**Table S1.** Bioactive natural products produced by octocoral associated microorganisms.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Microorganism** | **Host species and family** | **Compound and chemical class** | **Bioactivity** | **Reference** |
| *Bacteria* |  |  |  |  |
| ***Bacillus amyloliquefaciens*** Firmicutes Bacilli | *Junceella juncea* Ellisellidae | **macrolactin V**  **(2)**  macrolide | strongly antibacterial activity against *Escherichia. coli*, *Bacillus subtilis*, and *Staphylococcus aureus* | [1] |
| ***Pseudoalteromonas* sp.** Proteobacteria γ-proteobacteria | *Leptogorgia alba* Gorgoniidae | **alteramide A**  **(1)**  polyketide | antifungal activity | [2] |
| ***Pseudoalteromonas* sp.** Proteobacteria γ-proteobacteria | *Lobophytum crassum* Alcyoniidae | **pseudoalteromones A & B (18)** ubiquinone-monoterpenoids | anti-inflammatory activity - inhibition of release of elastase by human neutrophils; pseudoalteromone A also shows anticancer activity against MOLT-4 and T-47D cells | [3,4] |
| ***Streptomyces* sp.** Actinobacteria | unidentified soft coral (China) | **strepchloritide A & B**  **(17)**  polyketides | antibacterial activity against *S. aureus*; anticancer activity against MCF-7 cells | [5] |
| ***Vibrio* sp.** Proteobacteria  γ-proteobacteria | *Sinularia polydactyla* Alcyoniidae | **aqabamycin A–G**  **(3)**  maleimids | antibacterial, antifungal and anticancer activities | [6] |
| *Fungi* |  |  |  |  |
| ***Alternaria sp*.** Ascomycota Dothideomycetes | *Sarcophyton* sp. Alcyoniidae | **tetrahydroaltersolanol C** anthraquinone | active against the porcine reproductive and respiratory syndrome virus (PRRSV) | [7] |
| ***Alternaria sp.*** Ascomycota Dothideomycetes | *Sarcophyton* sp. Alcyoniidae | **alterporriols P & Q**  **(15)**  anthraquinones | alterporriol Q has antiviral activity against PRRSV; alterporriol P is anticancerous against PC-3 and HTC-116 | [7] |
| ***Aspergillus elegans*** Ascomycota Eurotiomycetes | *Sarcophyton* sp. Alcyoniidae | **4'-O-methoxyasperphenamate (4)**  pheylalanine derivative | antibacterial activity against *Staphylococcus epidermidis* | [8] |
| ***Aspergillus elegans*** Ascomycota Eurotiomycetes | *Sarcophyton* sp. Alcyoniidae | **asperphenamate** pheylalanine derivative | antibacterial activity against *S. epidermidis* | [8] |
| ***Aspergillus elegans*** Ascomycota Eurotiomycetes | *Sarcophyton* sp. Alcyoniidae | **aspochalasin D, I, J & H**  **(12)**  alkaloids / cytochalasins | strong antifouling activity against larval settlement of the barnacle *Balanus amphitrite* | [8] |
| ***Aspergillus fumigatus*** Ascomycota Eurotiomycetes | *Sinularia* sp. Alcyoniidae | **spirotryprostatin F**  **(25)**  cyclopetide-alkaloid | stimulatory phytoregulatory activity on sprout roots of soy, corn and buckwheat | [9] |
| ***Aspergillus ochraceus*** Ascomycota Eurotiomycetes | *Dichotella gemmacea* Ellisellidae | **ochralate A** pyrazinone derivative | antibacterial activity against *Enterobacter aerogenes* | [10] |
| ***Aspergillus ochraceus***  Ascomycota Eurotiomycetes | *Dichotella gemmacea* Ellisellidae | **ochromide B**  pyrazinone derivative | antibacterial activity against *E. aerogenes* | [10] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Muricella abnormalis* Acanthagorgiidae | **asperpeptide A**  **(5)**  cyclopeptide | antibacterial activity against *Bacillus cereus* and *S. epidermidis* | [11] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Muricella abnormalis* Acanthagorgiidae | **22-O-(NMe-L-valyl)-21-epi-aflaquinolone B**  **(14)**  hydroquinolone | very potent antiviral activity against respiratory syncytial virus (RSV). | [12] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Melitodes squamata* Melithaeidae | **aspergillipeptide C**  **(13)**  cyclopeptide | strong antifouling activity against *Bugula neritina* larvae settlement | [13] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Dichotella gemmacea* Ellisellidae | **aspergilone A**  **(20)**  benzylazaphilones | anticancer activity against HL-60, MCF-7 and A-549; potent antifouling activity against *B. amphitrite* larvae settlement | [14] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Dichotella gemmacea* Ellisellidae | **8-O-methylnidurufin** anthraquinone | antibacterial activity against *Micrococcus luteus* | [15] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Melitodes