Review

Natural Products of Marine Macroalgae from South Eastern Australia, with Emphasis on the Port Phillip Bay and Heads Regions of Victoria

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Received: 29 January 2020; Accepted: 26 February 2020; Published: 28 February 2020

Abstract: Marine macroalgae occurring in the south eastern region of Victoria, Australia, consisting of Port Phillip Bay and the heads entering the bay, is the focus of this review. This area is home to approximately 200 different species of macroalgae, representing the three major phyla of the green algae (Chlorophyta), brown algae (Ochrophyta) and the red algae (Rhodophyta), respectively. Over almost 50 years, the species of macroalgae associated and occurring within this area have resulted in the identification of a number of different types of secondary metabolites including terpenoids, sterols/steroids, phenolic acids, phenols, lipids/polyenes, pheromones, xanthophylls and phloroglucinols. Many of these compounds have subsequently displayed a variety of bioactivities. A systematic description of the compound classes and their associated bioactivities from marine macroalgae found within this region is presented.

Keywords: marine macroalgae; bioactivity; secondary metabolites

1. Introduction

The pharmaceutical industry has evolved as a result of research conducted in the areas of both synthetic organic chemistry and natural products extraction. During the period 1981–2014, approximately 42% of all U.S Food and Drug Administration (FDA) new drug approvals were based on either natural products or derivatives of a natural product pharmacophore [1]. Additionally, 49% of all anti-cancer drugs produced since the 1940s have been derived from a natural product source, or have been inspired by a natural product, and synthesized as a ‘natural product mimic’ [1].

Given the reduced effectiveness of traditional antibiotics to fight more resistant forms of bacterial infection in humans, together with the need for antibiotics in agriculture, there has been an increasing need to source new antibiotic drugs. Akin to this is the unabated need for bioactive compounds that show cytotoxic activity towards tumor cells for the effective treatment of cancers. This has provided much of the impetus for the research conducted within the field of natural product drug discovery, both from terrestrial and marine sources. While numerous drugs have been derived from terrestrial plants, there is still a huge untapped reserve of marine organisms that have been comparatively understudied. Terrestrial natural products (TNPs) have been exploited for their biological potency for many hundreds of years, whilst it is only recently, due to the increased use of SCUBA, that we have had access to the array of ocean-dwelling species, and this has led to an increase in the study of Marine Natural Products (MNPs). In fact, between 2014 and 2016, 203 new natural products were discovered from the study of macro algae (Green, Red and Brown) [2,3]. Many of these compounds displayed very
promising biological activity, making them serious contenders as anti-cancer and anti-bacterial drugs or drug leads. A recent cheminformatics study has highlighted the potential of MNPs to produce drug-like chemical compounds [4]. Despite this, MNPs remain less studied than TNPs, mostly due to the relative ease with which TNP specimens can be obtained and cultivated. Currently, there are 10 FDA-approved marine-derived pharmaceutical drugs, together with 30 potential candidates for application in a number of disease areas that are in different stages of clinical trials (Phase I, II and III) Figure 1 [5].

A number of reviews have also detailed the biologically active natural products that are sourced from marine organisms [6–10], highlighting marine organisms as an important resource for the production of new and unique compounds with potential medicinal value. Many of the compounds represented in Figure 1 have been isolated from sponges, ascidians and cyanobacteria. Marine macroalgae are underrepresented in the pharmaceutical pipeline despite the number of biologically active compounds. Marine algae have also been used in a number of other important areas including the food industry [11], agriculture [12] and as a source of third-generation bioplastics [13]. Compounds from marine algae have been shown to exhibit a number of biologically active properties such as anti-microbial [6,7,14], anti-cancer [15], anti-leishmanial [16], anti-inflammatory [17], anti-fouling [18] and anti-protozoal [19] activities. Historically, Australia has been an excellent source of novel marine
invertebrate chemistry. Australia has the largest Exclusive Economic Zone (EEZ) on the planet, which is made up of several diverse marine ecoregions. As a source of novel chemistry, Australia’s EEZ has been prolific, with its contribution representing the third largest of newly discovered MNPs during the period 1965–2012, only behind Japan and China, respectively. Of interest is the marine ecoregion of Port Phillip Bay, located on the south eastern coast of Australia in the state of Victoria. During the period 1995–2012, this marine ecoregion has been the dominant source of unreported natural products located within Australia’s EEZ [20]. The primary reason for this being the large amount of habitat variety that is present in this Bay, such as intertidal sandy beaches, mangroves and rocky shores along with tidal habitats like sand beds, seagrass beds and rocky reefs. Port Phillip Bay, located on the southern shore of Victoria (Figure 2), has an area of approximately 2000 square kilometers and an average depth of 13 m. It represents a unique habitat, being shallow enough to be in the photic zone throughout and is known for the cleansing activities of the microphyto- and zoo-benthos and continues to be a region of Australia that yields new species. It is home to approximately 200 different species of macroalgae, a figure which is subject to change due to introduced species that originate from shipping within the Port and is represented by all three major phyla, namely the brown (Ochrophyta), red (Rhodophyta) and the green algae (Chlorophyta).

Figure 2. Geographical location of Port Phillip Bay in relation to Australia.

In order to explore the potential of the Port Phillip Bay region as a continuing source for bioactive marine natural products, it is important to review and document the natural products that have been studied and the bioactivities that have been discovered for the marine algae occurring in this region. The methodology adopted to compile this review required that a species list for Port Phillip Bay macroalgae to be created using the Victorian Biodiversity Atlas in conjunction with the Melbourne Museum listings for algae species found within the Port Phillip Bay area [21–23]. Table 1 displays the listings of the species of Port Phillip Bay algae that this review focuses upon. A number of these species are not endemic to Port Phillip Bay, and have been sampled worldwide. Thus, this review will not be limited to natural products derived only from marine algae sampled from Port Phillip Bay, but will focus on the global study of natural products from each marine algae species that exists within the Port Phillip Bay region.

The purpose of this review is to provide a compilation of the natural products found in the marine macroalgae of Port Phillip Bay and discuss the associated trends in their biological activities. Emphasis has been placed on the three major phyla of algae, namely the green (Chlorophyta), the brown (Ochrophyta) and the red algae (Rhodophyta) and the study of their secondary metabolites between 1971 and early 2019. This review provides listings of compounds that are categorized under the following structure classes: terpenoids, sterols/steroids, phenolic acids, phenols, lipids/polyenes, pheromones, xanthophylls and phloroglucinols. Compound classes that include carbohydrates/sugars (polysaccharides, agars and carrageenans), tannins, tannic acids, phlorotannins and fatty acids have been excluded from this review, owing to their ubiquitous nature.
Table 1. Reported marine algae species of the Port Phillip Bay region [21,22].

| CHLOROPHYTA | RHODOPHYTA | OCHROPHYTA |
|--------------|------------|------------|
| ▲ Aphrodes lanceolatus | ▲ Carposoma falkax | ▲ Acerospermum ciliolatum |
| ▲ Bryopsis vesiculosa | ▲ Sargassum heteromorphum | ▲ Heterosiphonia gumianna |
| ▲ Caulerpa alternans | ▲ Sargassum linearifolium | ▲ Heterosiphonia muellerii |
| ▲ Caulerpa brownii | ▲ Sargassum paradoxi | ▲ Laurencia elongata |
| ▲ Caulerpa catapides | ▲ Sargassum sonderi | ▲ Laurencia elegans |
| ▲ Caulerpa cliftonii | ▲ Sargassum multinervosum | ▲ Laurencia filiformis |
| ▲ Caulerpa flexilis | ▲ Sargassum venustum | ▲ Lenormandia angustata |
| ▲ Caulerpa geminata | ▲ Sargassum vestitum | ▲ Lenormandia muelleri |
| ▲ Caulerpa longifolia | ▲ Scytophithion lomentaria | ▲ Mermaidavia nana |
| ▲ Caulerpa obscura | ▲ Sphacelaphora microphylla | ▲ Metagoniolithon radiatum |
| ▲ Caulerpa papillosa | ▲ Chaetomorpha valida | ▲ Metaphymenia auriculata |
| ▲ Caulerpa remotifolia | ▲ Caulerpa vesicularis | ▲ Metaphymenia auriculata |
| ▲ Caulerpa scalpelliformis | ▲ Caulocystis uvifera | ▲ Montastraea flabellina |
| ▲ Caulerpa semplicissima | ▲ Dictyota dichotoma | ▲ Pachymenia orbicularis |
| ▲ Caulerpa trifaria | ▲ Dictyota furcellata | ▲ Palisada tumida |
| ▲ Chaetomorpha coliformis | ▲ Dictyota guiniana | ▲ Periclimenes minutus |
| ▲ Chaetomorpha valida | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus alatus |
| ▲ Caulerpa simplicissima | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Caulerpa trigonaria | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Chlanodophora microphylla | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Codium australicum | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Codium duthiei | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Codium fragile | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Codium harveyi | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Codium lucasi | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Codium pomoides | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Dictyopteris sericea | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Ulva australis | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Ulva compressa | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Ulva lactuca | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Ulva longa | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Ulva rigida | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |
| ▲ Ulva taiutata | ▲ Dictyopteris acrostichoides | ▲ Phacelocarpus cariosus |

*Currently unaccepted name but is also mentioned in literature frequently; see Supporting Information S1 for new name.*  
★Species that are currently accepted name and have other names that are synonyms. *Species that are the currently accepted name and have no synonyms.*
2. Chlorophyta (Green Algae)

The phylum Chlorophyta are found to be distinctively green in color due to the presence of chlorophyll a and b occurring in high concentrations. Green algae proliferate within the euphotic zone of the ocean, or where there is sufficient sunlight to perform effective photosynthesis, usually growing within the intertidal zone up to depths of 50 meters. The most common and frequently studied species of green algae found in Port Phillip Bay are within the genera *Caulerpa*, *Codium* and *Ulva*. Many of the species that comprise the three mentioned genera can also be found in various tropical, sub-tropical and temperate marine climates around the world and are thus not exclusive to Port Phillip Bay. Common types of secondary metabolite classes found within the phylum Chlorophyta include diterpenes, sesquiterpenes, sterols and lipids. This review reports a total of 64 secondary metabolites distributed among 12 species of common green algae of Port Phillip Bay within the period 1971 to early 2019.

2.1. Terpenoids

2.1.1. Diterpenes

Algae from the genus *Caulerpa* would appear to have yielded the majority of diterpene compounds, comprised of both cyclic and acyclic C-20 diterpenes (1–20) (see Supporting Information Figure S2). Many of the cyclic diterpenoid compounds found within *Caulerpa* show a variety of biological activities. Compound 7, extracted and characterized in 1985 from *C. brownii*, was shown to exhibit anti-bacterial activity towards *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Vibrio anguillarum* utilizing the disc diffusion methodology at 100 µg/disc [24]. Metabolites (5 and 9) derived from *Caulerpa trifaria* displayed moderate cytotoxic behavior when tested using the brine shrimp assay [25]. Caulerpol (2) appears to be found in most species of the genus *Caulerpa*, usually as the dominant constituent of the crude extract. The isolation of caulerpol was of particular importance as it was the first compound with a retinol carbon skeleton isolated from a plant source and was later shown to be easily synthesized from (S)-(-)-α-cyclogeraniol [26]. A number of terpenoid esters (2a – 2f) were also found with R groups representing the fatty acids arachidonic, eicosapentanoic, oleic, linoleic, linolenic and hexadecatrienenoic acids [27]. The acyclic diterpenes of the genus *Caulerpa* exhibit both acetoxy and aldehyde functionalities, much the same as the cyclic diterpenes. A good example being the natural product trifarin (17) from *C. trifaria* which contains two acetoxy groups. The usual scenario for these diterpenes is to contain acetoxy groups or both aldehyde and acetoxy groups, but it is rare to observe diterpenes from green algae with two aldehyde functional groups, as seen in compounds 5 (C. brownii) and 20 (C. brownii) [27]. Diterpenes are also found outside the genus *Caulerpa*, but only within the species *Codium fragile*. Non-polar fractions of *C. fragile* have been shown to yield saturated terpenoid compounds such as trans-phytol (13) and its two derivatives, phytol acetate (14) and phytol palmitate (15) [28].

2.1.2. Sesquiterpenes

Sesquiterpenes (C-15) are found in a smaller number of *Caulerpa* species as diterpenes but have only been found within the genus *Caulerpa* for the reported green algae of Port Phillip Bay. Sesquiterpenes, with acetoxy and aldehyde functionalities (21–24), Figure 3, have been shown to be potent feeding deterrents and in some cases cytotoxic towards predatory species of herbivorous fish [29]. It has been suggested that caulerpeneyne (24), an acyclic acetylenic sesquiterpene found in *C. trifaria*, as a minor secondary metabolite and in *C. taxifolia*, as a major secondary metabolite, is a key player in the cytotoxicity of *Caulerpa* algae towards herbivores [30]. This sesquiterpene appears to contribute to the invasiveness of the genus *Caulerpa* by means of its inhibition of the key organic anion transporters, Oatp1d1 and Oct1. These transporters play a role in the toxicity defense of a herbivorous predator of the genus *Caulerpa*, the zebra fish (*Danio rerio*) [30]. Although this particular mechanism of action has only been demonstrated towards zebrafish, it appears
to provide some reasoning behind the apparent success of Caulerpa as an invasive species of algae [30]. Compound (23) was shown to display moderate anti-microbial activity against B. subtilis and the marine fungus Dreschleria haloides. Furthermore, this compound inhibited the cell division of fertilized sea urchin eggs, demonstrating its antipredatory attributes [31].

2.1.3. Cyclic geranylacetone

All cyclic geranylacetone compounds (25-29), Figure 4, that have been characterized were isolated from the ethyl acetate fraction of the green alga Ulva lactuca. Compounds of a similar structure type, namely, the apocarotenoids, have been studied for their potential germination and growth inhibition qualities [32,33]. Many similar types of C13 nor isoprenoids have been found largely in wine, particularly Rieslings. Many of these compounds have been isolated and studied for their floral aromas [34,35]. A distribution of the terpene compounds reported in this review by species and locality is shown in Table 2.

