrossRef] [PubMed]

73. Iwamoto, M.; Sumino, A.; Shimada, E.; Kinoshita, M.; Matsumori, N.; Oiki, S. Channel Formation and Membrane Deformation via Sterol-Aided Polymerization of Amphidinol 3. *Sci. Rep.* 2017, 7, 10782. [CrossRef] [PubMed]

74. Pejin, B.; Ciric, A.; Markovic, D.; Tommonaro, G.; Sokovic, M. In vitro avarol does affect the growth of *Candida* sp. *Nat. Prod. Res.* 2016, 30, 1956–1960. [CrossRef] [PubMed]

75. Quezada, M.; Licona-Cassani, C.; Cruz-Morales, C.; Cruz-Morales, C.; Marcellin, E.; Capon, R.J.; Barona-Gomez, F. Diverse Cone-Snail Species Harbor Closely Related Streptomyces Species with Conserved Chemical and Genetic Features, Including Polycyclic Tetramic Acid Macrolactams. *Front. Microbiol.* 2017, 8, 2305. [CrossRef] [PubMed]

76. Jiao, W.H.; Hong, L.L.; Sun, J.B.; Piao, S.J.; Chen, G.D.; Deng, H.; Wang, S.P.; Yang, F.; Lin, H.W. *±* (±)-Hipposporide J—a pair of unusual antifungal enantiomeric sesterterpenoids from the marine sponge *Hippospongia* lachne. *Eur. J. Org. Chem.* 2017, 2017, 3421–3426. [CrossRef]

77. Kildgaard, S.; Subko, K.; Phillips, E.; Goedts, V.; de la Cruz, M.; Diaz, C.; Gotfredsen, C.H.; Andersen, B.; Frisvad, J.C.; Nielsen, Z. Naturforsch. *C* 2017, 72, 43–48. [CrossRef] [PubMed]

78. Son, S.; Ko, S.K.; Jang, M.; Kim, J.W.; Kim, G.S.; Lee, J.K.; Jeon, E.S.; Futamura, Y.; Ryoo, I.J.; Lee, J.S.; et al. New Cyclic Tetramic Acid Macrolactams. *Angew. Chem., Int. Ed.* 2016, 55, 555–563. [CrossRef] [PubMed]

79. Topsis, E.; Unal, I.; Aich, S.; Bedir, E. Cytosine-type nucleosides from marine-derived Streptomyces rochei 06CM016. *J. Antibiot.* 2016, 69, 51–56. [CrossRef] [PubMed]

80. Yang, F.; Wang, R.P.; Xu, B.; Hu, Y.B.; Ma, G.Y.; Yang, G.F.; Dai, S.W.; Zhang, W.; Jiao, W.H.; Song, S.J.; et al. New antimalarial norterpene cyclic peroxides from *Xisha Islands* sponge *DACRUS arnoldi*. *Bioorg. Med. Chem. Lett.* 2016, 26, 2084–2087. [CrossRef] [PubMed]

81. Almaliti, J.; Malloy, K.L.; Glukhov, E.; Spadafora, C.; Gutierrez, M.; Gerwick, W.H. Dudawalamesides A-D, Antiparasitic Cyclic Depsipeptides from the Marine Cyanobacterium *Mooreoa* producens. *J. Nat. Prod.* 2017, 80, 1827–1836. [CrossRef] [PubMed]

82. Chan, S.T.; Nani, R.R.; Schauer, E.A.; Martin, G.E.; Williamson, R.T.; Sauri, J.; Buevich, A.V.; Schafer, W.A.; Joyce, L.A.; Goey, A.K.; et al. Characterization and Synthesis of Eudistidine C, a Bioactive Marine Alkaloid with an Intriguing Molecular Scaffold. *J. Org. Chem.* 2016, 81, 10631–10640. [CrossRef] [PubMed]

83. Buedenbender, L.; Grkovic, T.; Duffy, S.; Kurthboke, D.I.; Avery, V.K.; Carroll, A.R. Nasoseaazine C, a new anti-plasmodial dimeric diketopiperazine from a marine sediment derived *Streptomyces* sp. *Tetrahedron Lett.* 2016, 57, 5893–5895. [CrossRef]

84. Wang, J.; Pearce, A.N.; Chan, S.T.; Taylor, R.B.; Page, M.J.; Valentin, A.; Bourguet-Kondracki, M.L.; Dalton, J.P.; Wiles, S.; Copp, B.R. Biologically Active Acetylenic Amino Alcohol and N-Hydroxylated 1,2,3,4-Tetrahydro-beta-carboline Constituents of the New Zealand Ascidian *Pseudodistoma* sp. *J. Nat. Prod.* 2016, 79, 607–610. [CrossRef] [PubMed]

85. Campos, P.E.; Wolfender, J.L.; Queiroz, E.F.; Marcourt, L.; Al-Mourabit, A.; Frederich, M.; Bordignon, A.; De Voogd, N.; Illien, B.; Gauvin-Bialecki, A. Unguiculin A and Ptilomycalins E-H, Antimalarial Guanidine Alkaloids from the Marine Sponge *Monanchora* sp. *J. Nat. Prod.* 2016, 80, 1404–1410. [CrossRef]

86. White, A.M.; Dao, K.; Vrubliauskas, D.; Konst, Z.A.; Piersens, G.K.; Mandi, A.; Andrews, K.T.; Skinner-Adams, T.S.; Clarke, M.E.; Narbutas, P.T.; et al. Catalyst-Controlled Stereoselective Synthesis Secures the Structure of the Antimalarial Isocyanoterpene *Pustulosaisonitrile*-1. *J. Org. Chem.* 2017, 82, 13313–13323. [CrossRef]
139. Zhang, Y.; Adnani, N.; Braun, D.R.; Ellis, G.A.; Barns, K.J.; Parker-Nance, S.; Guzei, I.A.; Bugni, T.S. Micromonomohalimanes A and B: Antimicrobial Halimane-Type Diterpenoids from a Marine Micromonomospora Species. J. Nat. Prod. 2016, 79, 2968–2972. [CrossRef]

140. Zhou, S.L.; Wang, M.; Zhao, H.G.; Huang, Y.H.; Lin, Y.Y.; Tan, G.H.; Chen, S.L. Penicilazaphilone C, a new antineoplastic and antibacterial azaphilone from the Marine Fungus Penicillium sclerotiorum. Arch. Pharm. Res. 2016, 39, 1621–1627. [CrossRef]

141. He, K.Y.; Zhang, C.; Duan, Y.R.; Huang, G.L.; Yang, C.Y.; Lu, X.R.; Zheng, C.J.; Chen, G.Y. New chlorinated xanthone and anthaquinone produced from a mangrove-derived fungus Penicillium citrinum HL-5126. J. Antibiot. 2017, 70, 823–827. [CrossRef]

142. Kim, J.; Shin, D.; Kim, S.H.; Park, W.; Shin, Y.; Kim, W.K.; Lee, S.K.; Oh, K.B.; Shin, J.; Oh, D.C. Borrelidins C-E: New Antibacterial Macrolides from a Saltmarsh-Derived Halophilic Nocardiopsis sp. Mar. Drugs 2017, 15, 166. [CrossRef] [PubMed]

143. Li, J.L.; Chen, D.; Huang, L.; Ni, M.; Zhao, Y.; Fan, H.; Bao, X. Antichlamydial Dimeric Indole Derivatives from Marine Fungus Eurotium chevalieri KUFA 0006. Phytochemistry 2017, 141, 86–97. [CrossRef]

144. Niu, S.; Liu, D.; Shao, Z.; Proksch, P.; Lin, W. Eutypellazines N-S, new thiodiketopiperazines from a deep sea sediment derived fungus Eutyella sp. with anti-VRE activities. Tetrahedron Lett. 2017, 58, 3695–3699. [CrossRef]

145. Teta, R.; Marteinsson, V.T.; Longeon, A.; Klonowski, A.M.; Groben, R.; Bourguet-Kondracki, M.L.; Costantino, V.; Mangoni, A. Thermoactinoamide A, an Antibiotic Lipophilic Cyclopeptide from the Icelandic Thermophilic Bacterium Thermoactinomyces vulgaris. J. Nat. Prod. 2017, 80, 2530–2535. [CrossRef]

146. Wang, Q.; Zhang, Y.; Yang, M.; Tan, Y.; Hu, X.; He, H.; Xiao, C.; You, X.; Wang, Y.; Gan, M. Neo-actinomycins A and B, natural actinomycins bearing the 5H-oxazolo[4,5-b]phenoxazinone chromophore, from the marine-derived Streptomyces sp. IMB094. Sci. Rep. 2017, 7, 3591. [CrossRef]

147. Jamison, M.T.; Macho, J.; Molinski, T.F. Structure-activity of antifungal compounds inspired by aminobisabolenes from the sponge Halichondria sp. Biopros. Med. Chem. Lett. 2016, 26, 5244–5246. [CrossRef]