squamata* Melithaeidae | **9a,14-dihydroxy-6b-p-nitrobenzoylcinnamolide** alkaloid | strong antiviral activity against influenza virus H1N1 and H3N2 | [16] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Melitodes squamata* Melithaeidae | **7a,14-dihydroxy-6b-p-nitrobenzoylconfertifolin** alkaloid | moderate antiviral activit against H1N1 and H3N2 | [16] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Melitodes squamata* Melithaeidae | **aspergilliamide** aspergillic acid | weak toxicity to brine shrimp *Artemia salina* | [17] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Melitodes squamata* Melithaeidae | **ochratoxin A butyl ester** ochratoxin | significant toxicity to *Artemia salina* | [17] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Melitodes squamata* Melithaeidae | **5-hydroxy-3-isopropyl-4-methoxyfuranone**  γ-lactones | significant toxicity to *Artemia salina* | [18] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Dichotella gemmacea* Ellisellidae | **chrodrimanin B** terpenoid | insecticidal activity: potent blockers of insect GABA-gated chloride channels | [19,20] |
| ***Aspergillus* sp.** Ascomycota Eurotiomycetes | *Dichotella gemmacea* Ellisellidae | **methyl sydowate (7)** sesquiterpenoid | modest antibacterial activity against *S. aureus* | [21] |
| ***Aspergillus sydowii*** Ascomycota Eurotiomycetes | *Verrucella umbraculum* Ellisellidae | **fumiquinazoline D** indole alkaloid | antifouling activity towardsbryozoan *Bugula neritina* larvae settlement | [22] |
| ***Aspergillus sydowii*** Ascomycota Eurotiomycetes | *Verrucella umbraculum* Ellisellidae | **cyclotryprostatin B** indole alkaloid | antifouling activity towards *B. neritina* larvae settlement | [22] |
| ***Aspergillus terreus*** Ascomycota Eurotiomycetes | *Sinularia kavarattiensis* Alcyoniidae | **aspernolide A** aromatic butenolid | mild anticancer activity towards H460, ACHN, Calu, Panc1 and HCT-116 cell lines | [23] |
| ***Aspergillus terreus*** Ascomycota Eurotiomycetes | *Echinogorgia aurantiaca* Plexauridae | **asperterrestide A** cyclopeptide | antiviral activity against influenza virus strains H1N1 and H3N2; anticancer activity against human tumor cell lines | [24] |
| ***Aspergillus terreus*** Ascomycota Eurotiomycetes | *Echinogorgia aurantiaca* Plexauridae | **territrem D and E** lactones / territrem derivatives | territrem D shows potent antifouling activity against *B. amphitrite* larvae settlement and, together with territrem E, strong anti-neurodegenerative activity (acetylcholinesterase (AChE) inhibitors) | [25] |
| ***Aspergillus terreus*** Ascomycota Eurotiomycetes | *Echinogorgia aurantiaca* Plexauridae | **11a-dehydroxy-isoterreulactone A** lactone / territrem derivative | antiviral activity towards HSV-1 | [25] |
| ***Aspergillus terreus*** Ascomycota Eurotiomycetes | *Echinogorgia aurantiaca* Plexauridae | **isobutyrolactone II** lactone / butyrolactone derivative | antiviral activity towards HSV-1 | [25] |
| ***Aspergillus terreus*** Ascomycota Eurotiomycetes | *Sarcophyton subviride* Alcyoniidae | **versicolactone B**  **(23\*)**  lactone | antiinflammatory activity against nitric oxide (NO) production in RAW264.7 mouse macrophages | [26] |
| ***Aspergillus versicolor***  Ascomycota Eurotiomycetes | *Dichotella gemmacea* Ellisellidae | **aroyl uridine derivative 1, 2**  **(6)**  nucleosides | antibacterial activity against *S. epidermidis* and toxicity towards brine shrimp *A. salina* | [27] |
| ***Aspergillus versicolor***  Ascomycota Eurotiomycetes | *Cladiella* sp. Alcyoniidae | **tetraorcinol A**  **(24)**  phenol / orcinol | weak antioxidant activity/radical scavenger against the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical | [28] |
| ***Aspergillus versicolor*** Ascomycota Eurotiomycetes | *Cladiella* sp. Alcyoniidae | **cottoquinazoline D**  **(11)**  alkaloid | modest antifungal activity against *Candida albicans* | [29] |
| ***Chondrostereum* sp.** Basidiomycota Agaricomycetes | *Sarcophyton tortuosum*  Alcyoniidae | **chondrosterin J** sesquiterpenoid | potent anticancer activity y towards CNE-1 and CNE-2 cell lines | [30] |
| ***Chondrostereum* sp.** Basidiomycota Agaricomycetes | *Sarcophyton tortuosum*  Alcyoniidae | **chondrosterin A**  **(19)**  sesquiterpenoid | anticancer activity towards A549, CNE-2 and LoVo cancer cells | [31] |