![Figure 3. Chemical structure of sesquiterpenes 21-24.](image)

Table 2. Distribution of compounds 1 to 29.

| No. | Compound Type | Species | Origin | Ref |
|-----|---------------|---------|--------|-----|
| 1, 2 | Diterpene | C. brownii | Spring Beach, East Tasmania | [27] |
| 2a-f | Diterpene | C. brownii | Spring Beach, East Tasmania | [27] |
| 3, 4 | Diterpene | C. trifaria | Taroona Beach, Hobart, Tasmania | [25] |
| 5 | Diterpene | C. trifaria | Taroona Beach, Hobart, Tasmania | [25,27] |
| 6 | Diterpene | C. brownii | Spring Beach, East Tasmania | [27] |
| 7 | Diterpene | C. brownii | Spring Beach, East Tasmania | [27] |
| 8 | Diterpene | C. brownii | Spring Beach, East Tasmania | [27] |
| 9 | Diterpene | C. trifaria | Taroona Beach, Hobart, Tasmania | [25] |
| 10 | Diterpene | C. brownii | Spring Beach, East Tasmania | [27] |
| 11 | Diterpene | C. trifaria | Taroona Beach, Hobart, Tasmania | [25] |
| 12 | Diterpene | C. brownii | Spring Beach, East Tasmania | [27] |
| 13-15 | Diterpene | C. fragile | Qingdao Coastline, Shangdong, China | [28] |
| 16 | Diterpene | C. brownii | Spring Beach, East Tasmania | [27] |
| 17 | Diterpene | C. trifaria | Taroona Beach, Hobart, Tasmania | [25,36] |
| 18 | Diterpene | C. trifaria | Taroona Beach, Hobart, Tasmania | [25,27] |
| 19, 20 | Diterpene | C. brownii | Spring Beach, East Tasmania | [27] |
| 21, 22 | Sesquiterpene | C. flexilis | Cosy corner, Western Australia | [36] |
| 23 | Sesquiterpene | C. flexilis | Cosy corner, Western Australia | [36,37] |
| 24 | Sesquiterpene | C. trifaria | Taroona Beach, Hobart, Tasmania | [25] |
| 25-29 | Cyclic geranylacetone | U. lactuca | BoHai Coastline, China | [38] |
were found that include some lipids (49) Dictyosphaeria sericea. and Caulerpa[44]. Interestingly, compounds biological activities is provided in the Supporting Information (Table S7). compounds reported in this review by species and locality is shown in Table 3. A summary of the green algae (37) from the alga Codium fragile [44]. Interestingly, compounds 37–39 and 48 were all isolated and characterized from the alga C. fragile and following this study, it was suggested that sterol compounds may prove to be useful biomarkers for this genus allowing for easier taxonomic distinction between other members of the Codiceae family [44,45]. Much of the literature available for the genus Ulva involves biological activity studies on polysaccharides [46–49], many of the sterols found within this genus have shown promising in vitro bioactivity. In particular, the glycosidic sterol (47) from U. lactuca has been shown to be an effective anti-bacterial, anti-fungal and anti-inflammatory agent in vitro [41]. Compound 46, displaying an epoxide side chain functionality, appeared to display moderate recombinant aldose reductase inhibition when assayed at 3 µg/mL [39]. This compound outperformed all other sterols in this assay (41–45) of which, compounds 41, 42, 44 and 45 possess a hydroxyl vinyl moiety in place of the epoxide. This suggests that the epoxide side chain moiety must play a significant role in the inhibition shown by compound 46.

2.2. Steroids/Sterols

The sterols (see supporting information Figure S5) of U. lactuca (30–36, 40, 47) and U. australis (40, 41, 42, 44–46) have been studied extensively [39–43]. Many of the sterols found in the green algae of Port Phillip Bay appear to have a C-19 core skeleton with differing functionalities of the side chain. Of note, are compounds 41 and 42 derived from U. lactuca, which exhibit a keto group within the C-19 skeleton. Also of interest are the sterols 38, 47 and 48, which all appear to be variants of clerosterol, with 47 and 48 having attained a glycosidic moiety, whereas 38 has a long-chain ester attached. Acetylation of sterol fractions appears to be a tactic employed for easier isolation of these compounds, which was evident in the reported isolation of acetylated codisterol (37) from the alga Codium fragile [44]. Interestingly, compounds 37–39 and 48 were all isolated and characterized from the alga C. fragile and following this study, it was suggested that sterol compounds may prove to be useful biomarkers for this genus allowing for easier taxonomic distinction between other members of the Codiceae family [44,45]. Much of the literature available for the genus Ulva involves biological activity studies on polysaccharides [46–49], many of the sterols found within this genus have shown promising in vitro bioactivity. In particular, the glycosidic sterol (47) from U. lactuca has been shown to be an effective anti-bacterial, anti-fungal and anti-inflammatory agent in vitro [41]. Compound 46, displaying an epoxide side chain functionality, appeared to display moderate recombinant aldose reductase inhibition when assayed at 3 µg/mL [39]. This compound outperformed all other sterols in this assay (41–45) of which, compounds 41, 42, 44 and 45 possess a hydroxyl vinyl moiety in place of the epoxide. This suggests that the epoxide side chain moiety must play a significant role in the inhibition shown by compound 46.

2.3. Miscellaneous

Within the reported green algae of Port Phillip Bay, a number of miscellaneous compounds were found that include some lipids (49–52), bromophenolics (54–58) and a pigment (53), Figure 5. The di-indolo pigment caulerpin (53) was found exclusively within algae of the genus Caulerpa (trifaria, brownii, flexilis, racemosa and peltata), perhaps offering a useful chemotaxonomic marker for this genus [50]. The unprecedented bicyclic lipid dictyosphaerin (49) was isolated from the endemic Australian alga Dictyosphaeria sericea. This appears to be the only natural product reported in the literature for this species and is the only genus of reported Port Phillip Bay green algae outside of Caulerpa and Ulva that has shown the presence of lipidic compounds.

It should be noted that this compound was only partially characterized, as neither its relative nor absolute configuration have been described [51]. Compounds 50–52 were derived from the petroleum ether fraction of a methanolic extraction of U. lactuca along with isofucosterol and some fatty acid compounds [52]. In 1999 a profiling study of Eastern Australian marine algae, which included various green algae (Caulerpa cactoides, C. fragile, Codium galeatum, Codium lucasi and U. lactuca) [53], resulted in the identification of simple low molecular weight bromophenolic compounds 54–58 that were confirmed to be present in varying amounts. A distribution of the sterol, lipids and miscellaneous compounds reported in this review by species and locality is shown in Table 3. A summary of the biological activities is provided in the Supporting Information (Table S7).
number of secondary metabolites. Each of these species has shown the presence of an extensive range of phenolic compounds, diterpenoids, sesquiterpenoids and long-chain unsaturated lipids. Reported number of secondary metabolites. Each of these species has shown the presence of an extensive range.

\[ \text{Figure 5. Chemical structure of miscellaneous compounds 49–58.} \]

Table 3. Distribution of compounds 30 to 58.

| No. | Compound Type     | Species          | Origin                              | Ref    |
|-----|-------------------|------------------|-------------------------------------|--------|
| 30–36 | Steroid/Sterol    | *U. lactuca*     | Bay of Kotor, Southern Adriatic Sea | [40]   |
| 37   | Steroid/Sterol    | *C. fragile*     |                                     |        |
| 38, 39 | Steroid/Sterol   | *C. fragile*     | Qingdao Coastline, Shangdong, China | [28]   |
| 40   | Steroid/Sterol    | *U. lactuca*     | Abu Qir Bay, Alexandria, Egypt      | [40, 52] |
| 41–46 | Steroid/Sterol    | *U. australis*    | Dalian Coast, China                 | [39]   |
| 47   | Steroid/Sterol    | *U. lactuca*     | Abu Qir Bay, Alexandria, Egypt      | [41]   |
| 48   | Steroid/Sterol    | *C. fragile*     | Qingdao Coastline, Shangdong, China | [28]   |
| 49   | Lipid             | *D. sericea*     | Cape Schank and Point Lonsdale, Victoria | [51]   |
| 50–52 | Lipid             | *U. lactuca*     | Abu Qir Bay, Alexandria, Egypt      | [41]   |
| 53   | Di indolo pigment | *C. trifaria*    | Point Peron, WA                     | [50]   |
|      |                   | *C. brev.Xr*     | Augusta, WA                         |        |
|      |                   | *C. flexis*      | Augusta, WA                         |        |
|      |                   | *C. peltata*     | Big Nook Island, WA                 |        |
|      |                   | *C. racemosa*    | Big Nook Island, WA                 |        |
| 54   | Bromophenolic     | *U. lactuca*     | Bateau Bay, NSW                     | [54]   |
|      |                   | *C. lucasi*      | Bateau Bay, NSW                     |        |
|      |                   | *C. galeatum*    | Bateau Bay, NSW                     |        |
|      |                   | *C. cactoides*   | Bateau Bay, NSW                     |        |
| 55   | Bromophenolic     | *U. lactuca*     | Bateau Bay, NSW                     | [54]   |
|      |                   | *C. lucasi*      | Bateau Bay, NSW                     |        |
|      |                   | *C. galeatum*    | Bateau Bay, NSW                     |        |
|      |                   | *C. cactoides*   | Bateau Bay, NSW                     |        |
| 56   | Bromophenolic     | *U. lactuca*     | Bateau Bay, NSW                     | [54]   |
|      |                   | *C. lucasi*      | Bateau Bay, NSW                     |        |
|      |                   | *C. galeatum*    | Bateau Bay, NSW                     |        |
|      |                   | *C. fragile*     | Bateau Bay, NSW                     |        |
|      |                   | *C. cactoides*   | Bateau Bay, NSW                     |        |
| 57   | Bromophenolic     | *U. lactuca*     | Bateau Bay, NSW                     | [54]   |
|      |                   | *C. lucasi*      | Bateau Bay, NSW                     |        |
|      |                   | *C. galeatum*    | Bateau Bay, NSW                     |        |
|      |                   | *C. fragile*     | Bateau Bay, NSW                     |        |
|      |                   | *C. cactoides*   | Bateau Bay, NSW                     |        |
| 58   | Bromophenolic     | *U. lactuca*     | Bateau Bay, NSW                     | [54]   |
|      |                   | *C. lucasi*      | Bateau Bay, NSW                     |        |
|      |                   | *C. galeatum*    | Bateau Bay, NSW                     |        |
|      |                   | *C. fragile*     | Bateau Bay, NSW                     |        |
|      |                   | *C. cactoides*   | Bateau Bay, NSW                     |        |

3. Ochrophyta (Brown Algae)

The Ochrophyta phylum has been the most studied phylum of algae in Port Phillip Bay to date and has yielded the largest number and variety of natural products. *Caulocystis cephalornithos, Dictyota dichotoma* and *Nototheia anomala* represent the species of brown algae that have yielded the greatest number of secondary metabolites. Each of these species has shown the presence of an extensive range
of phenolic compounds, diterpenoids, sesquiterpenoids and long-chain unsaturated lipids. Reported herein is a total of 281 secondary metabolites isolated from 37 species of brown algae within the period 1971 to early 2019, representing several terpenoid classes, steroids/sterols, lipids and other miscellaneous compound classes.

3.1. Terpenoids

3.1.1. Tocotrienols

A part of the vitamin E family, the tocotrienols are a class of terpenoids that are characterized by their unsaturated farnesyl tails attached to a chromane ring, with variations between the types being expressed through substitutions on the aromatic ring or methylation of the hydroxyl group. There are four variations of the tocotrienol (α, β, γ and δ), two of the variants, γ (59) and δ (60), are reported herein. Two methylated variants of the tocotrienol compound class {61 and 62}, Figure 6, were also reported here but the identity of compound 62 was not confirmed, as the location of the methyl groups on the chromane ring was unclear. This could mean that the structure of 62 could be either β-tocotrienol or γ-tocotrienol [55]. All tocotrienols were found within the genus Cystophora, δ-tocotrienol (60) appeared to be the most prolific type being isolated as a secondary metabolite in Cystophora subfarcinata, Cystophora platylubium, Cystophora monilifera, Cystophora siliquosa and Cystophora retorta [55–58]. Both γ-tocotrienol and δ-tocotrienol have been reported to display a broad range anti-cancer activity including against colon carcinoma and lung cancer [57].

![Chemical structure of tocotrienols 59–62.](image)

3.1.2. Monoterpenes

Only five monoterpenes (C-10) were isolated from the brown algae listed in this review; in this instance, compounds 63–67, Figure 7, were all derived from the edible alga Undaria pinnatifida. All monoterpenes are in the form of loliolide derivatives, differing only in the stereochemistry of a tertiary alcohol and methyl group along with the degree of unsaturation. Loliolide monoterpenes have been well studied for their biological activities [59]. Compound 65, (+)-epiloliolide, was isolated from the brown alga Sargassum naozhouense and showed moderate antioxidant activity scavenging 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radicals. Further, epiloliolide proved to have anti-microbial properties as well as displaying resistance to the fungus Candida albicans and the two bacterial strains Escherichia coli and the methicillin-resistant Staphylococcus aureus (MRSA) [60]. More recently, loliolide (67) was reported to display allelopathic influence on the germination of surrounding plant seeds, which could be a contributor to the relative competitiveness of the brown alga Ul. pinnatifida [61].

![Chemical structure of monoterpenes 63–67.](image)
3.1.3. Prenylated Phenols

Prenylated phenols (68–80) (see Supporting Information Figure S10) are a significant group of compounds found in brown algae. They are identified from their terpenoid tails, of varying length, which are attached to a phenolic head group which is sometimes further cyclized as in compound 74. Prenylated phenols were discovered across three different genera and five different species of brown algae. To date, the *Sargassum* genus has yielded the greatest amount of prenylated phenols with compounds 68–71 and 77 derived from *Sargassum paradoxum*, and its relative *Sargassum fallax* only boasting two of the same phenols in 68 and 69 [62,63]. Of note was the moderate anti-tumor activity of compound 69 (sargahydroquinoic acid) against P388 (Murine Leukaemia cells) achieving an IC\(_{50}\) value of 14 \(\mu\)M, when tested at 1 mg/mL [63]. The dichloromethane (DCM) extract of *S. paradoxum* was assayed against a series of bacteria (*S. aureus*, MRSA and *S. pyogenes*) showing weak to moderate resistance. This was supported by compounds 68–71, isolated from the DCM extract, displaying a similar degree of anti-bacterial activity [62]. Compounds 75 and 76, isolated from *C. brownii*, are unique in this class and are of particular interest with respect to the molecular phylogeny of the *Cystophora* genus. These compounds display further complexity compared to their counterparts due to the incorporation of a furan ring in their terpenoid tails. Due to this fact, it is theorized that *C. brownii* is perhaps more phylogenically advanced than its *Cystophora* relatives. *C. torulosa*, on the other hand, appears to display only prenylated phenols with lower molecular weight and less relative complexity, such as compounds 78 and 79, perhaps suggesting that this *Cystophora* species is less phylogenically developed than *C. brownii* [56]. The study of *Perithalia caudata* from the family Sporochnaceae resulted in a number of simple prenylated phenols (72–74 and 80) being isolated with promising anti-bacterial assays [64–67]. It should be noted here that it was unclear if 74 was indeed a true natural product of *P. caudata* or perhaps an artefact of the isolation process formed by a ring closure of 72. Compound 72 was reported to show Minimum Inhibitory Concentrations (MICs) of 3.1 \(\mu\)g/mL for assays against both *C. albicans* and *Cryptococcus neoformans* and an MIC of 6.2 \(\mu\)g/mL against *B. subtilis* [65]. A distribution of the tocotrienols, monoterpenes and prenylated phenol compounds reported in this review by species and locality is shown in Table 4.