148. Zhu, Y.; Wang, Y.; Gu, B.; Yang, F.; Jiao, W.H.; Hu, G.; Yu, H.B.; Han, B.N.; Zhang, W.; Shen, Y.; et al. Antifungal bromopyrrole alkaloids from the South China Sea sponge Agelas sp. Tetrahedron 2016, 72, 2964–2971. [CrossRef]

149. Bertin, M.J.; Demirkiran, O.; Navarro, G.; Moss, N.A.; Lee, J.; Goldgof, G.M.; Vigil, E.; Winzeler, E.A.; Valeriote, F.A.; Gerwick, W.H. Kalkipyrone B, a marine cyanobacterial gamma-pyrone possessing cytotoxic and anti-fungal activities. Phytochemistry 2016, 122, 113–118. [CrossRef]

150. Villa-Perez, P.; Cueto, M.; Diaz-Marrero, A.R.; Lobatón, C.D.; Moreno, A.; Cozar-Castellano, I. Leptolide Improves Peripheral Nerve Regeneration in a Rat Model of Chronic Peripheral Nerve Injury. J. Neurosci. Res. 2017, 95, 1138–1149. [CrossRef]

151. Woo, J.K.; Ha, T.K.Q.; Oh, D.C.; Oh, W.K.; Oh, K.B.; Shin, J. Polyoxygensaturated Steroids from the Sponge Clathria gombawuiensis. J. Nat. Prod. 2017, 80, 3242–3253. [CrossRef]

152. Villa-Perez, P.; Cueto, M.; Diaz-Marrero, A.R.; Lobatón, C.D.; Moreno, A.; Perdomo, G.; Cozar-Castellano, I. Leptolide Improves Peripheral Nerve Regeneration in a Rat Model of Chronic Peripheral Nerve Injury. J. Neurosci. Res. 2017, 95, 1138–1149. [CrossRef]

153. Cui, H.; Liu, Y.; Nie, Y.; Liu, Z.; Chen, S.; Zhang, Z.; Lu, Y.; He, L.; Huang, X.; She, Z. Polypektides from the Mangrove-Derived Endophytic Fungus Nectria sp. HHX001 and Their alpha-Glucosidase Inhibitory Activity. Mar. Drugs 2016, 14, 86. [CrossRef]

154. Lin, X.; Wu, Q.; Yu, Y.; Liang, Z.; Liu, Y.; Zhou, L.; Zhang, T. Novel Penicillin C, a novel sesquiterpene methylcyclopentenone-dione from a deep sea-derived Penicillium strain with renoprotective activities. Sci. Rep. 2017, 7, 10757. [CrossRef]

155. Chen, Z.; Hao, J.; Wang, L.; Wang, Y.; Kong, F.; Zhu, W. New alpha-glucosidase inhibitors from marine algae-derived Streptomyces sp. OUCM02343. Sci. Rep. 2016, 6, 2016. [CrossRef]

156. Wiese, J.; Aldemir, H.; Schmaljohann, R.; Guldner, T.A.M.; Imhoff, J.F. Asperentin B, a New Inhibitor of the Protein Tyrosine Phosphatase 1B. Mar. Drugs 2017, 15, 191. [CrossRef]

157. Liu, S.; Liu, Z.; Liu, H.; Long, Y.; Chen, D.; Lu, Y.; She, Z. Lasiodiplactone A, a novel lactone from the mangrove endophyte fungus Lasiodiplodia theobromae ZJ-HQ1. Org. Biomol. Chem. 2017, 15, 6338–6341. [CrossRef]

158. Yang, F.; Wang, F.; Wang, Z.; Lv, W.; Wang, W.; Wang, Y. Glucose Uptake Activities of Bis (2, 3-Dibromo-4, 5-Dihydroxybenzyl) Ether, a Novel Marine Natural Product from Red Alga Odonthalia corymbifera with Protein Tyrosine Phosphatase 1B Inhibition, In Vitro and In Vivo. PLoS ONE 2016, 11, e0147748. [CrossRef] [PubMed]

159. Kim, E.A.; Lee, S.H.; Lee, J.H.; Kang, N.; Oh, J.Y.; Seun-heui, S.; Ahn, G.; Ko, S.C.; Fernandez, S.P.; Kim, S.Y.; et al. A marine algic polyphenol, dieckol, attenuates blood glucose levels by Akt pathway in alloxan induced hyperglycemia zebrafish model. RSC Adv. 2016, 6, 78570–78575. [CrossRef] [PubMed]

160. Chen, S.; Liu, Z.; Liu, H.; Long, Y.; Chen, D.; Lu, Y.; She, Z. Lasiodiplactone A, a novel lactone from the mangrove endophyte fungus Lasiodiplodia theobromae ZJ-HQ1. Org. Biomol. Chem. 2017, 15, 6338–6341. [CrossRef]

161. Zhang, L.; Niaz, S.I.; Khan, D.; Wang, Z.; Zhu, Y.; Zhou, H.; Lin, Y.; Li, J.; Liu, L. Induction of Diverse Bioactive Secondary Metabolites from the Mangrove Endophytic Fungus Trichoderma sp. (Strain 307) by Co-Cultivation with Acinetobacter johnsonii (Strain B2). Mar. Drugs 2017, 15, 35. [CrossRef]

162. Chen, S.; Liu, Y.; Liu, Z.; Cai, R.; Lu, Y.; Huang, X.; She, Z. Isocoumarins and benzofurans from the mangrove endophytic fungus Talaromyces amstelodami possess a-glucosidase inhibitory and antibacterial activities. RSC Adv. 2016, 6, 26412–26420. [CrossRef]

163. Zbakh, H.; Talero, E.; Avila, J.; Alcaide, A.; de Los, R.C.; Zubia, E.; Motilva, V. The Algal Meroterpenes 11-Hydroxy-1-O-Methylamandione Alomeliotides Dextran Sulfate Sodium-Induced Collitis in Mice. Mar. Drugs 2016, 14, 149. [CrossRef] [PubMed]
164. Jung, B.; Ku, S.K.; Gao, M.; Kim, K.M.; Han, M.S.; Choi, H.; Bae, J.S. Suppressive effects of three diketopiperazines from marine-derived bacteria on TGFB1p-mediated septic responses in human endothelial cells and mice. *Arch. Pharm. Res.* 2016, 39, 843–854. [CrossRef] [PubMed]

165. Kang, H.; Ku, S.K.; Choi, H.; Bae, J.S. Three diketopiperazines from marine-derived bacteria inhibit LPS-induced endothelial inflammatory responses. *Biorg. Med. Chem. Lett.* 2016, 26, 1873–1876. [CrossRef]

166. Ahmad, T.B.; Rugg, D.; Benkendorff, K.; Mahdi, L.K.; Pratt, K.A.; Dooley, L.; Wei, C.; Kotti, M. Brominated indoles from a marine mollusc inhibit inflammation in a murine model of acute lung injury. *PLoS ONE* 2017, 12, e0186904. [CrossRef]

167. El-Desoky, A.H.; Kato, H.; Angkouw, E.D.; Mangindaan, R.E.; de Voogd, N.J.; Tsukamoto, S. Ceylonamides A-F, Nitrogenous Spongian Diterpenes That Inhibit RANKL-Induced Osteoclastogenesis, from the Marine Sponge *Spongilla ceylonensis*. *J. Nat. Prod.* 2016, 79, 1922–1928. [CrossRef]

168. Hassan, H.M.; Boonlarppradab, C.; Fenical, W. Actinoquinolines A and B, anti-inflammatory quinoline alkaloids from a marine-derived *Streptomyces* sp., strain CNP975. *J. Antibiot.* 2016, 69, 511–514. [CrossRef] [PubMed]
Malyarenko, T.V.; Kharchenko, S.D.; Kicha, A.A.; Ivanchina, N.V.; Dmitrenok, P.S.; Chingizova, E.A.; Pisyagin, E.A.; Evtushenko, E.V.; Antokhina, T.I.; Minh, C.V.; et al. Anthenosides I-L, Steroidal Glycosides with Unusual Structural Features from the Starfish Anthena aspera. J. Nat. Prod. 2016, 79, 3047–3056. [CrossRef]

Fang, W.; Lin, X.; Wang, J.; Liu, Y.; Tao, H.; Zhou, X. Asperpyrone-Type Bis-Naphtho-gamma-Pyrones with COX-2-Inhibitory Activities from Marine-Derived Fungus Aspergillus niger. Molecules 2016, 21, 941. [CrossRef][PubMed]