| ***Chondrostereum* sp.** Basidiomycota Agaricomycetes | *Sarcophyton tortuosum*  Alcyoniidae | **incarnal**  sesquiterpenoid | potent anticancer activity against eight different cancer cell lines | [32] |
| ***Chondrostereum* sp.** Basidiomycota Agaricomycetes | *Sarcophyton tortuosum*  Alcyoniidae | **hirsutanol A**  sesquiterpenoid | potent anticancer activity is against 15 different cancer cell lines | [33] |
| ***Cochliobolus lunatus*** Ascomycota Dothideomycete | *Dichotella gemmacea* Ellisellidae | **cochliomycin A**  lactone | strong antifouling activity against *B. amphitrite* larvae settlement and moderate antibacterial activity against *S. aureus* | [34] |
| ***Nodulisporium* sp.**Ascomycota Sordariomycetes | unidentified soft coral (Thailand) | **nodulisporacid A**  **(22)**  lactone / tetronic acid | antimalarial activity against chloroquine resistant *Plasmodium falciparum* | [35] |
| ***Penicillium citrinum***  Ascomycota Eurotiomycetes | *Annella sp.* Supergorgiidae | **penicillanthranin A**  **(8)**  anthraquinone | antibacterial activity against *S. aureus* and methicillin resistant *S. aureus* (MRSA) | [36] |
| ***Penicillium commune*** Ascomycota Eurotiomycetes | *Muricella abnormalis* Acanthagorgiidae | **communols A–G**  **(9)**  polyketides | communols A, F and G are moderately active against *E. coli* and *Enterobacter aerogenes* | [37] |
| ***Penicillium oxalicum*** Ascomycota Eurotiomycetes | *Muricella flexuosa* Acanthagorgiidae | **oxalicumone A & B**  **(21)**  chromones | anticancer activity against A375 and SW-620 cancer cell lines; oxalicumone A is more potent | [38] |
| ***Penicillium* sp.** Ascomycota Eurotiomycetes | *Dichotella gemmacea* Ellisellidae | **6,8,50,60-tetrahydroxy-30-methylflavone**  polyketide | significant antifouling activity against *B. amphitrite* larvae settlement | [39] |
| ***Pestalotiopsis* sp.** Ascomycota Sordariomycetes | *Sarcophyton sp.* Alcyoniidae | **(+)- and ()-pestaloxazine A (16)**  polyketide-cyclopeptide | antiviral activity against EV71; ((+)-pestaloxazine A more potent and more selective | [40] |
| ***Pestalotiopsis* sp.** Ascomycota Sordariomycetes | *Sarcophyton sp.* Alcyoniidae | **()-pestalachloride D**  **(10)**  benzophenone derivative | moderate antibacterial activity against several Gram-negative bacteria | [41] |
| ***Phoma* sp.** Ascomycota Dothideomycetes | *Dichotella gemmacea* Ellisellidae | **phomaether A & C** dephenyl ethers | strong antibacterial activity against several Gram-positive and -negative pathogens | [42] |
| ***Scopulariopsis* sp.** *Ascomycota Sordariomycetes* | *Carijoa* sp*.*  Clavulariidae | **aniduquinolone A**  alkaloid | antifouling activity towards *B. amphitrite* larvae settlement | [43] |
| ***Scopulariopsis* sp.** Ascomycota Sordariomycetes | *Carijoa* sp.  Clavulariidae | **aflaquinolone A, D, F, G; 6-deoxyaflaquinolone E** alkaloid | antifouling activity towards *B. amphitrite* larvae settlement; deoxyaflaquinolone E shows broad spectrum antibacterial activity | [43] |
| ***Trichoderma aureoviride*** Ascomycota Sordariomycetes | *Annella sp.* Supergorgiidae | **trichodermaquinone** antthraquinone | weak activity against MRSA | [44] |
| ***Xylariaceae*** Ascomycota Sordariomycetes | *Melitodes squamata* Melithaeidae | **dicitrinin** (also penicitrinone) **A**  polyketide | strong antifouling activity against *B. neritina* larvae settlement | [45] |
| ***Xylariaceae*** Ascomycota Sordariomycetes | *Melitodes squamata* Melithaeidae | **(3R,4S)-(+)-4-hydroxy-6-deoxyscytalone**  polyketide | inhibitory activities towards SHP2, PTPlB, and IMPDH (anticancer) | [45] |
| ***Xylariaceae*** Ascomycota Sordariomycetes | *Melitodes squamata* Melithaeidae | **dihydrocitrinon**  polyketide | antifouling activity against *B. neritina* larvae settlement, inhibition of cathepsin B and the enzymes SHP2 and IMPDH (anticancer) | [45] |
| ***Xylariaceae*** Ascomycota Sordariomycetes | *Melitodes squamata* Melithaeidae | **phenol acid A**  polyketide | antifouling activity against *B. neritina* larvae settlement and cathepsin B inhibition (anticancer) | [45] |
| *Microalgae* |  |  |  |  |
| ***Symbiodinium* sp.**  Dinoflagellata  Dinophyceae | *Antillogorgia elisabethae*  Gorgoniidae | **Pseudopterosin A, B, C, D**  diterpene-glycoside | strong anti-inflammatory and analgesic activity | [46, 47] |