**Table 4. Distribution of compounds 59 to 80.**

| No. | Compound Type       | Species          | Origin处处 | Ref   |
|-----|---------------------|------------------|------------|-------|
| 59  | Tocotrienols        | *C. monilifera*  | Governor Reef, Indented Head, Victoria | [57]  |
| 60  | Tocotrienols        | *C. subfarcinata*| Queenslife, Victoria |       |
|     | *C. platycladum*    | *C. monilifera*  | Governor Reef, Indented Head, Victoria | [55–58]|
|     | *C. siliquosa*      | Sorrento Back Beach, Victoria |       |
|     | *C. retorta*        | Cowaramup Bay, WA |           |
| 61, 62| Tocotrienols      | *C. torulosa*    | Torquay, Victoria | [55]  |
| 63–66| Monoterpenes      | *U. pinnatifida* | Miura Peninsula, Japan | [59]  |
| 67  | Monoterpenes        | *U. pinnatifida* | Miura Peninsula, Japan | [59,68,69]|
|     | *C. piluliformis*   | *C. spongiosus*  | Tipaza, Algerian Mediterranean Coast |       |
| 68, 69| Prenylated Phenols | *S. paradoxum*   | Governor Reef, Indented Head, Victoria | [62,63]|
|     | *S. fallax*         | Governor Reef, Indented Head, Victoria |           |
| 70, 71| Prenylated Phenols| *S. paradoxum*   | Governor Reef, Indented Head, Victoria | [57]  |
| 72  | Prenylated Phenols  | *P. caudata*     | Flinders Reef, Victoria | [66]  |
| 73  | Prenylated Phenols  | *P. caudata*     | Ninepin point, D’Entrecasteaux Channel, Tasmania | [67]  |
| 74  | Prenylated Phenols  | *P. caudata*     | Flinders Reef, Victoria | [66]  |
| 75, 76| Prenylated Phenols | *C. brownii*     | Victor Harbour, SA | [56]  |
| 77  | Prenylated Phenols  | *S. paradoxum*   | Governor Reef, Indented Head, Victoria | [57]  |
| 78, 79| Prenylated Phenols| *C. torulosa*    | Cook Straight, Wellington, New Zealand | [58]  |
| 80  | Prenylated Phenols  | *P. caudata*     | Flinders Reef, Victoria | [66]  |
3.1.4. Meroditerpenoids

As with prenylated phenols, the meroditerpenoids are primarily found in the genus Sargassum with all but compound 81 being natural products of either S. paradoxum or S. fallax. The meroditerpenoids 82–88 and 90, Figure 8, isolated from S. paradoxum all displayed some level of anti-bacterial activity. Compounds 82, 84, 85, 87 and 88 displayed weak anti-bacterial activity against the Gram-positive bacterium S. pyogenes, whilst compound 86 outperformed the standard antibiotic ampicillin against the Gram-negative bacterium P. aeruginosa [57]. S. fallax yielded compounds 86–89 and 91, with compound 87 displaying moderate cytotoxicity towards P388 cancer cells (IC\textsubscript{50}: 17 \muM at 1 mg/mL). In contrast compounds 86 and 91 only had IC\textsubscript{50} values of 32 \muM and \textgtr 27–29 \muM, respectively, when measured under the same conditions. Compound 91 (fallachromenoic acid) is also of chemotaxonomic interest, as this is the first chlorinated meroditerpene isolated from S. fallax [63].

Interestingly, compounds 89–91 appear to all be derivatives of \( \delta \)-tocotrienol with carboxylic acid, aldehyde or halogen functionalities. Compound 81, technically a meromonoterpene, was isolated from the acetone extract of the plant Cystophora torulosa via Sephadex LH-20 size exclusion chromatography. As this is the first meromonoterpenoid isolated from C. torulosa, it was suggested that it be a candidate for assessing phylogenic relationships of the Cystophora genus [58].

3.1.5. Sesquiterpenes and Monoterpenes

Terpenoids that populate this class are both acyclic and cyclic and are identified by terminal ketone or aldehyde functional groups, followed by C-15 or C-20 terpenoid tails. There are multiple varieties of mono- and sesquiterpenes including farnesylacetone epoxides (92–94), cyclic farnesylacetones (102–110), farnesylacetones (95–97, 101), geranylacetones (100) and geranylgeranal epoxides (98, 99) (see Supporting Information Figure S12). All compounds in this class were isolated and characterised from the alga Cystophora moniliformis [58,68,70–72]. Taxonomically, this class of compounds is reported to consist of good indicators of the developmental progress of species within the genus Cystophora [68]. As these compounds are suspected to be derived from the ubiquitous tocotrienols, the higher abundance of them within C. moniliformis provides support to the claim that this alga is the most developed species of Cystophora. Many of these compounds have been shown to have weak or no anti-microbial activity, but an anti-tumor assay of a mixture of (107) and (110) present in a 3:1 ratio, respectively, showed it to possess moderate anti-cancer activity (IC\textsubscript{50}: 45 \muM at 1 mg/mL). Furthermore, this same mixture showed moderate anti-fungal ability via the disc diffusion assay against Trichophyton mentagrophytes [72]. Crude extracts of C. moniliformis have been shown to have quite potent anti-tumor activity against P388 cells, but no single compound has been isolated that appears to account for the high crude extract activity. This supports the idea that the collective effects of monoterpenes and sesquiterpenes are responsible for the anti-tumor activity observed in the crude extract [58,72]. A distribution of the meroditerpene, monoterpene and sesquiterpene compounds that are reported in this review by species and locality is shown in Table 5.
Table 5. Distribution of compounds 81 to 111.

| No. | Compound Type | Species       | Origin                                         | Ref   |
|-----|---------------|---------------|-----------------------------------------------|-------|
| 81  | Meroditerpenoids | *C. torulosa* | Cook Straight, Wellington, New Zealand         | [58]  |
| 82  | Meroditerpenoids | *S. paradoxum*| Governor Reef, Indented Head, Victoria         | [57]  |
| 83  | Meroditerpenoids | *S. paradoxum* | Governor Reef, Indented Head, Victoria         | [57]  |
| 84, 85 | Meroditerpenoids | *S. paradoxum* | Governor Reef, Indented Head, Victoria         | [57,63] |
| 86, 87 | Meroditerpenoids | *S. paradoxum* | Governor Reef, Indented Head, Victoria         | [57,63] |
| 88  | Meroditerpenoids | *S. paradoxum* | Governor Reef, Indented Head, Victoria         | [57]  |
| 89  | Meroditerpenoids | *S. fallax*   | Governor Reef, Indented Head, Victoria         | [63]  |
| 90  | Meroditerpenoids | *S. paradoxum* | Governor Reef, Indented Head, Victoria         | [57]  |
| 91  | Meroditerpenoids | *S. fallax*   | Governor Reef, Indented Head, Victoria         | [63]  |
| 92–94 | Farnesylacetone epoxide | *C. moniliformis* | Sarge Bay, Cape Leeuwin, WA                     | [58]  |
| 95–97 | Farnesylacetone | *C. moniliformis* | Port Phillip Bay, Victoria                     | [72]  |
| 98–100 | Geranylacetone, Geranylgeranal epoxide | *C. moniliformis* | North East side of West Island, SA            | [70]  |
| 101 | Farnesylacetone | *C. moniliformis* | Port Phillip Bay, Victoria                     | [71]  |
| 102, 103 | Cyclic farnesylacetone | *C. moniliformis* | Port Phillip Bay, Victoria                     | [72]  |
| 104, 105 | Cyclic farnesylacetone | *C. moniliformis* | Port Phillip Bay, Victoria                     | [72]  |
| 106, 107 | Cyclic farnesylacetone | *C. moniliformis* | Port Phillip Bay, Victoria                     | [72]  |
| 108 | Cyclic farnesylacetone | *C. moniliformis* | Port Phillip Bay, Victoria                     | [72]  |
| 109 | Cyclic farnesylacetone | *C. moniliformis* | North East side of West Island, SA            | [70]  |
| 110 | Cyclic farnesylacetone | *C. moniliformis* | Port Phillip Bay, Victoria                     | [72]  |
| 111 | Aromadendrene  | *C. moniliformis* | Port Phillip Bay, Victoria                     | [68]  |

3.1.6. Diterpenoids

The diterpenes (C-20) from brown algae have been extensively studied and reviewed, and none more so than the diterpenes derived from algae within the genus *Dictyota* [73]. The *Dictyota* genus is within the family Dictyotaceae and consists of some 221 species. In this instance, only one diterpene was found outside of the species *D. dichotoma*, a dolastane diterpene from the less studied *D. furcellata* (143) [74]. All other diterpenes (112–142, 144–192) (see Supporting Information Figures S13–S15) reported were from the species *D. dichotoma* which has been extensively studied. A recent review of the diterpenes in question suggested a grouping of diterpenes based on biosynthetic origins and also diterpene cyclization complexity [73]. The grouping separates the diterpenes into three groups, Group I (112–134, 136–140), Group II (135, 141–175) and Group III (176–192). Group I diterpenes are all compounds derived from the apparent first cyclization of the pre-cursor geranyl-geraniol between positions C-1 and C-10. Group II involves the same cyclization of geranyl-geraniol pre-cursor but between C-1 and C-11, while Group III involves cyclization between C-2 and C-10. Diterpenes of all three groups are reported to exhibit significant anti-tumor, anti-viral and some anti-fouling activities [73]. A distribution of the diterpene compounds reported in this review by species and locality is shown in Table 6.
Table 6. Distribution of compounds 112 to 192.

| No. | Compound Type | Species | Origin | Ref       |
|-----|---------------|---------|--------|-----------|
| 112 | Diterpene     | D. dichotoma | Northern Adriatic Sea | [73] |
| 113 | Diterpene     | D. dichotoma | Red Sea | [73] |
| 114 | Diterpene     | D. dichotoma | Saronicos Gulf, Greece | [73] |
| 115–117 | Diterpene | D. dichotoma | Tyrrhenian Sea | [73] |
| 118 | Diterpene     | D. dichotoma | Puerto Madryn | [73] |
| 119 | Diterpene     | D. dichotoma | Red Sea | [73] |
| 120 | Diterpene     | D. dichotoma | Northern Adriatic Sea | [73] |
| 121 | Diterpene     | D. dichotoma | Tyrrhenian Sea | [73] |
| 122–124 | Diterpene | D. dichotoma | Red Sea, Egypt | [73] |
| 125 | Diterpene     | D. dichotoma | Troitsa Bay, Russian Far East | [73] |
| 126–128 | Diterpene | D. dichotoma | Red Sea, Egypt | [73] |
| 129 | Diterpene     | D. dichotoma | Japan | [73] |
| 130 | Diterpene     | D. dichotoma | Red Sea, Egypt | [73] |
| 131, 132 | Diterpene | D. dichotoma | Patagonia | [73] |
| 133 | Diterpene     | D. dichotoma | Tyrrhenian Sea | [73] |
| 134 | Diterpene     | D. dichotoma | - | [73] |
| 135 | Diterpene     | D. dichotoma | Acicastello, Italy | [73] |
| 136, 137 | Diterpene | D. dichotoma | Russian Far East | [73] |
| 138, 140 | Diterpene | D. dichotoma | - | [73] |
| 141, 142 | Diterpene | D. dichotoma | Acicastello, Italy | [73] |
| 143 | Diterpene     | D. forcellata | Cape Peron, Shark Bay, WA | [73] |
| 144–151 | Diterpene | D. dichotoma | Indian Ocean | [73] |
| 152–157 | Diterpene | D. dichotoma | Acicastello, Italy | [73] |
| 158–164 | Diterpene | D. dichotoma | Indian Ocean | [73] |
| 165, 166 | Diterpene | D. dichotoma | Red Sea | [73] |
| 167, 168 | Diterpene | D. dichotoma | - | [73] |
| 169, 171 | Diterpene | D. dichotoma | Karachi Coast, Arabian Sea | [73] |
| 172, 173 | Diterpene | D. dichotoma | Red Sea | [73] |
| 174 | Diterpene     | D. dichotoma | Indian Ocean | [73] |
| 175 | Diterpene     | D. dichotoma | - | [73] |
| 176 | Diterpene     | D. dichotoma | Oshoro Bay, Hokkaido, Japan | [73] |
| 177–179 | Diterpene | D. dichotoma | Yagachi, Okinawa, Japan | [73] |
| 180 | Diterpene     | D. dichotoma | - | [73] |
| 181–183 | Diterpene | D. dichotoma | Oshoro Bay, Hokkaido, Japan | [73] |
| 184–186 | Diterpene | D. dichotoma | - | [73] |
| 187 | Diterpene     | D. dichotoma | Yagachi, Okinawa, Japan | [73] |
| 188 | Diterpene     | D. dichotoma | - | [73] |
| 189 | Diterpene     | D. dichotoma | Nagahama Beach, Ehime, Japan | [73] |
| 190, 191 | Diterpene | D. dichotoma | Troitsa Bay, Russian Far East | [73] |
| 192 | Diterpene     | D. dichotoma | - | [73] |

3.2. Steroids/Sterols

Brown algae are responsible for the production of several sterol compounds, but when compared with green algae, there are some differences. Firstly, green algae produce a greater variety of sterolic compounds, and secondly, some structural differences are apparent. Green algal derived sterols appear
to have a higher inclination towards glycosidic moieties along with long lipid esters that branch from the hydroxyl group on ring A of the steroid skeleton \(38, 47, 48\). Steroids derived from the brown algae appear to have no glycosidic attachments but display more diversity in the lipidic chains sprouting from the D ring \(200–202\). Furthermore, the brown algae \(C. brownii\) produces two new sterols \(201, 202\) which was of particular interest, as prior to this there had only been two other occasions where polyoxyxynated sterols had been isolated from brown algae. The steroid fucosterol \(200\) has been found in a number of brown algae \(S. linearfolium, C. sinuosa, D. dichotoma\) and \(C. spongiosum\) \(43,75,76\). This common steroid is of interest as it has been reported to be a potent acetylcholinesterase (AChE) inhibitor for symptomatic treatment of Alzheimer’s disease \(77\). Furthermore, fucosterol \(200\) has been shown to be a potent anti-malarial agent displaying an IC\(_{50}\) value of 7.48 µg/mL \(78\). Other common sterols such as cholesterol \(199\), desmosterol \(196\) and campesterol \(198\) were also found within \(C. sinuosa, Cladostephus spongiosus\) and \(C. brownii\). Also found among the same algae including the prolific \(D. dichotoma\) are the relatively common steroids Brassicasterol \(193\), dehydrocholesterol \(194\), Poriferasterol \(195\) and Clionasterol \(197\). A summary of the isolated steroids/sterols is given in the Supporting Information (Figure S16).