Su, Y.D.; Wen, Z.H.; Wu, Y.C.; Fang, L.S.; Chen, Y.H.; Chang, Y.C.; Sheu, J.H.; Sung, P.J. BRIARENOLIDES M-T, new bRIARANE DITERPENOIDS from a Formosan octocoral Briareum sp. Tetrahedron 2016, 72, 944–951. [CrossRef]

Su, Y.D.; Sung, C.S.; Wen, Z.H.; Chen, Y.H.; Chang, Y.C.; Chen, J.J.; Fang, L.S.; Wu, Y.C.; Sheu, J.H.; Sung, P.J. New 9-Hydroxybriarane DITERPENOIDS from a Gorgonian Coral Briareum sp. (Briareidae). Int. J. Mol. Sci. 2016, 17, 79. [CrossRef]

Wang, L.; Li, M.; Tang, J.; Li, X. Eremophilane Sesquiterpenes from a Deep Marine-Derived Fungus, Aspergillus sp. SCSIOW2, Cultivated in the Presence of Epigenetic Modifying Agents. Molecules 2016, 21, 473. [CrossRef]

Kwon, J.; Lee, H.; Ko, W.; Kim, D.; Kim, K.; Kwon, H.C. Chemical constituents isolated from Antarctic marine-derived Aspergillus sp. SF-5976 and their anti-inflammatory activities in LPS-stimulated RAW 264.7 and BV2 cells. Tetrahedron 2017, 73, 3905–3912. [CrossRef]

Hsu, Y.M.; Chang, F.R.; Lo, I.W.; Lai, K.H.; El-Shazly, M.; Wu, T.Y.; Du, Y.C.; Hwang, T.L.; Cheng, Y.B.; Wu, Y.C. Zoanthamine-Type Alkaloids from the Zoanthid Zoanthus kuroshio Collected in Taiwan and Their Effects on Inflammation. J. Nat. Prod. 2016, 79, 2674–2680. [CrossRef][PubMed]

Tseng, W.R.; Huang, C.Y.; Tsai, Y.Y.; Lin, Y.S.; Hwang, T.L.; Su, J.H.; Sung, P.J.; Dai, C.F.; Sheu, J.H. New cytotoxic and anti-inflammatory steroids from the soft coral Klyxum flavicidum. Bioorg. Med. Chem. Lett. 2016, 26, 3253–3257. [CrossRef][PubMed]

Tsai, Y.Y.; Huang, C.Y.; Tseng, W.R.; Chiang, P.L.; Hwang, T.L.; Su, J.H.; Sung, P.J.; Dai, C.F.; Sheu, J.H. Klyflaccaeroids K-M, bioactive steroidal derivatives from a soft coral Klyxum flavicidum. Bioorg. Med. Chem. Lett. 2017, 27, 1220–1224. [CrossRef]

Ahmed, A.F.; Teng, W.T.; Huang, C.Y.; Dai, C.F.; Hwang, T.L.; Sheu, J.H. Anti-Inflammatory Lobane and Prenyleudesmane DITERPENOIDS from the Soft Coral Lobophytum varium. Mar. Drugs 2017, 15, 300. [CrossRef]

Huang, C.Y.; Chang, C.W.; Tseng, Y.J.; Lee, J.; Sung, P.J.; Su, J.H.; Hwang, T.L.; Dai, C.F.; Wang, H.C.; Sheu, J.H. Bioactive Steroids from the Formosan Soft Coral Umbellulifera petasites. Mar. Drugs 2016, 14, 180. [CrossRef]

Su, Y.D.; Cheng, C.H.; Wen, Z.H.; Wu, Y.C.; Sung, P.J. New anti-inflammatory sterols from a gorgonian Pinnigorgia sp. Bioorg. Med. Chem. Lett. 2016, 26, 3060–3063. [CrossRef]

Chang, Y.C.; Kuo, L.M.; Su, J.H.; Hwang, T.L.; Kuo, Y.H.; Lin, C.S.; Wu, Y.C.; Sung, P.J. Pinnigorgiols A-C, 9,11-secoesters with a rare ring arrangement from a gorgonian coral Pinnigorgia sp. Tetrahedron 2016, 72, 999–1004. [CrossRef]

Chang, Y.C.; Hwang, T.L.; Sheu, J.H.; Wu, Y.C.; Sung, P.J. New Anti-Inflammatory 9,11-Seccosterols with a Rare Tricyclo[5,2,1,1]decane Ring from a Formosan Gorgonian Pinnigorgia sp. Mar. Drugs 2016, 14, 218. [CrossRef]

Chang, Y.C.; Kuo, L.M.; Hwang, T.L.; Yeh, J.; Wen, Z.H.; Fang, L.S.; Wu, Y.C.; Lin, C.S.; Sheu, J.H.; Sung, P.J. Pinnisterols A-C, New 9,11-secoesters from a Gorgonian Pinnigorgia sp. Mar. Drugs 2016, 14, 12. [CrossRef]

Chang, Y.C.; Hwang, T.L.; Kuo, L.M.; Sung, P.J. Pinnisterols D-J, New 11-Acetoxy-9,11-secoesters with a 1,4-Quinone Moiety from Formosan Gorgonian Coral Pinnigorgia sp. (Gorgoniidae). Mar. Drugs 2017, 15, 11. [CrossRef][PubMed]

Vien, L.T.; Hanh, T.T.; Huong, P.T.; Dang, N.H.; Thanh, N.V.; Lyakhova, E.; Cuong, N.X.; Nam, N.H.; Kim, P.V.; Kicha, A.; et al. Pyrrrole Oligoglycosides from the Starfish Acanthaster planci Suppress Lipopolysaccharide-Induced Nitric Oxide Production in RAW264.7 Macrophages. Chem. Pharm. Bull. 2016, 64, 1654–1657. [CrossRef]

Malyarenko, T.V.; Kicha, A.A.; Kalinovsky, A.I.; Ivanchina, N.V.; Popov, R.S.; Pisyagin, E.A.; Menchinskaya, E.S.; Padmakumar, K.P.; Stonik, V.A. Four New Steroidal Glycosides, Protolinciosides A-D, from the Starfish Protoreaster lincki. Chem. Biodivers. 2016, 13, 998–1007. [CrossRef]

Zhao, M.; Cheng, S.; Yuan, W.; Xi, Y.; Li, X.; Dong, J.; Huang, K.; Gustafson, K.R.; Yan, P. Cambranoids from a Chinese Collection of the Soft Coral Lobophytum crassum. Mar. Drugs 2016, 14, 111. [CrossRef][PubMed]

Huang, C.Y.; Tseng, Y.J.; Chokkalimang, U.; Hwang, T.L.; Hsu, C.H.; Dai, C.F.; Sung, P.J.; Sheu, J.H. Bioactive Isoprenoid-Derived Natural Products from a Dongsha Atoll Soft Coral Sinularia erecta. J. Nat. Prod. 2016, 79, 1339–1346. [CrossRef][PubMed]

Huang, C.Y.; Ahmed, A.F.; Su, J.H.; Sung, P.J.; Hwang, T.L.; Chiang, P.L.; Dai, C.F.; Liaw, C.C.; Sheu, J.H. Bioactive new withanolides from the cultured soft coral Sinularia brassica. Bioorg. Med. Chem. Lett. 2017, 27, 3267–3271. [CrossRef]

Huang, C.Y.; Su, J.H.; Liaw, C.C.; Sung, P.J.; Chiang, P.L.; Hwang, T.L.; Dai, C.F.; Sheu, J.H. Bioactive Steroids with Methyl Ester Group in the Side Chain from a Reef Soft Coral Sinularia brassica Cultured in a Tank. Mar. Drugs 2017, 15, 280. [CrossRef]

Torres-Mendoza, D.; Gonzalez, Y.; Gomez-Reyes, J.F.; Guzman, H.M.; Lopez-Perez, J.L.; Gerwick, W.H.; Fernandez, P.L.; Gutierrez, M.; Uprolides N, O and P from the Panamanian Octocoral Eunicea succinea. Molecules 2016, 21, 819. [CrossRef]

Pisyagin, E.A.; Manzhulo, I.V.; Dmitrenok, P.S.; Aminin, D.L. Cucumarioside A2-2 causes changes in the morphology and proliferative activity in mouse spleen. Acta Histochem. 2016, 118, 387–392. [CrossRef]

Pisyagin, E.A.; Manzhulo, I.V.; Goprenchenko, T.Y.; Dmitrenok, P.S.; Avilov, S.A.; Silchenko, A.S.; Wang, Y.M.; Aminin, D.L. Cucumarioside A(2)-2 Causes Macrophage Activation in Mouse Spleen. Mar. Drugs 2017, 15, 341. [CrossRef]