**MRSA** - methicillin resistant *Staphylococcus aureus.* **GABA** - *gamma-*aminobutyric acid neurotransmitter.

**Viruses:** **RSV** - respiratory syncytial virus; **PRRSV**- porcine reproductive and respiratory syndrome virus; **H1N1** and **H3N2**– Influenza A virus subtypes; **HSV-1** - Herpes simplex virus; **EV71** – human Enterovirus 71.

**Cancer cell lines:** **A375** – human malignant melanoma; **A549** – human lung carcinoma; **ACHN** - human kidney adenocarcinoma;

**Calu** – human lung carcinoma; **CNE-1** and **CNE-2** – nasopharyngeal carcinoma; **H460** – human lung cancer; **HCT-116** - human colon carcinoma; **HL-60** – human promyelocytic leukemia; **LoVo** – human colon metastasis; **MCF-7** - human breast cancer; **MOLT-4** – lymphoblastic leukemia; **Panc1** – human pancreas; **PC-3** - human prostate adenocarcinoma; **SW-620** – human colon adenocarcinoma; **T-47D** – human breast tumor.

**IMPDH** – Inosine-5'-monophosphate dehydrogenase; **SHP2** and **PTPlB** - protein tyrosine phosphatases; IMPDH, SHP2 & PTPlB are associated with cell proliferation; cathepsin B is upregulated in several cancers.

**(23\*) versicolactone B** refers to compound 23 with the sum formula C24H24O6 as shown in figure 4 and described by [26,48]. However, the compound name likely needs revision since several *Aspergillus* derived lactones with different chemical structures and sum formula share this name.

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