### 3.3. Lipids

Brown algae are known to produce large amounts of straight-chain fatty acids and saturated or polyunsaturated lipids. Lipidic compounds were found to be highly abundant in the brown alga \(C. cephalornithos\), where they were present as saturated fats \(210–214\), unsaturated fats \(215–219\), straight-chain ketones \(203–209, 222\) and diketones \(223\) as well as secondary alcohols \(220, 221\) \(79\) (see Supporting Information Figure S17). A study that yielded the lipids reported herein from the brown alga \(C. cephalornithos\) showed large variance in relative amounts of lipids based on collection site and season. For example, a larger amount of the alkene \(215\) was present when the alga was collected during September from sites around Tasmania (Spring). This was suggested to be due to an increase in alkene production during rapid growth of the alga or potentially due to smaller alkene losses in the Southern hemisphere winter \(79\). The brown alga \(Lobophora variegata\), commonly found in the Canary Islands, was also shown to yield saturated and unsaturated ketones \(225–227\) \(80\). This particular species of algae has been reported to suffer extremely low levels of microbial infection and has also been studied in an ecological perspective with particular interest in its role in absorbing heavy metal ions \(81\). A 2015 study examined the anti-bacterial properties of the compound lobophorone E \(227\) against both Gram-negative and Gram-positive bacteria, but it was shown to be significantly outperformed by the positive control ciprofloxacin \(80\).

#### 3.3.1. Polyenes

The polyenes detailed in this review where distributed in the following algae: \(N. anomala\) \(228–231\) \(82\), \(C. torulosa\) \(228, 231\) \(55\) and \(C. retorta\) \(228, 231\) \(58\) (see Supporting Information Figure S17). It appears that the genus \(Cystophora\) exhibited the more highly unsaturated polyenes, whereas the polyenes \(229\) and \(230\) were only found in the alga \(N. anomala\). Compounds \(228\) and \(231\) were reported to be potent lipoxygenase inhibitors, with this type of inhibition being important in the prevention of psoriasis, asthma, rhinitis and arthritis, with IC\(_{50}\) values of 40 µM and 5.0 µM, respectively \(83\).

#### 3.3.2. Oxy/Epoxy lipids

All Oxylipids and Epoxylipids were found in the brown alga \(N. anomala\) (see Supporting Information Figure S18). Of interest are the Oxylipids \(232\) and \(233\) \(84\), which have been targets of synthetic studies due to their interesting 2, 5-disubstituted-3-oxygenated tetrahydrofuranyl motif \(85\) that appears to be responsible for the biological activity of both compounds. Compounds \(232\) and \(233\) have both shown potent nematocidal activity against the parasitic nematode species \(Trichostrongylus colubriformis\) and \(Haemonchus contortus\) \(84\). A possible biosynthetic pathway to Oxylipids \(232, 233, 246–254\) was suggested via C-18, C-20 and C-22 lipidic pre-cursors, showing a possible link to the
epoxylipid structure also found in *N. anomala* (234–245) [86]. A distribution of the steroids, lipids, polyenes and oxy/epoxy lipids compounds reported in this review by species and locality is shown in Table 7.

Table 7. Distribution of compounds 193 to 254.

| No. | Compound Type | Species | Origin | Ref |
|-----|---------------|---------|--------|-----|
| 193–195 | Steroids/Sterols | *C. sinuosa* | Cap Vert, Dakar | [76] |
| | | *D. dichotoma* | | |
| 196 | Steroids/Sterols | *C. sinuosa* | Cap Vert, Dakar | [43,76] |
| | | *C. spongiosus* | Praia do quebrado, Portugal | |
| | | *D. dichotoma* | | |
| 197 | Steroids/Sterols | *C. sinuosa* | Cap Vert, Dakar | [76] |
| | | *D. dichotoma* | | |
| 198, 199 | Steroids/Sterols | *C. sinuosa* | Cap Vert, Dakar | [42,43,76] |
| | | *C. spongiosus* | Praia do quebrado, Portugal | |
| | | *L. variegata* | St Thomas, Virgin Islands | |
| | | *D. dichotoma* | Cap Vert, Dakar | |
| 200 | Steroids/Sterols | *S. linearfolium* | Bateau Bay, NSW | [43,75,76] |
| | | *C. sinuosa* | Cap Vert, Dakar | |
| | | *D. dichotoma* | Cap Vert, Dakar | |
| | | *C. spongiosus* | Praia do quebrado, Portugal | |
| 201 | Steroids/Sterols | *C. brownii* | Victor Harbour, SA | [56] |
| 202 | Steroids/Sterols | *C. brownii* | Victor Harbour, SA | [56,76] |
| | | *C. sinuosa* | Cap Vert, Dakar | |
| 203–221 | Lipid | *C. cephalornithos* | Southern and South Eastern Tasmania | [79] |
| 222 | Lipid | *C. cephalornithos* | Victorian Coastline | [87] |
| 223 | Lipid | *C. cephalornithos* | Southern and South Eastern Tasmania | [79] |
| 224 | Lipid | *C. cephalornithos* | Victorian Coastline | [87] |
| 225–227 | Lipid | *L. variegata* | Tenerife, Canary Islands | [80] |
| 228 | Polyene | *N. anomala* | Bells Beach, Victoria | [55,58,86] |
| | | *C. torulosa* | Torquay, Victoria | |
| | | *C. retorta* | Cowaramup Bay, WA | |
| 229, 230 | Polyene | *N. anomala* | Bells Beach, Victoria | [86] |
| 231 | Polyene | *N. anomala* | Bells Beach, Victoria | [58,86] |
| | | *C. torulosa* | Cook Straight, Wellington, New Zealand | |
| | | *C. retorta* | Cowaramup Bay, WA | |
| 232, 233 | Oxylipid | *N. anomala* | Bells Beach, Victoria | [84] |
| 234 | Epoxylipid | *N. anomala* | Torquay, Victoria | [82] |
| 235 | Epoxylipid | *N. anomala* | Southern and South Eastern Tasmania | [88] |
| 236–245 | Epoxylipid | *N. anomala* | Bells Beach, Victoria | [86,89] |
| 246–254 | Oxylipid | *N. anomala* | Bells Beach, Victoria | [86,89] |

3.4. Phenols

3.4.1. Phloroglucinols

Phloroglucinols appear to be one of the most widely spread classes of secondary metabolite within the phylum Ochrophyta when considering the 13 species of brown algae that show the presence of phloroglucinols. Although widely spread at the species level, this compound class was
only found among two genera of algae, namely, *Cystophora* and *Zonaria*. It has been stated that the phloroglucinols are of taxonomic importance to *Cystophora* algae providing an alternate means of tracking evolutionary development of species within this genus [58]. However, this method of tracking phylogeny has shown apparent deviations to the current theory of species evolution within this genus [90]. The species *C. subfarcinata* (255, 256, 259–262, 265, 269–271), *C. monilifera* (255, 259, 261, 262, 265, 266, 269, 270, 272), *C. retroflexa* (255, 262, 263, 265, 269–271) and *Z. spiralis* (257, 258, 264, 273–275) (see Supporting Information Figure S19) represent the brown algae that have produced the greatest number of phloroglucinol compounds [57,58,91,92]. An interesting trend appears within the species *Z. spiralis*, where it is observed that rather than yielding primarily monocyclic phloroglucinols, as in the genus *Cystophora*, *Z. spiralis* appears to mainly produce bicyclic derivatives expressed as hemiketals and chromones [94]. Other members of the *Zonaria* genus, including *Z. turneri*ana, *Z. crenata* and *Z. angustata* which also show monocyclic phloroglucinols as the major secondary metabolites [94]. Hemiketals and chromones (273–275) from *Z. spiralis* have shown inhibitory activity against prominent neurodegenerative disease kinase targets and also anti-bacterial activity (257, 258, 273, 275) against *B. subtilis*, with all compounds having IC₅₀ values between 2.5 and 10.0 µM [93]. Other monocyclic phloroglucinols from *C. subfarcinata* (252 and 267) and *C. monilifera* (255, 262, 266 and 270) have displayed weak anti-bacterial activity against the Gram-positive bacteria *Streptococcus pyogenes*, only showing minimal inhibition zones when tested using the disc diffusion assay at 1 mg/mL. Compound 256 showed equal activity against Gram-positive and Gram-negative bacteria, *S. aureus* and *P. aeruginosa*, respectively, but once again, all compounds from *C. monilifera* were substantially outperformed by the standard antibiotic ampicillin [57]. Compounds 265 and 268 both found within *Cystophora* and *Zonaria* have each shown moderate anti-bacterial activity against *S. aureus* and *B. subtilis* [95].

3.4.2. Phenols/Phenolic acids/Resorcinols

Phenolic compounds are found throughout brown algae, primarily in the form of a phenolic, phenolic acid or a benzopyranone head group attached to a lipidic tail. These types of phenols have been found across four genera including the prolific *Cystophora* and *Sargassum* as well as *Caulocystis, Colpomenia* and *Lobophora*. The benzopyranones (276, 277) were found in this instance only within the species *C. cephalornithos*. These particular compounds, found also in the plant *Ginkgo biloba* L., have been shown to be biological derivatives of ginkgolic acids, which are themselves a form of the anti-inflammatory agent salicylic acid [96]. In contrast to salicylic acid, these compounds, in the form of ginkgolic acid or benzopyranone, are responsible for allergic contact dermatitis (ACD) [96]. *C. cephalornithos* also yielded several resorcinols (285 and 286), phenolic acids (278–282), phenols (283 and 284) and dihydroxy phenolic acids (288, 289). Compounds similar to 285–287 and 290, 291 have been studied previously for their anti-cancer properties. In particular they have been found to have strong activity against human colon cancer cells (HCT-116 and HT-29) [97]. The resorcinol 286 was shown to have the highest cytotoxicity with IC₅₀ values of 31.45, 35.27 and 24.28 µg/mL against SMMC7721, K562 and HeLa, respectively [98]. This class of lipidic resorcinol has also been shown to exhibit various anti-tuberculosis activities [99]. Polar extracts of the alga *C. peregrina* yielded a number of common low molecular weight aromatic acids such as compounds 292–295. These low molecular weight compounds were identified on the basis of GC–MS experiments [100]. Compounds 296 and 297, isolated from the brown alga *L. variegata*, were shown to exhibit small to moderate inhibition against the Gram-positive bacteria *S. aureus* [80]. A summary of the phenols/phenolic acids/resorcinols is given in the Supporting Information (Figure S20). A distribution of the phloroglucinols, benzopyranones, phenolic acids, phenols and resorcinol compounds reported in this review by species and locality is shown in Table 8.
Table 8. Distribution of compounds 255 to 297.

| No. | Compound Type | Species | Origin | Ref |
|-----|---------------|---------|--------|-----|
| 255 | Phloroglucinol | C. subfarcinata | Queenscliff, Victoria | [57,58,91] |
|     |               | C. monilifera | Governor Reef, Indented Head, Victoria | |
|     |               | C. retroflexa | Governor Reef, Indented Head, Victoria | |
|     |               | C. retorta | Cowaramup Bay, WA | |
| 256 | Phloroglucinol | C. torulosa | Torquay, Victoria | [55,57,58] |
|     |               | C. subfarcinata | Queenscliff, Victoria | |
|     |               | C. elliptica | Sorrento Back Beach | |
|     |               | C. monilifera | Cowaramup Bay, WA | |
| 257, 258 | Phloroglucinol | Z. spiralis | North Walkerville, Victoria | [93] |
| 259 | Phloroglucinol | C. subfarcinata | Governor Reef, Indented Head, Victoria | [57] |
|     |               | C. monilifera | Governor Reef, Indented Head, Victoria | |
| 260 | Phloroglucinol | C. subfarcinata | Queenscliff, Victoria | [57] |
| 261 | Phloroglucinol | C. subfarcinata | North Eastern West Island, SA | |
| 262 | Phloroglucinol | C. retroflexa | Governor Reef, Indented Head, Victoria | [57,91] |
|     |               | C. monilifera | Governor Reef, Indented Head, Victoria | |
| 263 | Phloroglucinol | C. retroflexa | Governor Reef, Indented Head, Victoria | [91] |
| 264 | Phloroglucinol | Z. spiralis | North Walkerville, Victoria | [93] |
| 265 | Phloroglucinol | C. subfarcinata | Governor Reef, Indented Head, Victoria | [57,91] |
|     |               | C. monilifera | Governor Reef, Indented Head, Victoria | |
|     |               | C. retroflexa | Governor Reef, Indented Head, Victoria | |
| 266 | Phloroglucinol | C. monilifera | Governor Reef, Indented Head, Victoria | [57] |
| 267, 268 | Phloroglucinol | Z. turneriana | Tinderbox, Tasmania | [94] |
|     |               | Z. crenata | Tinderbox, Tasmania | |
|     |               | Z. angustata | Sisters Beach, Tasmania | |
| 269, 270 | Phloroglucinol | C. subfarcinata | Queenscliff, Victoria | [57,91] |
|     |               | C. monilifera | Governor Reef, Indented Head, Victoria | |
|     |               | C. retroflexa | Governor Reef, Indented Head, Victoria | |
| 271 | Phloroglucinol | C. subfarcinata | Queenscliff, Victoria | [57,91] |
|     |               | C. monilifera | Governor Reef, Indented Head, Victoria | |
|     |               | C. retroflexa | Governor Reef, Indented Head, Victoria | |
| 272 | Phloroglucinol | C. monilifera | Governor Reef, Indented Head, Victoria | [57] |
| 273–275 | Phloroglucinol | Z. spiralis | North Walkerville, Victoria | [93] |
| 276, 277 | Benzopyranones | C. cephalornithos | Southern and South Eastern Tasmania | [79] |
| 278 | Phenolic Acid | C. cephalornithos | Southern and South Eastern Tasmania | [79,91] |
|     |               | S. decipiens | Governor Reef, Indented Head, Victoria | |
| 279 | Phenolic Acid | C. cephalornithos | Southern and South Eastern Tasmania | [79] |
| 280 | Phenolic Acid | C. cephalornithos | Southern and South Eastern Tasmania | [79,91] |
|     |               | S. decipiens | Governor Reef, Indented Head, Victoria | |
| 281, 282 | Phenolic Acid | C. cephalornithos | Southern and South Eastern Tasmania | [79] |
| 283 | Phenol | C. cephalornithos | Southern and South Eastern Tasmania | [79,91] |
|     |               | S. decipiens | Governor Reef, Indented Head, Victoria | |
| 284 | Phenol | C. cephalornithos | Southern and South Eastern Tasmania | [79] |
| 285 | Resorcinol | C. cephalornithos | Southern and South Eastern Tasmania | [79,91] |
|     |               | S. decipiens | Governor Reef, Indented Head, Victoria | |
| 286 | Resorcinol | C. cephalornithos | Southern and South Eastern Tasmania | [55,79] |
|     |               | C. torulosa | Torquay, Victoria | [55] |
| 287 | Resorcinol | C. torulosa | Torquay, Victoria | [55] |
| 288, 289 | Phenolic Acid | C. cephalornithos | Southern and South Eastern Tasmania | [79] |
| 290 | Resorcinol | C. torulosa | Cook Straight, Wellington, New Zealand | [58] |
| 291 | Resorcinol | C. torulosa | Torquay, Victoria | [55] |
| 292–295 | Phenolic Acid | C. peregrina | Bulgarian Coast | [100] |
| 296, 297 | Phenolic Acid | L. variegata | Tenerife, Canary Islands | [80] |