Sanchez, J.A.; Alfonso, A.; Rodriguez, I.; Alonso, E.; Cifuentes, J.M.; Bermudez, R.; Rateb, M.E.; Jaspars, M.; Houssen, W.E.; Ebel, R.; et al. Spongionella Secondary Metabolites, Promising Modulators of Immune Response through CD147 Receptor Modulation. Front. Immunol. 2016, 7, 452. [CrossRef]
213. Sanchez, J.A.; Alfonso, A.; Leiros, M.; Alonso, E.; Rateb, M.E.; Jaspers, M.; Houssen, W.E.; Ebel, R.; Tabadrujv, J.; Botana, L.M. Identification of Spongionella compounds as cyclosporine A mimics. Pharmaco. Res. 2016, 107, 407–414. [CrossRef]

214. Becker, K.; Hartmann, A.; Ganzera, M.; Fuchs, D.; Gostner, J.M. Immunomodulatory Effects of the Mycosporine-Like Amino Acids Shinorine and Porphyra-334. Mar. Drugs 2016, 14, 119. [CrossRef] [PubMed]

215. Chung, T.W.; Li, Y.R.; Huang, W.Y.; Su, J.H.; Chan, H.L.; Lin, S.H.; Liu, C.S.; Lin, S.C.; Lin, C.C.; Lin, C.H. Sinularioid suppresses LPS-induced phenotypic and functional maturation of dendritic cells. Mol. Med. Rep. 2017, 16, 6992–7000. [CrossRef] [PubMed]

216. Gao, Y.Y.; Liu, Q.M.; Liu, B.; Xie, C.L.; Cao, M.J.; Yang, X.W.; Liu, G.M. Inhibitory Activities of Compounds from the Marine Actinomycete Williamsia sp. MCC11A1233 Variant on IgE-Mediated Mast Cells and Passive Cutaneous Anaphylaxis. J. Agric. Food Chem. 2017, 65, 10749–10756. [CrossRef] [PubMed]

217. Chen, S.; Wang, J.; Lin, X.; Zhao, B.; Wei, X.; Li, G.; Kaliaperumal, K.; Liao, S.; Yang, B.; Zhou, X.; et al. Chrysamides A-C, Three Dimeric Nitrophenyl trans-Epoxydienes Produced by the Deep-Sea-Derived Fungus Penicillium chrysogenum SCSIO1001. Org. Lett. 2016, 18, 3650–3653. [CrossRef]

218. Gunasekera, S.P.; Li, Y.; Ratnayake, R.; Luo, D.; Lo, J.; Reibenspies, J.H.; Xu, Z.; Clare-Salzler, M.J.; Ye, T.; Paul, V.J.; et al. Discovery, Total Synthesis and Key Structural Elements for the Immunosuppressive Activity of Cocosolide, a Symmetrical Glycosylated Macrolide Dimer from Marine Cyanobacteria. Chemistry 2016, 22, 8158–8166. [CrossRef] [PubMed]

219. Einarsdottir, E.; Liu, H.B.; Freysdottir, J.; Gottfredsen, C.H.; Omarsdottir, S. Immunomodulatory N-acyl Dopamine Glycosides Derived from the Icelandic Marine Sponge Myxilla incrustans Collected at a Hydrothermal Vent Site. Planta Med. 2016, 82, 903–909. [CrossRef]

220. Kawase, O.; Ohno, O.; Suenaga, K.; Xuan, X. Immunological Adjuvant Activity of Pectinioside A, the Steroidal Saponin from the Starfish Patiria pectinifera. Nat. Prod. Commun. 2016, 11, 605–606. [CrossRef]

221. Liu, H.; Chen, S.; Liu, W.; Liu, Y.; Huang, X.; She, Z. Polyketides with Immunosuppressive Activities from Mangrove Endophytic Actinomycete Acids Shinorine and Porphyra-334. Mar. Drugs 2016, 14, 217. [CrossRef] [PubMed]

222. Jiang, S.; Tae, H.S.; Xu, S.; Shao, X.; Adams, D.J.; Wang, C. Identification of a Novel O-Conotoxin Reveals an Unusual and Potent Inhibitor of the Human alpha9alpha10 Nicotinic Acetylcholine Receptor. Mar. Drugs 2017, 15, 678. [CrossRef] [PubMed]

223. Botic, T.; Defant, A.; Zanini, P.; Zuzeck, M.C.; Frangese, R.; Janussen, D.; Kersken, D.; Knez, Z.; Mancini, I.; Sepic, K. Discorhabdin Mimetics with Antinociceptive Properties. J. Med. Chem. 2016, 59, 2381–2395. [CrossRef]

224. Fung, C.W.; Hung, H.C.; Huang, S.Y.; Chen, C.H.; Chen, Y.R.; Chen, C.Y.; Yang, S.N.; Wang, H.D.; Sung, P.J.; Sheu, J.H.; et al. Neuroprotective Effect of the Marine-Derived Compound 11-Dehydrosinulariolide through DJ-1-Related Pathway in In Vitro and In Vivo Models of Parkinson’s Disease. Mar. Drugs 2016, 14, 187. [CrossRef] [PubMed]

225. Botic, T.; Defant, A.; Zanini, P.; Zuzeck, M.C.; Frangese, R.; Janussen, D.; Kersken, D.; Knez, Z.; Mancini, I.; Sepic, K. Discorhabdin alkaloids from Antarctic Latruncanlia spp. sponges as a new class of cholinesterase inhibitors. ACS Chem. Neurosci. 2017, 8, 1609–1617. [CrossRef]

226. Jiang, S.; Tae, H.S.; Xu, S.; Shao, X.; Adams, D.J.; Wang, C. Identification of a Novel O-Conotoxin Reveals an Unusual and Potent Inhibitor of the Human alpha9alpha10 Nicotinic Acetylcholine Receptor. Mar. Drugs 2017, 15, 170. [CrossRef] [PubMed]

227. Brust, A.; Croker, D.E.; Colless, B.; Ragnarsson, L.; Andersson, A.; Jain, K.; Garcia-Caraballo, S.; Castro, J.; Brierley, S.M.; Alewood, P.F.; et al. Conopeptide-Derived kappa-Opioid Agonists (Conorphins): Potent, Selective, and Metabolic Stable Dynorphin A Mimetics with Antinociceptive Properties. J. Med. Chem. 2016, 59, 2381–2395. [CrossRef]

228. Feng, C.W.; Hung, H.C.; Huang, S.Y.; Chen, C.H.; Chen, Y.R.; Chen, C.Y.; Yang, S.N.; Wang, H.D.; Sung, P.J.; Sheu, J.H.; et al. Neuroprotective Effect of the Marine-Derived Compound 11-Dehydrosinulariolide through DJ-1-Related Pathway in In Vitro and In Vivo Models of Parkinson’s Disease. Mar. Drugs 2016, 14, 67. [CrossRef] [PubMed]

229. Chu, Y.; Jiang, S.; Tae, H.S.; Xu, S.; Shao, X.; Adams, D.J.; Wang, C. Identification of a Novel O-Conotoxin Reveals an Unusual and Potent Inhibitor of the Human alpha9alpha10 Nicotinic Acetylcholine Receptor. Mar. Drugs 2017, 15, 678. [CrossRef] [PubMed]

230. Kong, L.; Huang, L.; Yu, J.; Xiang, S.; Wang, J.; Zhang, J.; Yan, X.; Cui, W.; He, S.; Wang, Q. Fucoxanthin, a Marine Carotenoid, Reverses Scopolamine-Induced Cognitive Impairments in Mice and Inhibits Acetylcholinesterase in Vitro. Mar. Drugs 2016, 14, 67. [CrossRef] [PubMed]

231. Zhang, L.; Wang, H.; Fan, Y.; Gao, Y.; Li, X.; Hu, Z.; Deng, K.; Wang, Y.; Wang, X. Fucoxanthin provides neuroprotection in models of traumatic brain injury via the Nrf2-ARE and Nrf2-autophagy pathways. Sci. Rep. 2017, 7, 46763. [CrossRef] [PubMed]
235. Fang, F.; Zhao, J.; Ding, L.; Huang, C.; Naman, C.B.; He, S.; Wu, B.; Zhu, P.; Luo, Q.; Gerwick, W.H.; et al. 5-Hydroxyxycollencinone, a New beta-Amyloid Fibrillation Inhibitor from a Sponge-Derived Fungus Trichoderma sp. HP1Q-34. *Mar. Drugs* 2017, 15, 260. [CrossRef]

236. Flores, P.L.; Rodriguez, E.; Zapata, E.; Carbo, R.; Farias, J.M.; Martinez, M. Maitoxin Is a Potential Selective Activator of the Endogenous Transient Receptor Potential Canonical Type 1 Channel in Xenopus laevis Oocytes. *Mar. Drugs* 2017, 15, 198. [CrossRef]

237. Alonso, E.; Alvarino, R.; Leiros, M.; Tabudravu, J.N.; Feusser, K.; Dam, M.A.; Rateb, M.E.; Jaspars, M.; Botana, L.M. Evaluation of the Antioxidant Activity of the Marine Pyrroloquinoneinisoquinoline Makulavamines. *Mar. Drugs* 2016, 14, 197. [CrossRef]

238. Abdelhameed, R.; Elgawish, M.; Mira, A.; Ibrahim, A.; Ahmed, S.; Shimizu, K.; Yamada, K. Anti-choline esterase activity of ceramides from the Red Sea marine sponge Mycale eupalotelitoles. *RSC Adv.* 2016, 6, 20422–20430. [CrossRef]

239. Uchimasu, H.; Matsumura, M.; Tsuda, M.; Kumagai, K.; Akakabe, M.; Fujieda, M.J.; Sakai, R. Mellpaladines and dopargimine, novel neuroactive guanidine alkaloids from a Palauan Didemnidae tunicate. *Tetrahedron* 2016, 72, 7185–7193. [CrossRef]

240. Yang, Y.; Bae, M.; Kim, B.; Park, Y.K.; Koo, S.I.; Lee, J.Y. Astaxanthin prevents and reverses the activation of mouse primary hepatic stellate cells. *J. Nutr. Biochem.* 2016, 29, 21–26. [CrossRef]

241. Kim, J.J.; Kang, Y.J.; Shin, S.A.; Bak, D.H.; Lee, J.W.; Lee, K.B.; Yoo, Y.C.; Kim, D.K.; Lee, B.H.; Kim, D.W.; et al. Phlorofucofuroeckol Acredinones on Osteoclastogenic and Osteoblastogenic Activity. *J. Nat. Prod.*

242. Naman, C.B.; Almaliti, J.; Armstrong, L.; Caro-Diaz, E.J.; Pierce, M.L.; Glukhov, E.; Fenner, A.; Spadafora, C.; Debonsi, H.M.; et al. Structure and Biological Activity of a Turripeptide from Unedogemmula bisaya Venom. *Toxicon* 2017, 60, 56–66. [CrossRef]

243. Caplan, S.L.; Zheng, B.; Dawson-Scully, K.; White, C.A.; West, L.M. Pseudopterosin A: Protection of Synaptic Function and Potential as a Neuromodulatory Agent. *Mar. Drugs* 2016, 14, 55. [CrossRef]

244. Perni, M.; Galvagnion, C.; Maltsev, A.; Meisl, G.; Muller, M.B.; Challa, P.K.; Kirkegaard, J.B.; Flagmeier, P.; Cohen, S.I.; Cascella, R.; et al. A novel specific inhibitor of the Shaker K(+) channel. *Eur. J. Med. Chem.* 2017, 140, 1246–1257. [CrossRef]

245. Boccitto, M.; Lee, N.; Sakamoto, S.; Spruce, L.A.; Hanada, H.; Clardy, J.; Seeholzer, S.H.; Kalb, R.G. The Neuroprotective Marine Compound Psammaplycene B Binds the RNA-Binding Protein HNRNPK. *Bioorg. Med. Chem. Lett.* 2016, 26, 499–504. [CrossRef]

246. Naman, C.B.; Almaliti, J.; Armstrong, L.; Caro-Diaz, E.J.; Pierce, M.L.; Glukhov, E.; Fenner, A.; Spadafora, C.; Debonsi, H.M.; Dorrestein, P.C.; et al. Discovery and Synthesis of Caracolamide A, an Ion Channel Modulating Dichlorovinylidene Containing Phenylylamide from a Panamanian Euplectelleridae sp. *J. Nat. Prod.* 2016, 79, 2238–2334. [CrossRef]

247. Campos-Lira, E.; Carrillo, E.; Aguilar, M.B.; Gajewiak, J.; Gomez-Lagunas, F.; Lopez-Vera, E. Conopeptide CNQ-027. *Mar. Drugs* 2017, 15, 2328–2334. [CrossRef]

248. Yeon, J.T.; Kim, H.; Kim, K.J.; Lee, J.; Won, D.H.; Nam, S.J.; Kim, S.H.; Kang, H.; Son, Y.J. Acredinone C and the Effect of Acredinones on Osteoclastogenic and Osteoblastogenic Activity. *J. Nat. Prod.* 2016, 79, 1730–1736. [CrossRef] [PubMed]

249. Yang, Y.; Bae, M.; Kim, B.; Park, Y.K.; Koo, S.I.; Lee, J.Y. Astaxanthin prevents and reverses the activation of mouse primary hepatic stellate cells. *J. Nutr. Biochem.* 2016, 29, 21–26. [CrossRef]

250. Boccitto, M.; Lee, N.; Sakamoto, S.; Spruce, L.A.; Hanada, H.; Clardy, J.; Seeholzer, S.H.; Kalb, R.G. The Neuroprotective Marine Compound Psammaplycene B Binds the RNA-Binding Protein HNRNPK. *Bioorg. Med. Chem. Lett.* 2016, 26, 499–504. [CrossRef]

251. Dorrestein, P.C.; et al. Discovery and Synthesis of Caracolamide A, an Ion Channel Modulating Dichlorovinylidene Containing Phenylylamide from a Panamanian Euplectelleridae sp. *J. Nat. Prod.* 2016, 79, 2238–2334. [CrossRef]

252. Campos-Lira, E.; Carrillo, E.; Aguilar, M.B.; Gajewiak, J.; Gomez-Lagunas, F.; Lopez-Vera, E. Conopeptide CNQ-027. *Mar. Drugs* 2017, 15, 2328–2334. [CrossRef]

253. Boccitto, M.; Lee, N.; Sakamoto, S.; Spruce, L.A.; Hanada, H.; Clardy, J.; Seeholzer, S.H.; Kalb, R.G. The Neuroprotective Marine Compound Psammaplycene B Binds the RNA-Binding Protein HNRNPK. *Bioorg. Med. Chem. Lett.* 2016, 26, 499–504. [CrossRef]

254. Ding, B.; Wang, Z.; Huang, X.; Liu, Y.; Chen, W.; She, Z. Bioactive alpha-pyrole meroterpenoids from mangrove endophytic fungus *Penicillium* sp. *Nat. Prod. Res.* 2016, 30, 2805–2812. [CrossRef] [PubMed]

255. Omaga, C.A.; Carpio, L.D.; Imperial, J.S.; Daly, N.L.; Gajewiak, J.; Flores, M.S.; Espino, S.S.; Christensen, S.; Filchakova, O.M.; Lopez-Vera, E.; et al. Structure and Biological Activity of a Turripeptide from Unedogemmula bisaya Venom. *Biochemistry* 2017, 56, 6051–6060. [CrossRef] [PubMed]

256. Yeon, J.T.; Kim, H.; Kim, K.J.; Lee, J.; Won, D.H.; Nam, S.J.; Kim, S.H.; Kang, H.; Son, Y.J. Acredinone C and the Effect of Acredinones on Osteoclastogenic and Osteoblastogenic Activity. *J. Nat. Prod.* 2016, 79, 1730–1736. [CrossRef] [PubMed]

257. Yang, Y.; Bae, M.; Kim, B.; Park, Y.K.; Koo, S.I.; Lee, J.Y. Astaxanthin prevents and reverses the activation of mouse primary hepatic stellate cells. *J. Nutr. Biochem.* 2016, 29, 21–26. [CrossRef]

258. Abdjul, D.B.; Kanno, S.I.; Yamazaki, H.; Uki, K.; Namikoshi, M. A dimeric urea of the bisabolene sesquiterpene from the Okinawan marine sponge *Axinopsis* sp. inhibits protein tyrosine phosphatase 1B activity in Huh-7 human hepatoma cells. *Bioorg. Med. Chem. Lett.* 2016, 26, 315–317. [CrossRef]
259. Lai, K.H.; Liu, Y.C.; Su, J.H.; El-Shazly, M.; Wu, C.F.; Du, Y.C.; Hsu, Y.M.; Yang, J.C.; Weng, M.K.; Chou, C.H.; et al. Antileukemic Scalarane Sesterterpenoids and Meroditerpenoid from Carteriospongia Phyllospiong sp., Induce Apoptosis via Dual Inhibitory Effects on Topoisomerase II and Hsp90. Sci. Rep. 2016, 6, 36170. [CrossRef]

260. Uchida, R.; Nakajyo, K.; Kobayashi, K.; Ohshtiro, T.; Terahara, T.; Imada, C.; Tomoda, H. 7-Chlorofolipastatin, an inhibitor of sterol O-acetytransferase, produced by marine-derived Aspergillus unguii NKH-807. J. Antibiot. 2016, 69, 647–651. [CrossRef]

261. Esposito, G.; Bourguet-Kondracki, M.L.; Mai, L.H.; Leone, A.; Teta, R.; Meijer, L.; Van, S.R.; Mangoni, A.; Costantino, V. Chloromethylhalicyclamine B, a Marine-Derived Protein Kinase CK1delta/epsilon Inhibitor. J. Nat. Prod. 2016, 79, 2953–2960. [CrossRef]