3.5. Miscellaneous

Several other secondary metabolite classes have been isolated and characterized from the brown algae considered in this review. Classes include 1-deoxysphingoid bases, pheromones, bromophenolics and xanthophylls. The 1-deoxysphingoid base 298 (3-epi-xestoaminol C) was isolated from the brown
algae *Xiphophora chondrophylla* and was the first 1-deoxysphingoid that had been isolated from brown algae [101]. Compound 298 had its absolute configuration determined using the Mosher method and was subsequently reported to have quite remarkable multifaceted bioactivity [101]. Initial studies demonstrated antitubercular activity with an IC₅₀ value of 19.4 µM with inhibition against *Myobacterium tuberculosis* (H37Ra). This was followed by confirmation of growth inhibition against both *S. aureus* and *S. cerevisiae* with IC₅₀ values 17.0 µM and 17.1 µM, respectively. 3-epi-xestoaminol C showed great promise when assayed against human leukemia cells (HL-60) achieving an IC₅₀ of 8.8 µM, which was followed by an IC₅₀ of 18.0 µM when assayed against human embryonic kidney cells (HEK) [101].

Brown algae have long been known to possess a variety of pheromone compounds with a number of functions contributing to the reproductive cycle, which have been studied extensively across a number of species. A study on the species *Dictyopteris acrostichoides* showed the largest number of C-11 pheromones (299–305, 313, 316 and 317). These compounds were isolated from extracts of female gametes of *D. acrostichoides* [102]. Many of these compounds are produced by the organism with the primary function of attracting male gametes to complete sexual reproduction, but some have also been shown to function as effective anti-predation agents, or may even be used to interfere with other pheromone communication systems of competing alga [103,104]. Many species of brown algae reported herein, including *X. chondrophylla*, *Scytosphilon lomentaria* and *Hormosira banksii*, have been found to produce the sexual pheromone hormosirene (309), suggesting that this is a particularly important pheromone for the phylum Ochrophyta [103,105]. The brown alga *C. peregrina* has been found to exhibit the pheromone (304), which has long been suspected as a sperm attractant for this and many other species [106]. A mixture of miscellaneous pheromone compounds has also been found distributed across seven species of brown algae including *D. acrostichoides* (306, 313), *X. chondrophylla* (307), *S. lomentaria* (307), *H. banksii* (308), *P. caudata* (310–312), *C. spongiosus* (313, 315), *Macrocystis pyrifera* (314) and *U. pinnatifida* (314).

The simple low molecular weight brom phenolic compounds 318–322 were found to be present in varying amounts in many Australian algae including *C. spongiosus*, *C. sinuosa*, *E. radiata*, *Homoeostrichus sinclairii*, *H. banksii* and *Phyllospora comosa*, and this was confirmed by a bromophenolic distribution study of many brown, red and green algae [54]. Interestingly, a rare bromophenolic of the C-6 C-4 C-6 arrangement was isolated from the brown alga *Colpomenia sinuosa* (323) via a bio-activity directed isolation. This metabolite was found to be responsible for the cytotoxicity that the crude extracts of this alga displayed [107].

Xanthophyll compounds such as fucoxanthin (329) have been found consistently throughout brown algae and have been the topic of a number of review articles due to their potential anti-cancer/anti-tumor applications [108,109]. Fucoxanthin has been found in a number of brown algae species (*U. pinnatifida*, *S. lomentaria*, *C. spongiosus*, *Halopteris pseudospicata*, *Sargassum vestitum*) and has, among some studies, largely contributed to the anti-cancer activity of crude extracts [109]. Due to the significant activity and interest in fucoxanthin (329), some work has been undertaken to explore the metabolism of this compound when consumed via edible brown algal species such as *U. pinnatifida*. The compounds fucoxanthinol (328) and amarouci xanthan the A (327) are the natural metabolites of fucoxanthin (329) and are thought to play a key role in the anti-cancer activity that has been associated with diets high in fucoxanthin containing algae [108,110]. A number of studies have also described the isolation of apo-carotenoids from the brown algae *S. lomentaria* (324–326), *C. spongiosus* (325, 326) and *Z. spiralis* (326). These apo-carotenoids are known to be oxidized derivatives of fucoxanthin (329) and appear to display some feeding deterrent activity (325, 326) [69,93,111].

Non-polar extracts of the brown alga *A. paniculata* were found to be a rich source of the furanic esters 330 and 331. These compounds are closely related to the furan fatty acids obtained from the sap of the rubber tree *Hevea brasiliensis* that plays a major role in the fabrication of latex [112]. The common low molecular weight compounds picolinic acid (332) and trimethylamine (333) were identified in trace quantities in the brown alga *C. peregrina* through use of GC–MS [100].
An interesting polyketide macrolide was isolated from the brown alga *L. variegata*, with the compound lobophorolide (334) being isolated as $1.2 \times 10^{-4}$% of the algal dry mass. Lobophorolide was assayed for both its anti-fungal and anti-tumor properties and found to exhibit good potency in both assays [113]. Although this study noted that due to the shared structural motifs of lobophorolide (334) with that of bacterial natural products, it was possible that this compound was derived from a symbiont of *L. variegata* which was further substantiated by the relatively low isolation yield of the natural product. In a 2015 study, several polyketides (335–339) were isolated from *L. variegata* of which only 335 displayed any notable biological activity. When assayed against *S. aureus*, compound 335 displayed significant growth inhibition, but was relatively ineffective against both *E. coli* and *E. faecalis* [80].

A summary of the miscellaneous compounds isolated from brown algae is given in the Supporting Information (Figure S21). A distribution of the miscellaneous compounds reported in this review by species and locality is shown in Table 9. A summary of the biological activities for compounds isolated from brown algae is given in the Supporting Information (Figure S22).

| No. | Compound Type | Species | Origin | Ref |
|-----|---------------|---------|--------|-----|
| 298 | Xestoaminol   | X. chondrophylla | Hen and Chicken Islands, New Zealand | [101] |
| 299–303 | Pheromone | D. acrostichoides | Point Lonsdale and Sorrento, Victoria | [102] |
| 304, 305 | Pheromone | D. acrostichoides | Point Lonsdale and Sorrento, Victoria | [102] |
| 306 | Pheromone | D. acrostichoides | Point Lonsdale and Sorrento, Victoria | [102] |
| 307 | Pheromone | X. chondrophylla | Point Lonsdale and Sorrento, Victoria | [108] |
| 308 | Pheromone | H. banksii | Flinders Reef, Victoria | [103] |
| 309 | Pheromone | X. chondrophylla | Point Lonsdale and Sorrento, Victoria | [108] |
| 310–312 | Pheromone | P. casdata | - | [114] |
| 313 | Pheromone | C. spongiosus | Point Lonsdale and Sorrento, Victoria | [102,115] |
| 314 | Pheromone | M. purpurea | Point Lonsdale and Sorrento, Victoria | [108] |
| 315 | Pheromone | C. spongiosus | Flinders Reef, Victoria | [115] |
| 316, 317 | Pheromone | D. acrostichoides | Point Lonsdale and Sorrento, Victoria | [102] |
| 318–322 | Bromophenolic | C. spongiosus | Bateau Bay, NSW | - |
| 323 | Bromophenolic | C. spongiosus | Bateau Bay, NSW | [54] |
| 324 | Xanthophyll | S. lomentaria | Aikappu, Akkeshi, Hokkaido | [111] |
| 325 | Xanthophyll | S. spongiosa | Aikappu, Akkeshi, Hokkaido | [69,111] |
| 326 | Xanthophyll | S. spongiosa | Aikappu, Akkeshi, Hokkaido | [69,93,111] |
| 327, 328 | Xanthophyll | U. pinnatifida | North Walkerville, Victoria | [108] |
| 329 | Xanthophyll | U. pinnatifida | Aikappu, Akkeshi, Hokkaido | [69,91,108,111] |
| 330, 331 | Furans | A. paniculata | Port MacDonnell | [116] |
| 332 | Pyridine | C. peregrina | Bulgarian Coast | [100] |
| 333 | Amine | C. peregrina | Bulgarian Coast | [100] |
| 334 | Polyketide Macrolide | L. variegata | Cay Lobos, Bahamas | [113] |
| 335–339 | Polyketides | L. variegata | Tenerife, Canary Islands | [80] |
4. Rhodophyta (Red Algae) of Port Phillip Bay

The red algae of Port Phillip Bay are the least studied phylum of algae, but appear to display the most diverse chemistry, much of which has been reported to display significant biological activity. In particular, the genera Laurencia and Plocamium have been the source of many of the natural products. The red algae of Port Phillip Bay appear to display a number of terpenoid like compounds, but unlike brown or green algae, many of the red algae contain highly halogenated terpenoids. This appears to set them apart in terms of both structural diversity and biological activity. This review documents 163 natural products that have been derived from 22 species of red algae.

4.1. Terpenoids

4.1.1. Halogenated Monoterpenes

The halogenated monoterpenes of the phylum Rhodophyta have been found distributed across the species Plocamium angustum (348–353), Plocamium mertensii (340–347), Plocamium costatum (351, 354–364) and Plocamium leptophyllum (365). P. mertensii was first reported to contain halogenated monoterpenes in a 1977 study where compound 346 was reported to be a major metabolite of this species [117]. This class of secondary metabolite has been notoriously difficult to secure the correct structures for, primarily due to the high number of halogenated substituents. As a result, a number of previously identified secondary metabolites have had structure re-assignments, many of which were reported in a study of P. mertensii [118]. The natural product originally assigned structure 346 was subsequently corrected to 340 (mertensene), using both on-line and off-line methodologies to achieve unequivocal structure characterization. This compound, together with compound 341, has previously shown insecticidal and growth inhibition against some insect species [119]. Compounds 340–342 were all shown to be effective antifeedant agents against a range of pest insect species, all of which displayed some toxicity towards at least one species of insect [120]. Compound 342 showed moderate antitubercular activity and cytotoxicity as well as high potency anti-algal activity toward the alga Chlorella fusca [121]. It should also be noted that 3:1 methanol:dichloromethane crude extracts of the red alga P. mertensii displayed anti-tumor, anti-viral and anti-fungal activities [118]. In a more recent study of the red alga P. angustum, the compounds plocamenone (352) and isoplocamenone (353) were isolated and characterized. Plocamenone was subsequently tested for cytotoxicity against P388 tumour cells showing promising IC$_{50}$ values of 157.5 ng/mL and >97.5 ng/mL when derived from two separate samples. This same study assayed a mixture of plocamenone and isoplocamenone which achieved an IC$_{50}$ value of >97.5 ng/mL, but isoplocamenone was unable to be assayed individually due to its instability [122]. The alga P. costatum was revisited and studied using HPLC–UV–MS–SPE–NMR analysis yielding, among others, the natural products 357, 358, 361–364. All compounds from this study underwent anti-microbial screening against C. albicans, M. smegmatis, S. aureus and E. coli, but were all found to be inactive [125]. The compound aplysiaterpenoid A (365) was isolated from the red alga P. leptophyllum in a bioassay guided fractionation using antifeedant activity as the guiding factor in isolation. In this situation aplysiaterpenoid A (365) demonstrated potent antifeedant activity against a number of gastropods and other herbivores, achieving complete inhibition with only 40 µg of compound. Inhibited herbivorous species included the gastropods; Omphalius pfeifferi and Turbo cornutus, the abalone Haliotis discus and the sea urchin Strongylocentrotus intermedius [126]. A summary of the halogenated monoterpenes isolated from red algae is given in Supporting Information (Figure S23).
4.1.2. Parguerenes

Investigations of the parguerenes as secondary metabolites have revealed the presence of at least two substructure classes; deoxyparguerenes (366–371) and parguerenes (372, 373) together with the isolation of a potential biosynthetic intermediate to the parguerenes (374) [127,128]. All compounds reported herein have been isolated from the red alga Laurencia filiformis, but this compound class has also been found in the sea hare Aplysia dactylomela. The parguerenes have been reported to have highly cytotoxic properties, and as a class have been studied on a structure activity basis. Studies such as these have shown that the cytotoxicity of parguerene compounds is dependent upon the presence of acetoxy groups at the C-2 position and bromine at the C-15 position. This is evident in the high growth inhibition activity of 367 against P388 and HeLa cell types, achieving IC\textsubscript{50} values of 8.5 and 6.3 µg/mL, respectively [129]. In a separate study, this compound was also shown to act as a potent feeding deterrent against the abalone Haliotis discus hannai and the young sea urchins Strongylocentrotus nudus and Strongylocentrotus intermedius [130]. Compound 366, which contains the C-2 acetoxy and C-15 bromine motif, also showed moderate cytotoxicity towards Ehrlich carcinoma. More impressive though, was this compound’s ability to act as an anthelmintic agent, taking only 30 mins at a concentration of 10% w/v to achieve paralysis of the worm species Allolobophora caliginosa, whereas the standard drug mebendazole takes 4 hours to achieve the same result [131]. Furthermore, both compounds 366 and 367 have been studied for their ability to act as P-glycoprotein inhibitors, indicating potentially significant applications in chemotherapeutic treatment, specifically against multidrug resistant cancers [128]. A summary of the parguerenes isolated from red algae is given in Supporting Information (Figure S23).

4.1.3. Chamigrenes

Algae of the genus Laurencia have been known to produce chamigrene-type compounds since the 1970s [132]. The two species that have been shown to produce a number of these chamigrene-type compounds are Laurencia filiformis (377, 379–385) and Laurencia elata (375–378, 381) (see Supporting Information Figure S24). The chamigrenes differ from other red algae derived terpenoids as they are both polyhalogenated and contain spiro centres, providing a challenge for structure elucidation, as was the case for pacifenol (377) [133]. Chamigrenes, as a class of compounds, have been reported to express anthelmintic behavior and some cytotoxic properties have also been demonstrated [134,135]. By far the most studied chamigrenes appear to be elatol (378) and pacifenol (377). Elatol exhibits a chloro vinyl moiety and is the major constituent of the red alga L. elata (now reclassified as Corynecladia elata see Supporting Information Table S1) [132]. This compound exhibits potent cytotoxicity against HeLa and Hep-2 cells (IC\textsubscript{50} 1.3 µM and 2.0 µM, respectively) [134]. Elatol also appeared to have moderate to high antibiofouling properties inhibiting the seaweed pathogens Alteromonas sp1., Alteromonas sp2., Proteus mirabilis, Proteus sp., Cytophaga-Flavobacterium, Vibrio sp. and also showing mild inhibition towards the human pathogen S. aureus [136]. An interesting 2017 study also indicated that elatol (378) appears to play a large role in the predation of red algae of the genus Laurencia by the sea hares Aplysia with theories that this compound appears to be a useful foraging cue for Aplysia [137]. Compounds 379, 380 and 381 have shown moderate activity in the brine shrimp (Artemia salina) bioassay, but the strongest activity was observed for pacifenol (377) where 90% mortality was observed at a concentration of 23 µg/mL after 24 h [138]. A distribution of the Halogenated monoterpenes, parguerenes and chamigrene compounds reported in this review by species and locality is shown in Table 10.
Table 10. Distribution of compounds 340 to 385.

| No.  | Compound Type          | Species     | Origin                          | Ref          |
|------|------------------------|-------------|---------------------------------|--------------|
| 340–342 | Halogenated Monoterpene | *P. mertensii* | Queenscliffe, Victoria          | [118]        |
| 343   | Halogenated Monoterpene | *P. mertensii* | Carnac Island, WA               | [139]        |
| 344, 345 | Halogenated Monoterpene | *P. mertensii* | Queenscliffe, Victoria          | [118]        |
| 346   | Halogenated Monoterpene | *P. mertensii* | -                               | [117]        |
| 347   | Halogenated Monoterpene | *P. mertensii* | Queenscliffe, Victoria          | [118]        |
| 348   | Halogenated Monoterpene | *P. angustum* | Cape Northumberland, SA         | [140]        |
| 349, 350 | Halogenated Monoterpene | *P. angustum* | Rocky Point, Torquay, Victoria  | [141]        |
| 351   | Halogenated Monoterpene | *P. angustum* | Queenscliffe, Victoria          | [122,123]    |
| 352, 353 | Halogenated Monoterpene | *P. angustum* | Queenscliffe, Victoria          | [122]        |
| 354   | Halogenated Monoterpene | *P. costatum* | Robe, South Australia          | [123]        |
| 355   | Halogenated Monoterpene | *P. costatum* | Port MacDonnell, South Australia| [124]        |
| 356   | Halogenated Monoterpene | *P. costatum* | Deep Glen Bay, Tasmania         | [142]        |
| 357   | Halogenated Monoterpene | *P. costatum* | Pandalowie Bay, South Australia | [125]        |
| 358   | Halogenated Monoterpene | *P. costatum* | Pandalowie Bay, South Australia | [125]        |
| 359, 360 | Halogenated Monoterpene | *P. costatum* | Deep Glen Bay, Tasmania         | [142]        |
| 361–364 | Halogenated Monoterpene | *P. costatum* | Pandalowie Bay, South Australia | [125]        |
| 365   | Halogenated Monoterpene | *P. leptophyllum* | Toyama Bay, Japan               | [126]        |
| 366–374 | Parguerene          | *L. filiformis* | South Australia                  | [127,128]    |
| 375, 376 | Chamigrene          | *L. elata*  | St. Pauls Beach, Sorrento, Victoria | [133]        |
| 377   | Chamigrene           | *L. filiformis* | Taroona Beach, Hobart, Tasmania | [133,138]    |
| 378   | Chamigrene           | *L. elata*  | St. Pauls Beach, Sorrento, Victoria | [133,138]    |
| 379, 380 | Chamigrene          | *L. filiformis* | Taroona Beach, Hobart, Tasmania | [138]        |
| 381   | Chamigrene           | *L. filiformis* | New South Wales Coast            | [132,138]    |
| 382–385 | Chamigrene          | *L. filiformis* | Stella Maris Beach, Salvador, Brazil | [143]        |

4.1.4. Laurenes

Laurene (389) and its structurally related derivatives (see Supporting Information Figure S25) are known to be prevalent throughout the genus *Laurencia*. These compounds are also thought to be the source of sesquiterpenes found within the sea hares of the genus *Aplysia* as they are frequently grazing on *Laurencia* algae [144]. All laurennes reported herein have been derived from the red alga
was further studied using the crystalline sponge methodology in 2016 as the absolute configuration of Elatenyne (157). Synthetic approaches to producing elatenyne were also investigated and yielded a pair of diastereomers of elatenyne (159). In another study of the same compound Gage-Including Atomic Orbital (GIAO) modelling calculations were used on 13C NMR spectra in an attempt to solve the relative stereochemistry of this compound but was only able to narrow down the relative stereochemistry to a small number of diastereoisomers (157). Elatenyne was further studied using the crystalline sponge methodology in 2016 as the absolute configuration of Elatenyne (157). Synthetic approaches to producing elatenyne were also investigated and yielded a pair of diastereomers of elatenyne (159).

4.1.6. Lauroxocanes (C15 acetogenins)

In the context of Port Phillip Bay marine algae, lauroxocane compounds have been found in the red algae Laurencia (386–397) and are all variations of compound 389 (laurene) which is found throughout this genus. Biosynthesis of these compounds has been postulated and discussed (145). Compounds 386, 390, 393 and 397 showed cytotoxicity toward P388 cancer cells with IC50 values ranging from >34–43 µM when tested at a concentration of 1 mg/mL, although it should be noted that compounds 390 and 397 were unstable and degraded during the course of the assays (146). Compounds 387 and 390 were assayed for their anti-cancer activity and whilst compound 390 exhibited strong cytotoxicity against the cancer cell line NSCLC-N6 (IC50 26.5 µM), compound 387 was found to possess only weak cytotoxicity (147). It was also found that compound 386 appeared to have significant anti-bacterial activity against methicillin-resistant Staphylococcus aureus (2 × MIC of 6.25 µg/mL) and moderate activity against vancomycin (VCM)-susceptible Enterococcus faecium (148). In a separate study, this particular compound exhibited inhibition of Mycobacterium tuberculosis (149).

All sesquiterpenes were isolated from the genus Laurencia, Figure 9. Heterocladol (400), isolated from Laurencia filiformis collected in both South Australia (145) and Victoria (146), first had its absolute configuration determined in 1977 via crystallographic methods (145). This was followed by the discovery of australad acetate (398) and australadiacetate (399) in a separate study in 1982, thereby cementing eudesmane sesquiterpenes as a prominent secondary metabolite of Laurencia filiformis (150). The compound alysistatin (401) was isolated from Laurencia filiformis in 1981, along with hydroxyaplysistatin (402) (151).

Alysistatin (401) was subjected to a biological activity assessment in subsequent studies and displayed anti-malarial, anti-inflammatory and selective enzymatic suppression activities, the results of which were summarized in recent reviews (152–154). As a result of both the interesting biological activity of alysistatin and also its relatively unique oxepane ring system, it has been extensively studied in order to achieve a stereo selective synthesis (155). The compound elatenyne was first isolated and characterized from the non-polar extracts of the red alga Laurencia elata (156), and initially assigned the structure 403 (156), but was re-assigned the structure 404 in a later study (133). In another study of the same compound Gage-Including Atomic Orbital (GIAO) modelling calculations were used on 13C NMR spectra in an attempt to solve the relative stereochemistry of this compound but was only able to narrow down the relative stereochemistry to a small number of diastereoisomers (157). Elatenyne was further studied using the crystalline sponge methodology in 2016 as the absolute configuration of 404 still remained unknown, and this method provided the unequivocal absolute configuration of Elatenyne (404) (158). Synthetic approaches to producing elatenyne were also investigated and yielded a pair of diastereomers of elatenyne (159).

4.1.5. Sesquiterpenes

Figure 9. Chemical structure of sesquiterpenes 398–404.
408, have been isolated from Laurencia obtusa and have been shown to have insecticidal activity against the ant species Pheidole pallidula [161]. The lauroxocane 408 was tested for anti-cancer activity and showed no appreciable activity [133], which was in accordance with many of the other lauroxocanes that have been found to have poor cytotoxicity [162]. The compound cis-dihydrorhodophytin (405) along with other lauroxocanes isolated from the sea hare Aplysia brasiliana displayed antifeedant activity. This compound was applied to small beetle larvae and offered to swordtail fish (Xiphophorus helleri) along with controls and it was observed that the beetle larvae with 405 applied were usually outright rejected by the fish, whereas the controls were consumed without hesitation [163]. A distribution of the lauren, sesquiterpenes and lauroxocane compounds reported in this review by species and locality is shown in Table 11.

![Figure 10. Chemical structure of lauroxocanes 405-408.](image)

Table 11. Distribution of compounds 386 to 408.

| No. | Compound Type | Species | Origin | Ref |
|-----|---------------|---------|--------|-----|
| 386 | Laurene       | L. filiformis | Hamelin Bay, Perth, WA Shoalwater Bay, Perth, WA Cottesloe Beach, Perth, WA Lancelin, Perth, WA | [164] |
| 387, 388 | Laurene | L. filiformis | Shoalwater Bay, Perth, WA Cottesloe Beach, Perth, WA | [164] |
| 389 | Laurene       | L. filiformis | South Australian Coast | [144] |
| 390 | Laurene       | L. filiformis | St. Pauls Beach, Sorrento, Victoria | [146] |
| 391 | Laurene       | L. filiformis | Shoalwater Bay, Perth, WA | [164] |
| 392 | Laurene       | L. filiformis | Port MacDonnell Beach, South Australia | [145] |
| 393, 394 | Laurene | L. filiformis | Shoalwater Bay, Perth, WA | [164] |
| 395, 396 | Laurene | L. filiformis | St. Pauls Beach, Sorrento, Australia | [146] |
| 397 | Laurene       | L. filiformis | Port MacDonnell Beach, South Australia | [145] |
| 398, 399 | Sesquiterpenoids | L. filiformis | Western Australia, South Australia | [127,150] |
| 400 | Sesquiterpenoids | L. filiformis | Port MacDonnell Beach, South Australia St. Pauls Beach, Sorrento, Australia | [145,146] |
| 401, 402 | Sesquiterpenoids | L. filiformis | Port Peron, WA | [151] |
| 403, 404 | Sesquiterpenoids | L. elata | Batemans Bay, New South Wales St. Pauls Beach, Sorrento, Australia | [133] |
| 405, 406 | Lauroxocane | L. filiformis | Western Australia | [150] |
| 407, 408 | Lauroxocane | L. filiformis | St. Pauls Beach, Sorrento, Australia | [133] |

4.1.7. Polyhalogenated Indoles

All polyhalogenated indole compounds (see Supporting Information Figure S28) reported in this review were isolated from Rhodophyllis membranacea (409–424), a red alga sampled from Moa Point [165] and also Seal Reef [166], New Zealand. Isolation of the bromochloroiodoindoles 410–412 and 417 is of note, as they contain three types of halogen which is observed very rarely in marine natural products derived from algae. Compounds 409, 413, 415, 410, 421 and 424 were assayed against the HL-60 cell
line and were found to have anti-cancer activity displaying IC₅₀ values of 38, 78, 61, 49, 28 and 61 µM, respectively. It was determined, via re-extraction, that compound 422 was isolated as an artefact of compound 424. This artefact is believed to have occurred through aldol condensation of the keto moiety of 424 with acetone that was used during purification. This was verified after a re-extraction of R. membranacea was performed in the absence of acetone. Compounds 409, 413, 415, 410, 421 and 424 were all found to have anti-fungal activity, compound 421 showed activity (IC₅₀ 23 µM) comparable to the standard cycloheximide.

4.1.8. Polyhalogenated Hydrocarbons

This class of secondary metabolites has been reported to be particularly difficult to characterize due to the number of substituted heteroatoms. A large amount of substituted bromines, non-aromatic double bonds, hydroxyl groups and acetoxy functionalities make this class of compound distinct, but also challenging to determine in terms of absolute structures. These compounds have been reported in only two species within this review, Ptilonia australasica (425–430, 432, 433) [167,168] and Delisea pulchra (427, 431, 434) [169,170] (see Supporting Information Figure S29). Most compounds reported here were studied for their anti-microbial properties. Compound 427 only displayed moderate to low activity against Gram-positive bacteria (M. luteus) inhibiting at 5 µg. Similarly, compounds 431 and 434 also showed low to moderate activity against the Gram-positive Bacteria M. luteus but was also able to inhibit the growth of Gram-negative bacteria (E. coli). All three compounds displayed moderate anti-fungal properties against the fungus Puccinia oxalis [171]. Interestingly, compound 431 also showed the ability to moderately inhibit the enzyme tyrosine kinase with a % Residual Enzyme Activity (REA) of 31.7% being achieved at a concentration of 200 µg/mL [171]. Compound 425 isolated from the alga P. australasica was assayed against PC3 cells where it demonstrated some promising anti-cancer activity achieving an IC₅₀ value of 0.44 µM. This compared favorably to the positive control, doxorubicin, which was reported to have an IC₅₀ value of 0.360 µM [168].

4.1.9. Halogenated Furanones

The red alga Delisea pulchra (435–466) has been a prolific source of halogenated furanones and this species produces large amounts of this class of secondary metabolite. D. pulchra has been sampled from the New South Wales Coast and as far south as Palmer station on the Antarctic Coast [171,172]. Samples of D. pulchra were found to contain large amounts of halogenated furanone compounds when sampled from both locations. The furanones isolated vary in structure primarily by locality and the type of halogen substitutions present. Regarding sampling locality, algae sampled from the Antarctic coast (Palmer station) appear to exhibit different halogenated furanones to those sampled from the east coast of Australia. For example, the novel compounds known as the pulchralides A–C of P. australasica also showed the ability to moderately inhibit the enzyme tyrosine kinase with a % Residual Enzyme Activity (REA) of 31.7% being achieved at a concentration of 200 µg/mL [171]. Compound 425 isolated from the alga P. australasica was assayed against PC3 cells where it demonstrated some promising anti-cancer activity achieving an IC₅₀ value of 0.44 µM. This compared favorably to the positive control, doxorubicin, which was reported to have an IC₅₀ value of 0.360 µM [168].
the active compounds have both an exocyclic double bond adjoining the lactone ring and also either a hydroxyl or acetyl functionality. A summary of the halogenated furanones isolated from red algae has been provided in the Supporting Information (Figure S30).