262. Serrill, J.D.; Wan, X.; Hau, A.M.; Jang, H.S.; Coleman, D.J.; Indra, A.K.; Alani, A.W.; McPhail, K.L.; Ishmael, J.E. Coibamidine A, a natural lariat depsipeptide, inhibits VEGFA/VEGFR2 expression and suppresses tumor growth in glioblastoma xenografts. Invest. New Drugs 2016, 34, 24–40. [CrossRef] [PubMed]

263. Issac, M.; Aknin, M.; Gauvain-Blaiecki, A.; De Voogd, N.; Ledoux, A.; Frederich, M.; Kashman, Y.; Carmeli, S. Cyclotheonellalozes A-C, Potent Protease Inhibitors from the Marine Sponge Theonella aff. swinhoei. J. Nat. Prod. 2017, 80, 1110–1116. [CrossRef] [PubMed]

264. Vaden, R.M.; Oswald, N.W.; Potts, M.B.; MacMillan, J.B.; White, M.A. FUSION-Guided Hypothesis Development Leads to the Identification of N(6),N(6)-Dimethyladenosine, a Marine-Derived AKT Pathway Inhibitor. Mar. Drugs 2017, 15, 75. [CrossRef] [PubMed]

265. Hwang, H.R.; Tai, B.Y.; Cheng, P.Y.; Chen, P.N.; Sung, P.J.; Wen, Z.H.; Hsu, C.H. Excavatolide B Modulates the Electrophysiological Characteristics and Calcium Homeostasis of Atrial Myocytes. Mar. Drugs 2017, 15, 25. [CrossRef]

266. Ma, S.Y.; Park, W.S.; Lee, D.S.; Choi, G.; Yim, M.J.; Lee, J.M.; Jung, W.K.; Park, S.G.; Seo, S.K.; Park, S.J.; et al. Fucoxanthin inhibits fibroblast protein expression in vitro and attenuates bleomycin-induced lung fibrosis in vivo. Eur. J. Pharmacol. 2017, 811, 199–207. [CrossRef]

267. Lee, H.Y.; Jang, E.J.; Bae, S.Y.; Jeon, J.E.; Park, H.J.; Shin, J.; Lee, S.K. Anti-Melanogenic Activity of Gagunin D, a Highly Oxygenated Diterpenoid from the Marine Sponge Phorbas sp., via Modulating Tyrosinase Expression and Degradation. Mar. Drugs 2016, 14, 212. [CrossRef]

268. Kim, K.; Leutou, A.S.; Jeong, H.; Kim, D.; Seong, C.N.; Nam, S.J.; Lim, K.M. Anti-Pigmentary Effect of (-)-4-Hydroxysattabacin and Protozoan DYRK & CLK Kinases. Mar. Drugs 2017, 15, 81. [CrossRef] [PubMed]

269. Williams, D.E.; Izard, F.; Arnould, S.; Dalisay, D.S.; Tantapakul, C.; Maneerat, W.; Matainaho, T.; Julien, E.; Anderssen, R.J. Structures of Nahuco Acid B-Produced in Culture by a Streptomyces sp. Isolated from a Marine Sediment and Evidence for the Inhibition of the Histone Methyl Transferase SETDB8 in Human Cancer Cells by Nahuco Acid A. J. Org. Chem. 2016, 81, 1324–1332. [CrossRef] [PubMed]

270. Hwang, J.S.; Kim, G.J.; Choi, H.G.; Kim, M.C.; Hahn, D.; Nam, J.W.; Nam, S.J.; Kwon, H.C.; Chi, J.; Cho, S.J.; et al. Identification of Antiangiogenic Potential and Cellular Mechanisms of Napyradiomycin A1 Isolated from the Marine-Derived Streptomyces sp. YP127. J. Nat. Prod. 2017, 80, 2269–2275. [CrossRef] [PubMed]

271. Loae, N.; Attanasio, E.; Villiers, B.; Durieu, E.; Tahtouh, T.; Cam, M.; Davis, R.A.; Alencar, A.; Roue, M.; Bourguet-Kondracki, M.L.; et al. Marine-Derived 2-Aminoimidazolone Alkaloids. Leucettamine B-Related Polyandrocarpamines Inhibit Mammalian and Protozoan DYRK & CLK Kinases. Mar. Drugs 2017, 15, 316. [CrossRef]

272. Zakarias, J.; Poerzgen, P.; Layugan, K.; Kawabata, K.G.; Goto, J.I.; Suzuki, S.; Myers, G.; Kelly, M.; Penner, R.; Fleig, A.; et al. Scalaradial Is a Potent Inhibitor of Transient Receptor Potential Melastatin 2 (TRPM2) Ion Channels. Mar. Drugs 2017, 15, 136. [CrossRef] [PubMed]

273. Starkus, J.G.; Laban, Y.; Marcon, F.; Gopinath, B.; Hsu, S.; Kunath, M.; Morishita, M.; Villanueva, J.R.; Wheaton, S.; Wiborg, C.; et al. Chara1 and Chara2 Inhibit Transient Receptor Potential Melastatin 2 (TRPM2) and TRPM8. Mar. Drugs 2017, 15, 138. [CrossRef] [PubMed]

274. Espiritu, R.A.; Cornelio, K.; Kinoshita, M.; Matsumori, N.; Murata, M.; Nishimura, S.; Kakeya, H.; Yoshida, M.; Matsunaga, S. Marine sponge cyclic peptide theonellamide A disrupts lipid bilayer integrity without forming distinct membrane pores. Biochim. Biophys. Acta 2016, 1858, 1373–1379. [CrossRef]
Garcia-Caballero, M.; Blacher, S.; Paupert, J.; Quesada, A.R.; Medina, M.A.; Noel, A. Novel application assigned to tolualquin: Inhibition of lymphangiogenesis by interfering with VEGF-C/VEGFR-3 signalling pathway. Br. J. Pharmacol. 2016, 173, 1966–1987. [CrossRef]

Yang, Z.; Zhu, M.L.; Li, D.H.; Zeng, R.; Han, B.N. N-Me-trichodermamide B isolated from Penicillium janthinellum, with antioxidant properties through NRF2-mediated signaling pathway. Bioorg. Med. Chem. 2017, 25, 6614–6622. [CrossRef]

Chen, R.; Cheng, Z.; Huang, J.; Liu, D.; Wu, C.; Guo, P.; Lin, W. Versicotides D–F, new cyclopeptides with lipid-lowering activities. RSC Adv. 2017, 7, 49235–49243. [CrossRef]

Abdul, B.B.; Yamazaki, H.; Kanno, S.I.; Wewengkang, D.S.; Rotinsulu, H.; Sumilat, D.A.; Uki, K.; K apojos, M.M.; Namikoshi, M. Furanoterpenes, new types of protein tyrosine phosphatase 1B inhibitors, from two Indonesian marine sponges, Ircinia and Spongia spp. Bioorg. Med. Chem. Lett. 2017, 27, 1159–1161. [CrossRef] [PubMed]

Zhang, Y.; Meng, T.; Zuo, L.; Bei, Y.; Zhang, Q.; Su, Z.; Huang, Y.; Pang, J.; Xiang, Q.; Yang, H. Xyloketal B attenuates fatty acid-induced lipid accumulation via the SREBP-1c pathway in NAFLD models. Mar. Drugs 2017, 15, 163. [CrossRef] [PubMed]

Mohamad, H.; Muhammad, R.; Andriani, Y.; Bakar, K.; Ismail, N.; Saidin, J.; Latip, J.; Musa, N.; Parentenzi, A. Potential secondary metabolites from marine sponge Aaptors aaptos for atherosclerosis and virosis treatments. Nat. Prod. Commun. 2017, 12, 1227–1230.

Tan, C.; Liu, Z.; Chen, S.; Huang, X.; Cui, H.; Long, Y.; Yu, L.; She, Z. Antioxidative Polyketones from the Mangrove-Derived Fungus Ascomycota sp. SK2YWS-L. Sci. Rep. 2016, 6, 36609. [CrossRef]

Leoutou, A.S.; Yun, K.; Khong, T.T.; Leutou, A.S.; Kim, G.D.; Hong, J.; Lee, C.H.; Son, B.W. Cristazine, a new cytotoxic dioxopiperazine from the alga-derived fungi Penicillium lividum Westling. Phytochem. Lett. 2016, 15, 7–12. [CrossRef]

Wu, B.; Wiese, J.; Schmaljohann, R.; Imhoff, J.F. Biscognauxiane, a new isopyrroloanthraquinone Compound from the Fungus Biscognauxia mediterranea Isolated from Deep-Sea Sediments. Mar. Drugs 2016, 14, 204. [CrossRef]

Oleinikova, G.K.; Denisenko, V.A.; Berdyshev, D.V.; Pushilin, M.V.; et al. New metabolites from the alga-derived fungi Penicillium thomii Maire and Penicillium lidivum Westling. Phytochem. Lett. 2016, 17, 135–139. [CrossRef]

El-Desoky, A.H.; Kato, H.; Kagiyama, I.; Hitora, Y.; Losung, F.; Mangindaan, R.E.; de Voogd, N.J.; Tsukamoto, S. Ceylonins A–F, new metabolites from the mangrove-derived fungus Ascomycota sp. SK2YWS-L. Sci. Rep. 2016, 6, 36609. [CrossRef]

Li, Y.; Liu, D.; Cheng, Z.; Proksch, P.; Lin, W. Cytotoxic trichothecene-type sesquiterpenes from the sponge-derived fungus Stachylidium Interacting N-Methylated Peptides from the Sponge-Derived Fungus Stachylidium Interacting N-Methylated Peptides from the Sponge-Derived Fungus Stachylidium sp. Marine Sponge. J. Nat. Prod. 2017, 80, 90–95. [CrossRef]

Li, Y.; Liu, D.; Cheng, Z.; Proksch, P.; Lin, W. Cytotoxic trichothecene-type sesquiterpenes from the sponge-derived fungus Stachylidium Interacting N-Methylated Peptides from the Sponge-Derived Fungus Stachylidium sp. Marine Sponge. J. Nat. Prod. 2017, 80, 90–95. [CrossRef]

Noinart, J.; Buttachon, S.; Dethoup, T.; Gales, L.; Pereira, J.A.; Urbatzka, R.; Freitas, S.; Lee, M.; Silva, A.M.S.; Pinto, M.M.M.; et al. A New Ergosterol Analog, a New Bis-Anthrquinone and Anti-Obesity Activity of Anthraquinones from the Marine Sponge-Associated Fungus Talaromyces stipitatus KUFA 0207. Mar. Drugs 2017, 15, 139. [CrossRef]

Li, X.; Xia, Z.; Tang, J.; Wu, J.; Tong, J.; Li, M.; Ju, J.; Chen, H.; Wang, L. Identification and Biological Evaluation of Secondary Metabolites from Marine Derived Fungi Aspergillus sp. SCSIGW3, Cultivated in the Presence of Epigenetic Modifying Agents. Molecules 2017, 22, 1302. [CrossRef]

Yun, K.; Khong, T.T.; Leoutou, A.S.; Kim, G.D.; Hong, J.; Lee, C.H.; Son, B.W. Cristazine, a New Cytotoxic Dioxopiperazine Alkaloid from the Mudflat-Sediment-Derived Fungus Chaetomium cristatum. Chem. Pharm. Bull. 2016, 64, 59–62. [CrossRef] [PubMed]

Long, H.; Cheng, Z.; Huang, W.; Wu, Q.; Li, X.; Cui, J.; Proksch, P.; Lin, W. Diasteltoxins A–C, Asteltoxin-Based Dimers from a Mutant of the Sponge-Associated Emmeria variicella Fungus. Org. Lett. 2016, 18, 4678–4681. [CrossRef] [PubMed]

Goey, A.K.; Chau, C.H.; Sissung, T.M.; Cook, K.M.; Venzon, D.J.; Castro, A.; Ransom, T.R.; Henrich, C.J.; McKee, T.C.; McMahon, J.B.; et al. Screening and Biological Effects of Marine Pyrroloiminoquinone Alkaloids: Potential Inhibitors of the HIF-1alpha/p300 Interaction. J. Nat. Prod. 2016, 79, 1267–1275. [CrossRef] [PubMed]

Arai, M.; Shin, D.; Kamiya, K.; Ishida, R.; Setiawan, A.; Kobayashi, M. Marine sponge polyborinated diphenyl ethers, selective growth inhibitors against cancer cells adapted to glucose starvation, inhibits mitochondrial complex II. J. Nat. Med. 2017, 71, 44–49. [CrossRef] [PubMed]

Jiao, W.H.; Shi, G.H.; Xu, T.T.; Chen, G.D.; Gu, B.B.; Wang, Z.; Peng, S.; Wang, S.P.; Li, J.; Han, B.N.; et al. Dysiederols A–C and Dysideanone E, Cytotoxic and NF-kappaB Inhibitory Tetracyclic Meroterpenes from a Dysidea sp. Marine Sponge. J. Nat. Prod. 2016, 79, 406–411. [CrossRef] [PubMed]

Vasileva, E.A.; Mishchenko, N.P.; Zadorozhnaya, P.A.; Fedoreyev, S.A. New Aminonaphthoquinone from the Sea Urchins Strongylocentrotus pallidus and Mesocentrotus nudus. Nat. Prod. Commun. 2016, 11, 821–824. [CrossRef]

Almeida, C.; El, M.F.; Kehraus, S.; Schnakenburg, G.; Konig, G.M. Endolides A and B, Vasopressin and Serotonin-Receptor Interacting N-Methylated Peptides from the Sponge-Derived Fungus Stachylidium sp. Org. Lett. 2016, 18, 528–531. [CrossRef]

Meng, L.H.; Mandi, A.; Li, X.M.; Liu, Y.; Kurtan, T.; Wang, B.G. Isolation, Stereochemical Study, and Antioxidant Activity of Benzo(furan)-Derivatives from a Mangrove-Derived Fungus Eutromus rubrum MA-150. Chirality 2016, 28, 581–584. [CrossRef] [PubMed]
303. Manda, S.; Sharma, S.; Wani, A.; Joshi, P.; Kumar, V.; Guru, S.K.; Bharate, S.S.; Bhushan, S.; Vishwakarma, R.A.; Kumar, A.; et al. Discovery of a marine-derived bis-indole alkaloid fascaplysin, as a new class of potent P-glycoprotein inducer and establishment of its structure-activity relationship. *Eur. J. Med. Chem.* 2016, 107, 1–11. [CrossRef] [PubMed]

304. Huang, R.Y.; Chen, W.T.; Kurtan, T.; Mandi, A.; Ding, J.; Li, J.; Li, X.W.; Guo, Y.W. Bioactive isoquinolinequinone alkaloids from the South China Sea nudibranch Jorunna funebris and its sponge-prey *Xestospongia* sp. *Future Med. Chem.* 2016, 8, 17–27. [CrossRef] [PubMed]

305. Hahn, D.; Kim, H.; Yang, I.; Chin, J.; Hwang, H.; Won, D.H.; Lee, B.; Nam, S.J.; Ekins, M.; Choi, H.; et al. The Halicylindramides, Farnesoid X Receptor Antagonizing Desipeptides from a *Petrosia* sp. Marine Sponge Collected in Korea. *J. Nat. Prod.* 2016, 79, 499–506. [CrossRef]

306. Abdjul, D.B.; Yamazaki, H.; Takahashi, O.; Kirikoshi, R.; Ukai, K.; Namikoshi, M. Isopetrosynol, a New Protein Tyrosine Phosphatase 1B Inhibitor from the Marine Sponge Halichondria cf. panicea Collected at Iriomote Island. *Chem. Pharm. Bull.* 2016, 64, 733–736. [CrossRef]

307. Cui, J.; Morita, M.; Ohno, O.; Kimura, T.; Teruya, T.; Watanabe, T.; Suenaga, K.; Shibasaki, M. Leptolyngbybolides, Cytotoxic Macrolides from the Marine Cyanobacterium *Leptolyngbya* sp.: Isolation, Biological Activity, and Catalytic Asymmetric Total Synthesis. *Chemistry* 2017, 23, 8500–8509. [CrossRef]

308. Nazari, M.; Serrill, J.D.; Yan, X.; Nguyen, M.H.; Anklin, C.; Gallegos, D.A.; Smith, A.B.; III, Ishmael, J.E.; McPhail, K.L. New Mandelalides Expand a Macrolide Series of Mitochondrial Inhibitors. *J. Med. Chem.* 2017, 60, 7800–7862. [CrossRef]

309. Wiese, J.; Imhoff, J.F.; Gulder, T.A.; Labes, A.; Schmaljohann, R. Marine Fungi as Producers of Benzocoumarins, a New Class of Quinones/Hydroquinones from the Marine Sponge *Spongia pertusa* Esper. *Mar. Drugs* 2017, 15, 6. [CrossRef]

310. Korolkova, Y.; Makarieva, T.; Tabakmakher, K.; Shubina, L.; Kudryashova, E.; Andreev, Y.; Mosharova, I.; Lee, H.S.; Lee, Y.J.; Kozlov, S. Marine Cyclic Guanidine Alkaloids Monanchomycalin B and Urupocidin A Act as Inhibitors of TRPV1, TRPV2 and TRPV3, but not TRPA1 Receptors. *Mar. Drugs* 2017, 15, 87. [CrossRef]