4.2. Steroids

All sterol compounds reported here were found in the red alga *A. armata* (467–473) (see Supporting Information Figure S31). The sterol composition of this alga was studied quantitatively, and it was found that the major sterol constituent was cholesterol (471) [43]. This agrees with the conventional idea that cholesterol is generally present in algae of the phylum Rhodophyta as the major constituent of sterol extracts [173]. Sterol constituents for this alga were extracted using dichloromethane and saponified using potassium hydroxide and ethanol with a period of reflux in diethyl ether. Varieties of steroids found in *A. armata* do not differ greatly from the steroid classes found in the algae of Chlorophyta and Ochrophyta, but simply differ in the number of steroids that have been reporte [43]. A distribution of the Polyhalogenated indoles, polyhalogenated hydrocarbons, polyhalogenated furanones and steroid compounds reported in this review by species and locality is shown in Table 12.

**Table 12. Distribution of compounds 409 to 473.**

| No.    | Compound Type           | Species     | Origin                  | Ref          |
|--------|-------------------------|-------------|-------------------------|--------------|
| 409–424| Polyhalogenated Indole  | *R. membranacea* | Moa Point, New Zealand | [165,166]    |
| 425–426| Polyhalogenated Hydrocarbon | *P. australasica* | Pearsons Point, Tasmania | [168]        |
| 427    | Polyhalogenated Hydrocarbon | *D. pulchra*  | Cape Banks, New South Wales | [167,169,170]|
| 428–430| Polyhalogenated Hydrocarbon | *P. australasica* | Tasmania | [167]        |
| 431    | Polyhalogenated Hydrocarbon | *D. pulchra*  | Cape Banks, New South Wales | [169,170]    |
| 432    | Polyhalogenated Hydrocarbon | *P. australasica* | Pearsons Point, Tasmania | [168]        |
| 433    | Polyhalogenated Hydrocarbon | *P. australasica* | Tasmania | [167]        |
| 434    | Polyhalogenated Hydrocarbon | *D. pulchra*  | Cape Banks, New South Wales | [169]        |
| 435    | Polyhalogenated Furanones | *D. pulchra*  | Cape Banks, New South Wales | [169]        |
| 436    | Polyhalogenated Furanones | *D. pulchra*  | Cape Banks, New South Wales Palmer Station, Antarctica | [170,172]    |
| 437, 438| Polyhalogenated Furanones | *D. pulchra*  | Cape Banks, New South Wales | [169,170]    |
| 439–442| Polyhalogenated Furanones | *D. pulchra*  | Cape Banks, New South Wales | [170,171]    |
| 443    | Polyhalogenated Furanones | *D. pulchra*  | Cape Banks, New South Wales Palmer Station, Antarctica | [170–172]     |
| 444–448| Polyhalogenated Furanones | *D. pulchra*  | Cape Banks, New South Wales | [170,171]    |
| 449    | Polyhalogenated Furanones | *D. pulchra*  | New South Wales | [174]        |
| 450    | Polyhalogenated Furanones | *D. pulchra*  | Cape Banks, New South Wales | [169]        |
| 451–462| Polyhalogenated Furanones | *D. pulchra*  | Cape Banks, New South Wales | [171,175]    |
| 463–465| Polyhalogenated Furanones | *D. pulchra*  | Palmer Station, Antarctica | [172]        |
| 466    | Polyhalogenated Furanones | *D. pulchra*  | Cape Banks, New South Wales | [169]        |
| 467, 468| Steroid                 | *A. armata*  | -                       | [176]        |
| 469–472| Steroid                 | *A. armata*  | Praia do Quebrado, Portugal | [43]         |
| 473    | Steroid                 | *A. armata*  | Portugal                | [177]        |
4.3. Miscellaneous

Simple bromophenolics were found to be present in a number of red algae species including *C. officinale* (474–478), *P. lucida* (474–478), *C. secundatus* (474–478), *A. anceps* (474–478), *J. sagittata* (474–478), *D. pulchra* (474–478) and *S. robusta* (474–478) and *P. angustum* (475–478) [54]. This was to be expected with the large number of higher molecular weight brominated terpenoids and laurenes that populate the algae of this phylum. As with brown algae, a number of red algae exhibited the presence of xanthophyllic compounds such as fucoxanthin (479) and β, β-Carotene (484). These have been studied in detail for their anti-cancer properties [108,109].

Xanthophyll compounds such as Fucoxanthin (479) and zeaxanthin (482) were isolated in abundance from a number of red algae such as *L. botryoides* (480, 483, 484), *M. abscissa* (480, 484, 496, 498, 499), *A. ciliolatum* (481, 482, 484), *C. clavulatum* (481, 482, 496, 498) and *P. capillacea* (481, 482, 484, 496).

Macrocyclic γ-Pyrone (486–488) were obtained from the red alga *Phacelocarpus peperocarpos* collected in South Australia. This has been the only instance of secondary metabolite isolation from this species, but many other varieties of γ- and α-pyrone have also been found within the alga *Phacelocarpos labillardieri*, which is also considered to be synonymous with *P. peperocarpos* [178–180]. It has also been suggested that biosynthesis of these compounds could occur through a pathway that utilizes a linear diketo acid [179]. To date, macrocyclic enol pyrones of this type have not been found in other natural sources, suggesting that this could potentially prove an important marker for this genus of red algae. γ-Pyrone have also been found within the species *Ptilonia australasica*, with compounds (490–492) representing the only halogenated γ-Pyrone reported in this review [167,168]. These compounds were found to be more prevalent in the non-polar extracts of *P. australasica*. Compound 490 was assayed against human prostate adenocarcinoma (PC3) cells displaying an IC₅₀ value of 10.0 µM, however this was outperformed by the positive control compounds of taxol and doxorubicin that achieved IC₅₀ values of 0.002 µM and 0.360 µM, respectively [168].

The red alga *L. filiformis* was shown to have two miscellaneous metabolites, an aromadendrene (485) and a lipid with an aldehyde functionality (489). A cyclic lipid was found to present in *C. clavulatum* (497). The alga *P. costatum* was also shown to have a linear diterpene compound (500). *G. filicina*, a red alga from the coast of Japan (now reclassified as *G. subpectinata* see Supporting Information Table S1), was shown to contain both pyrogallol compounds (493, 494) and a cyclic ketone (495) [181,182] which were examined for their biological activity. In a 2012 study a methylated derivative of compound 493 was isolated from the pacific oyster *Crassostrea gigas*. This compound was shown to be an active antioxidant agent displaying potent activity in DPPH assays [183,184]. A summary of all the miscellaneous classes of compounds isolated from red algae is given in the Supporting Information Figure S32. A distribution of the miscellaneous compounds reported in this review by species and locality is shown in Table 13. A summary of the biological activities for compounds isolated from red algae is given in Supporting Information Figure S33.
Table 13. Distribution of compounds 474 to 500.

| No. | Compound Type | Species                  | Origin                      | Ref  |
|-----|---------------|--------------------------|-----------------------------|------|
| 474 | Bromophenolic  | C. officinale            | Bateau Bay, NSW             | [54] |
|     |               | P. lucida                | Bateau Bay, NSW             |      |
|     |               | G. secundada             | Batemans Bay, NSW           |      |
|     |               | A. anceps                | Bateau Bay, NSW             |      |
|     |               | J. sagittata             | Bateau Bay, NSW             |      |
|     |               | D. pulchra               | Botany Bay, NSW             |      |
|     |               | S. robusta               | Batemans Bay, NSW           |      |
| 475 | Bromophenolic  | C. officinale            | Bateau Bay, NSW             | [54] |
|     |               | P. angustum              | Bateau Bay, NSW             |      |
|     |               | P. lucida                | Batemans Bay, NSW           |      |
|     |               | G. secundada             | Batemans Bay, NSW           |      |
|     |               | A. anceps                | Bateau Bay, NSW             |      |
|     |               | J. sagittata             | Bateau Bay, NSW             |      |
|     |               | D. pulchra               | Botany Bay, NSW             |      |
|     |               | S. robusta               | Batemans Bay, NSW           |      |
| 479 | Xanthophyll   | L. filiformis            | Australia                   | [185]|
|     |               | L. botryoides            | Australia                   |      |
| 480 | Xanthophyll   | L. botryoides            | Australia                   | [185]|
|     |               | M. abscissa              | Leigh, New Zealand          |      |
| 481 | Xanthophyll   | A. ciliolatum            | Ensenada, Baja, California  | [186]|
|     |               | C. clavulatum            | Ensenada, Baja, California  |      |
|     |               | P. capillacea            | Ensenada, Baja, California  |      |
| 482 | Xanthophyll   | L. botryoides            | Australia                   | [185]|
|     |               | A. ciliolatum            | Ensenada, Baja, California  | [186]|
|     |               | C. clavulatum            | Ensenada, Baja, California  |      |
|     |               | M. abscissa              | Leigh, New Zealand          | [186]|
|     |               | P. capillacea            | Ensenada, Baja, California  |      |
| 485 | Aromadendrene | L. filiformis            | South Australia             | [127]|
| 486 | γ−Pyrones     | P. peperocarpos          | South Australia             | [178]|
| 489 | Lipid         | L. filiformis            | Taroona Beach, Hobart,      | [138]|
|     |               |                          | Tasmania                    |      |
| 490 | γ−Pyrones     | P. australasica          | Pearsons Point, Tasmania    | [168]|
| 491 | γ−Pyrones     | P. australasica          |                          | [167]|
| 493 | Pyrogallols   | G. filicina              | Bay of Hiroshima, Japan     | [181]|
| 494 | Cyclic lipid  | G. filicina              | Bay of Hiroshima, Japan     | [182]|
| 495 | Xanthophyll   | C. clavulatum            | Ensenada, Baja, California  | [186]|
|     |               | M. abscissa              | Leigh, New Zealand          |      |
|     |               | P. capillacea            | Ensenada, Baja, California  |      |
| 496 | Xanthophyll   | C. clavulatum            | Ensenada, Baja, California  | [186]|
|     |               | M. abscissa              | Leigh, New Zealand          | [186]|
|     |               | P. capillacea            | Ensenada, Baja, California  |      |
| 497 | Cyclic lipid  | C. clavulatum            | East Coast of Sicily, Italy | [187]|
| 498 | Xanthophyll   | C. clavulatum            | Ensenada, Baja, California  | [186]|
|     |               | M. abscissa              | Leigh, New Zealand          | [186]|
| 499 | Xanthophyll   | M. abscissa              | Leigh, New Zealand          | [188]|
| 500 | Diterpene     | P. costatum              | Deep Glen Bay, Tasmania     | [142]|
5. Conclusions

This review describes the distribution of 508 natural products derived from algae that can be found within the Port Phillip Bay region in Victoria, Australia. Of the 193 species of algae that are commonly found within Port Phillip Bay, 71 species have been studied and documented for phytochemical purposes and have yielded an array of natural products. Figure 11 displays the distribution of these natural products among phyla and from how many species they were derived from. Figures 12–14 show the distribution of compound class amongst the species discussed in this review.

Brown algae have shown the largest number of natural products along with the largest number of species that have been studied for biological activity, whether by crude extract or pure compound evaluation. Green algae and red algae appear to be less studied, both in a natural product capacity, and as a source of crude extract bioactivity, yielding 9 and 5 species that display crude extract or pure compound bioactivity, respectively. Many studies have contributed to the isolation and identification of the large number of compounds that have been chemically profiled and discovered utilising hyphenated techniques such as HPLC–NMR and HPLC–MS [57,62,91,118,122,133,157,189]. This has expedited the process of dereplication and allowed for a more efficient pathway to the isolation and characterization of bioactive components present in crude extracts. As there can often be issues with the instability of compounds isolated from marine sources, these techniques limit the amount of exposure to the atmosphere or light that any purified sample would have by, promptly analyzing these samples after separation. Further use of such techniques could see an increase in the total number of natural products discovered, particularly from marine sources. Many studies included in this review appear to approach the isolation and characterization of natural products from a chemical perspective rather than by means of a bioassay guided fractionation. This provides an opportunity for utilizing these methodologies to attempt a more targeted natural product isolation, with the aim of furnishing more information about the bioactivity of crude extracts from marine organisms, and so increase the number of species studied.

![Distribution of Natural Products](image)

**Figure 11.** Total number of natural products isolated from marine algae common to Port Phillip Bay, represented by phylum.
Fig. 12. Heat maps of compound class distribution for Ochrophyta algae.
Figure 13. Heat maps of compound class distribution for Chlorophyta algae.

Figure 14. Heat maps of compound class distribution for Rhodophyta algae.
## Supplementary Materials:

The following are available online at http://www.mdpi.com/1660-3397/18/3/142/s1:

- Table S1: Taxonomic Revisions, Figure S2: Diterpenes Isolated from Green Algae, Figure S3: Sesquiterpenes Isolated from Green Algae, Figure S4: Cyclic Geranyl Acetones Isolated from Green Algae, Figure S5: Steroids/Sterols Isolated from Green Algae, Figure S6: Miscellaneous Compounds Isolated from Green Algae, Figure S7: Biological Activity Summary of Green Algae (Chlorophyta), Figure S8: Tocotrienols Isolated from Brown Algae, Figure S9: Meroditerpenoids Isolated from Brown Algae, Figure S10: Prenylated Phenols Isolated from Brown Algae, Figure S11: Meroditerpenoids Isolated from Brown Algae, Figure S12: Sesquiterpenes and Monoterpenes Isolated from Brown Algae, Figure S13: Diterpenoids Isolated from Brown Algae, Figure S14: Diterpenoids Isolated from Brown Algae (continued), Figure S15: Diterpenoids Isolated from Brown Algae (continued), Figure S16: Steroids/Sterols Isolated from Brown Algae, Figure S17: Lipids and Polyenes Isolated from Brown Algae, Figure S18: Oxylipids and Epoxylipids Isolated from Brown Algae, Figure S19: Phloroglucinols Isolated from Brown algae, Figure S20: Phenols/phenolic acids/resorcins Isolated from Brown algae, Figure S21: Miscellaneous Compounds Isolated from Brown Algae, Figure S22: Biological Activity Summary of Brown Algae (Ochrophyta), Figure S23: Halogenated Monoterpenes and Parguerenes Isolated from Red Algae, Figure S24: Chamigrenes Isolated from Red Algae, Figure S25: Laurenes Isolated from Red Algae, Figure S26: Sesquiterpenes Isolated from Red Algae, Figure S27: Lauroxocanes Isolated from Red Algae, Figure S28: Polyhalogenated Indoles Isolated from Red Algae, Figure S29: Polyhalogenated Hydrocarbons Isolated from Red Algae, Figure S30: Halogenated Furanes Isolated from Red Algae, Figure S31: Steroids Isolated from Red Algae, Figure S32: Miscellaneous Classes of Compounds Isolated from Red Algae, and Figure S33: Biological Activity Summary of Red Algae (Rhodophyta).