311. Chianese, G.; Yu, H.B.; Yang, F.; Sirignano, C.; Luciano, P.; Han, B.N.; Khan, S.; Lin, H.W.; Taglialetela-Scafati, O. PPAR Modulating Polyketides from a Chinese Plakortis simplex and Clues on the Origin of Their Chemodiversity. *J. Org. Chem.* 2016, 81, 5135–5143. [CrossRef]

312. Yue, D.Q.; Liu, H.L.; Chen, S.H.; Mollo, E.; Gavagnin, M.; Li, J.; Li, X.W.; Guo, Y.W. 5-Alkylpyrrrole-2-carboxaldehyde derivatives from the Chinese sponge Mycale lissocelha and their PTP1B inhibitory activities. *Chinese Chem. Lett.* 2017, 28, 1190–1193. [CrossRef]

313. Wang, J.; Mu, F.R.; Jiao, W.H.; Huang, J.; Hong, L.L.; Yang, F.; Xu, Y.; Wang, S.P.; Sun, F.; Lin, H.W. Meroterpenoids with Protein Tyrosine Phosphatase 1B Inhibitory Activity from a *Hyrtios* sp. Marine Sponge. *J. Nat. Prod.* 2017, 80, 2509–2514. [CrossRef] [PubMed]

314. Fukushima, K.; Takada, K.; Okada, S.; Matsunaga, S. Nazumazoles D–F, Cyclic Pentapeptides That Inhibit Chymotrypsin, from the Marine Sponge Theonella swinhoei. *J. Nat. Prod.* 2016, 79, 1694–1697. [CrossRef] [PubMed]

315. Wiese, J.; Imhoff, J.F.; Guder, T.A.; Labes, A.; Schmaljohann, R. Marine Fungi as Producers of Benzocoumarins, a New Class of Inhibitors of Glycogen-Synthase-Kinase 3beta. *Mar. Drugs* 2016, 14, 200. [CrossRef] [PubMed]

316. Ding, H.; Zhang, D.; Zhou, B.; Ma, Z. Inhibitors of BRD4 Protein from a Marine-Derived Fungus *Alternaria* sp. NH-F6. *Mar. Drugs* 2017, 15, 76. [CrossRef]

317. Tanokashira, N.; Kukita, S.K.; Kato, H.; Nehira, T.; Angkouw, E.D.; Mangindaan, R.E.; Devoogd, N.J.; Tsukamoto, S. Petroquinones: Anti-Inflammatory Agents from Tetrahedron Trimeric and dimeric xestoquinone derivatives isolated from the marine sponge *Petrosia* alfani. *Mar. Drugs* 2016, 14, 5530–5540. [CrossRef] [PubMed]

318. El-Desoky, A.H.; Kato, H.; Tsukamoto, S. Ceylonins G–I: Spongian diterpenes from the marine sponge *Spongia ceylonensis*. *J. Nat. Prod.* 2016, 79, 2983–2990. [CrossRef]

319. Imperatore, C.; Luciano, P.; Aiello, A.; Vitalone, R.; Irace, C.; Santamaria, R.; Li, J.; Guo, Y.W.; Menna, M. Structure and Configuration of Phosphoeleganin, a Protein Tyrosine Phosphatase 1B Inhibitor, from the Mediterranean Ascidian *Sidnyum elegans*. *Eur. J. Med. Chem.* 2017, 131, 1186–1193. [CrossRef]

320. Georgetta, P.; Ioannou, E.; Eavin-Bana, E.; Bagrel, D.; Martinet, N.; Vagias, C.; Roussis, V. Sesquiterpenes with inhibitory activity against CDC25 phosphatases from the soft coral *Pseudopterogorgia rigida*. *Tetrahedron* 2016, 72, 3262–3269. [CrossRef]

321. El-Desoky, A.H.; Kato, H.; Tsukamoto, S. Ceylonins G–I: Spongian diterpenes from the marine sponge *Spongia ceylonensis*. *J. Nat. Prod.* 2017, 80, 1144–1148. [CrossRef]

322. Ortega, M.J.; Pantoya, J.J.; de Los, R.C.; Zubia, E. 5-Alkylresorcinol Derivatives from the Bryozoan *Schizomavella* mammillata: Isolation, Synthesis, and Antioxidant Activity. *Mar. Drugs* 2017, 15, 344. [CrossRef]

323. Shi, J.; Fu, Q.; Wu, W.; Cai, M.; Zhou, X.; Zhang, Y. Producing Novel Fibrinolytic Isoindolinone Derivatives in Marine Fungus *Stachybotrys* longispora FG216 by the Rational Supply of Amino Compounds According to Its Biosynthesis Pathway. *Mar. Drugs* 2017, 15, 214. [CrossRef]

324. Zhao, Y.; Liu, D.; Proksch, P.; Yu, S.; Lin, W. Isoocoumarin Derivatives from the Sponge-Associated Fungus *Peyronellaea* glomerata isolated with Antioxidant Activities. *Chem. Biodivers.* 2016, 13, 1186–1193. [CrossRef]

325. Lee, M.S.; Chen, W.T.; Kurtan, T.; Mandi, A.; Ding, J.; Li, J.; Li, X.W.; Guo, Y.W. Bioactive isoquinolinequinone alkaloids from the South China Sea nudibranch Jorunna funebris and its sponge-prey *Xestospongia* sp. *Future Med. Chem.* 2016, 8, 17–27. [CrossRef] [PubMed]

326. Ortega, M.J.; Pantoya, J.J.; de Los, R.C.; Zubia, E. 5-Alkylresorcinol Derivatives from the Bryozoan *Schizomavella* mammillata: Isolation, Synthesis, and Antioxidant Activity. *Mar. Drugs* 2017, 15, 344. [CrossRef]
354. Chiesa, G.; Busnelli, M.; Manzini, S.; Parolini, C. Nutraceuticals and Bioactive Components from Fish for Dyslipidemia and Cardiovascular Risk Reduction. *Mar. Drugs* 2016, 14, 113. [CrossRef] [PubMed]

355. Alghazwi, M.; Kan, Y.Q.; Zhang, W.; Gai, W.P.; Yan, X.X. Neuroprotective Activities of Marine Natural Products from Marine Sponges. *Curr. Med. Chem.* 2016, 23, 360–382. [CrossRef]

356. Huang, Y.; Peng, C.; Yi, Y.; Gao, B.; Shi, Q. A Transcriptomic Survey of Ion Channel-Based Conotoxins in the Chinese Tubular Cone Snail (*Conus betulinus*). *Mar. Drugs* 2017, 15, 228. [CrossRef] [PubMed]

357. Molgo, J.; Marchot, P.; Araoz, R.; Bemoit, E.; Iorga, B.I.; Zakarian, A.; Taylor, P.; Bourne, Y.; Servent, D. Cyclic imine toxins from dinoflagellates: A growing family of potent antagonists of the nicotinic acetylcholine receptors. *J. Neurochem.* 2017, 142 (Suppl. 2), 41–51. [CrossRef]

358. Sadeghi, M.; McArthur, J.R.; Finol-Urdaneta, R.K.; Adams, D.J. Analgesic conopeptides targeting G protein-coupled receptors reduce excitability of sensory neurons. *Neuropharmacology* 2017, 127, 116–123. [CrossRef]

359. Bai, H.; Kong, W.W.; Shao, C.L.; Li, Y.; Liu, Y.Z.; Liu, M.; Guan, F.F.; Wang, C.Y. Zebrafish Embryo Toxicity Microscale Model for Ichthyotoxicity Evaluation of Marine Natural Products. *Mar. Biotechnol.* 2016, 18, 264–270. [CrossRef]

360. Agrawal, S.; Adholeya, A.; Deshmukh, S.K. The Pharmacological Potential of Non-ribosomal Peptides from Marine Sponge and Tunicates. *Front. Pharmacol.* 2016, 7, 333. [CrossRef]

361. García-Vilas, J.A.; Martinez-Poveda, B.; Quesada, A.R.; Medina, M.A. Aeroplysinin-1, a Sponge-Derived Multi-Targeted Bioactive Marine Drug. *Mar. Drugs* 2016, 14, 1. [CrossRef]

362. Alfonso, A.; Vieytes, M.R.; Botana, L.M. Yessotoxin, a Promising Therapeutic Tool. *Mar. Drugs* 2016, 14, 30. [CrossRef]

363. Valeur, E.; Gueret, S.; Adihou, H.; Gopalakrishnan, R.; Lemurell, M.; Waldmann, H.; Grossman, T.; Plowright, A. New Modalities for Challenging Targets in Drug Discovery. *Angew. Chem. Int. Ed.* 2017, 56, 10294–10323. [CrossRef] [PubMed]