## Funding:

JL would like to thank RMIT university his postgraduate scholarship funding that supported this research.

## Acknowledgments:

The authors of this paper would like to thank Associate Colin Rix for his ongoing support and help throughout this project.

## Conflicts of Interest:

The authors declare no conflict of interest.

## References

1. Newman, D.J.; Cragg, G.M. Natural Products as Sources of New Drugs from 1981 to 2014. *J. Nat. Prod.* 2016, 79, 629–661. [CrossRef] [PubMed]

2. Blunt, J.W.; Carroll, A.R.; Copp, B.R.; Davis, R.A.; Keyzers, R.A.; Prinsep, M.R. Marine natural products. *Nat. Prod. Rep.* 2018, 35, 8–53. [CrossRef] [PubMed]

3. Blunt, J.W.; Copp, B.R.; Keyzers, R.A.; Munro, M.H.G.; Prinsep, M.R. Marine natural products. *Nat. Prod. Rep.* 2017, 34, 235–294. [CrossRef]

4. Shang, J.; Hu, B.; Wang, J.; Zhu, F.; Kang, Y.; Li, D.; Sun, H.; Kong, D.X.; Hou, T. Cheminformatic Insight into the Differences between Terrestrial and Marine Originated Natural Products. *J. Chem. Inf. Model.* 2018, 58, 1182–1193. [CrossRef] [PubMed]

5. Mayer, A.M. Marine pharmacology in 2009-2011: Marine compounds with antibacterial, antidiabetic, antifungal, anti-inflammatory, antiprotzoal, antituberculosis, and antiviral activities; affecting the immune and nervous systems, and other miscellaneous mechanisms of action. *Mar. Drugs* 2013, 11, 2510–2573.

6. Cheung, R.C.; Wong, J.H.; Pan, W.L.; Chan, Y.S.; Yin, C.M.; Dan, X.L.; Wang, H.X.; Fang, E.F.; Lam, S.K.; Ngai, P.H.; et al. Antifungal and antiviral products of marine organisms. *Appl. Microbiol. Biotechnol.* 2014, 98, 3475–3494. [CrossRef]

7. Gyawali, R.; Ibrahim, S.A. Natural products as antimicrobial agents. *Food Control*. 2014, 46, 412–429. [CrossRef]

8. Michalak, I.; Chojnacka, K. Algae as production systems of bioactive compounds. *Eng. Life Sci*. 2015, 15, 160–176. [CrossRef]

9. Zhou, Z.-F.; Guo, Y.-W. Bioactive natural products from Chinese marine flora and fauna. *Acta Pharmacol. Sin.* 2012, 33, 1159–1169. [CrossRef]

10. Zhou, Z.-F.; Menna, M.; Cai, Y.-S.; Guo, Y.-W. Polyacetylenes of Marine Origin: Chemistry and Bioactivity. *Chem. Rev.* 2014, 115, 1543–1596. [CrossRef]

11. Scieszka, S.; Klewiccka, E. Algae in food: a general review. *Crit Rev. Food Sci Nutr.* 2018. [CrossRef] [PubMed]

12. Bouissil, S.; Pierre, G.; Alaoui-Talibi, Z.E.; Michaud, P.; El Modafar, C.; Dalatte, C. Applications of Algal Polysaccharides and Derivatives in Therapeutic and Agricultural Fields. *Curr. Pharm.* 2019, 25, 1187–1199. [CrossRef] [PubMed]

13. Mata, T.M.; Martins, A.A.; Caetano, N.S. Microalgae for biodiesel production and other applications: A review. *Renew. Sust. Energ. Rev.* 2010, 14, 217–232. [CrossRef]
14. Perez, M.J.; Falque, E.; Dominguez, H. Antimicrobial Action of Compounds from Marine Seaweed. Mar. Drugs 2016, 14, 52. [CrossRef] [PubMed]
15. Alves, C.; Silva, J.; Pinteus, S.; Gaspar, H.; Alpoim, M.C.; Botana, L.M.; Pedrosa, R. From Marine origin to therapeutics: The antitumor potential of marine algae-derived compounds. Front. Pharmacol. 2018, 9, 1–24. [CrossRef]
16. Tchokouaha Yamthe, L.R.; Appiah-Opong, R.; Tsouh Fokou, P.V.; Tsabang, N.; Fekam Boyom, F.; Kwadwo Nyarko, A.; Wilson, M. Marine algae as a source of novel antileishmanial drugs: A review. Mar. Drugs 2017, 15, 323. [CrossRef] [PubMed]
17. Fernando, I.S.; Nah, J.W.; Jeon, Y.J. Potential anti-inflammatory natural products from marine algae. Environ. Toxicol. Pharmacol. 2016, 48, 22–30. [CrossRef]
18. Dahms, H.U.; Dobretsov, S. Antifouling compounds from marine macroalgae. Mar. Drugs 2017, 15, 265. [CrossRef]
19. Torres, F.A.E.; Passalacqua, T.G.; Velasquez, A.M.A.; de Souza, R.A.; Colepicolo, P.; Graminha, M.A.S. New drugs with antiprototzoal activity from marine algae: A review. Rev. Bras. Farmacogn. 2014, 24, 265–276. [CrossRef]
20. Leal, M.C.; Munro, M.H.; Blunt, J.W.; Puga, J.; Jesus, B.; Calado, R.; Rosa, R.; Madeira, C. Biogeography and biodiscovery hotspots of macroalgal marine natural products. Nat. Prod. Rep. 2013, 30, 1380–1390. [CrossRef]
21. Womersley, H.B.S. Port Phillip Survey 1957–1963. Mem. Nat. Mus. Vict. 1966, 27, 133–153. [CrossRef]
22. Edgar, G. Australian Marine Life: The Plants and Animals of Temperate Waters; Reed New Holland: Sydney, Australia, 2000.
23. VictorianStateGovernment. Victorian Biodiversity Atlas. Available online: https://www.environment.vic.gov.au/biodiversity/victorian-biodiversity-atlas (accessed on 10 October 2018).
24. Paul, V.J.; Fenical, W. Diterpenoid metabolites from the Pacific marine algae of the order Caulerpales (Chlorophyta). Phytochemistry 1985, 24, 2239–2243. [CrossRef]
25. Handley, J.T.; Blackman, A.J. Monocyclic Diterpenes from the Marine Alga Caulerpa trifaria (Chlorophyta). Aust. J. Chem. 2000, 53, 67–71. [CrossRef]
26. Masaki, Y.; Hashimoto, K.; Iwai, H.; Kaji, K. Synthesis of optically active natural caulerpol. Chem. Lett. 1978, 1203–1204. [CrossRef]
27. Handley, J.T.; Blackman, A.J. Secondary Metabolites from the Marine Alga Caulerpa brownii (Chlorophyta). Aust. J. Chem. 2005, 58, 39–46. [CrossRef]
28. Yin, S-W.; Wang, C-Y.; Li, X-M.; Wang, B-G. A new clerosterol derivative, trans-phytol, and related metabolites from marine green alga Codium fragile (Codiaceae) and their chemotaxonomic significance. Biochem. Syst. Ecol. 2005, 33, 1288–1292. [CrossRef]
29. Sun, H.H.; Fenical, W. Rhipocephalin and rhipocephenal; Toxic feeding deterrents from the tropical marine alga Rhizophyllum Phoenix. Tetrahedron Lett. 1979, 8, 685–688. [CrossRef]
30. Maric, P.; Ahel, M.; Senta, I.; Terzic, S.; Mikac, I.; Zuljevic, A.; Smital, T. Effect-directed analysis reveals inhibition of zebrafish uptake transporter Oatp1d1 by caulerpenyne, a major secondary metabolite from the invasive marine alga. Caulerpa Taxifolia Chemosphere 2017, 174, 643–654. [CrossRef]
31. Paul, V.J.; Fenical, W. Bioactive terpenoids from Caribbean marine algae of the genera penicillus and udotea (Chlorophyta). Tetrahedron 1984, 40, 2913–2918. [CrossRef]
32. D’Abrosca, B.; Dellagreca, M.; Fiorentino, A.; Monaco, P.; Oriano, P.; Temussi, F. Structure elucidation and phytotoxicity of C13 nor-isoprenoids from Cenartium Parqui. Phytochemistry 2004, 65, 497–505. [CrossRef]
33. Dellagreca, M.; Marino, C.D.; Zarrelli, A.; D’Abrosca, B. Isolation and Phytotoxicity of Apocarotenoids from Chenopodium album. J. Nat. Prod. 2004, 67, 1492–1495. [CrossRef] [PubMed]
34. Dollmann, G.F.; Schreier, P.; Winterhalter, P.; Guntert, M.; Sommer, H. Synthesis and Enantiodifferentiation of Riesling Acetals. Phytochem. Anal. 1995, 6, 106–111. [CrossRef]
35. Strauss, C.R.; Dimitriadis, E.; Wilson, B.; Williams, P.J. Studies on the Hydrolysis of Two Megastigma-3, 6, 9-triols Rationlizing the Origins of Some Volatile C13 Norisoprenoids of Vitis vinifera Grapes. J. Agric. Food Chem. 1986, 34, 145–149. [CrossRef]
36. Capon, R.J.; Ghisalberti Emilio, L.; Jeffries Phillip, R. New Sesquiterpenes from Caulerpa flexilis var. muelleri. Aust. J. Chem. 1981, 34, 1775–1778. [CrossRef]
37. Blackman, A.J.; Wells, R.J. Flexilin and trifarin, Terpene 1, 4-diacetoxybuta-1, 3-dienes from two caulerpa species. Tetrahedron Lett. 1978, 33, 3063–3064. [CrossRef]
38. Sun, Y.; Zhan, Y.C.; Sha, Y.; Pei, Y.H. Norisoprenoids from Ulva lactuca. J. Asian Nat. Prod. Res. 2007, 9, 321–325. [CrossRef]
39. Li, G.-L.; Guo, W.-J.; Wang, G.-B.; Wang, R.-R.; Hou, Y.-X.; Liu, K.; Liu, Y.; Wang, W. Sterols from the Green Alga Ulva australis. Mar. Drugs 2017, 15, 299. [CrossRef]
40. Kapetanovic, R.; Sladic, D.; Popov, S.; Zlatovic, M.; Kljajic, Z.; Gasic, M. Sterol composition of the Adriatic sea algae Ulva lactuca, Codium dichotomum, Cystoseira adriatica and Fucus virsoides. J. Serb. Chem. Soc. 2005, 70, 1395–1400. [CrossRef]
41. Awad, N.E. Biologically active steroid from the green Alga Ulva lactuca. Phytother. Res. 2000, 14, 641–643. [CrossRef]
42. Govindan, M.; Hodge, J.D.; Brown, K.A.; Nunez-Smith, M. Distribution of cholesterol in Caribbean marine algae. Steroids 1993, 58, 178–180. [CrossRef]
43. Lopes, G.; Sousa, C.; Bernardo, J.; Andrade, P.B.; Valentão, P.; Ferreres, F.; Mouga, T. Sterol Profiles in 18 Macroalgae of the Portuguese Coastl. J. Phycol. 2011, 47, 1210–1218. [CrossRef] [PubMed]
44. Rubinstein, I.; Goad, L.J. Sterols of the siphonous marine alga Codium fragile. Phytochemistry 1974, 13, 481–484. [CrossRef]
45. Romeo, G.; Toscano, M.A. The isolation and characterization of (24S)-24-Methylcholesta-5, 25-dien-3β-ol from the siphonous marine alga Codium bursa. J. Nat. Prod. 1983, 46, 187–189. [CrossRef]
46. Olasehindé, T.A.; Mabinaya, L.V.; Olaniran, AO.; Okoh, A.I. Chemical characterization of sulfated polysaccharides from Gracilaria gracilis and Ulva lactuca and their radical scavenging, metal chelating, and cholinesterase inhibitory activities. Int. J. Food Prop. 2019, 22, 100–110. [CrossRef]
47. He, J.; Xu, Y.; Chen, H.; Sun, P. Extraction, Structural Characterization, and Potential Antioxidant Activity of the Polysaccharides from Four Seaweeds. Int. J. Mol. Sci. 2016. 17. [CrossRef]
48. Kammoun, I.; Bhairia, I.; Ben Abdallah, F.; Jaballi, I.; Ktari, N.; Boudawara, O.; Nasri, M.; Gharsallah, N.; Hakim, A.; Ben Amara, I. Potential protective effects of polysaccharide extracted from Ulva lactuca against male reprotoxicity induced by thiacloprid. Arch. Physiol. Biochem. 2017, 123, 334–343. [CrossRef]
49. MAhmed, O. Anti-Proliferative and Apoptotic Efficacies of Ulvan Polysaccharides against Different Types of Carcinoma Cells In Vitro and In Vivo. J. Canc. Sci. Ther. 2016, 4, 202–208.
50. Capon, R.J.; Ghisalberti Emilio, L.; Jefferies Phillip, R. Metabolites of the green algae, Caulerpa species. Phytochemistry 1983, 22, 1465–1467. [CrossRef]
51. Rochfort, S.J.; Watson, R.; Capon Robert, J. Dictyosphaerina: A Novel bicyclic lipid from a Southern Australian marine green algae, Dictyosphaerina sericea. J. Nat. Prod. 1996, 59, 1154–1156. [CrossRef]
52. El Sayed, H.; Choudhary, M.I.; Kandil, S.H.; El Nemr, A.; Gulzar, T.; Shobier, A.H. Studies on the constituents of the green alga Ulva lactuca. Chem. Nat. Comp. 2011, 47, 335–338.
53. Flodin, C.; Whitfield Frank, B. 4-Hydroxybenzoic acid: A likely precursor of 2, 4, 6-tribromophenol in Ulva lactuca. Phytochemistry 1999, 51, 249–255. [CrossRef]
54. Whitfield, F.B.; Heldoniotis, F.; Shaw, K.J.; Svoronos, D. Distribution of bromophenols in species of marine algae from Eastern Australia. J. Agric. Food Chem. 1999, 47, 2367–2373. [CrossRef]
55. Gregson, R.P.; Kazlauskas, R.; Murphy, P.T.; Wells, R.J. New Metabolites from the Brown Alga Cystophora torulosa. Aust. J. Chem. 1977, 30, 2527–2532. [CrossRef]
56. Bian, B.; Van Altena, I.A. Four new compounds from the Australian brown alga Cystophora brownii. Aust. J. Chem. 1998, 51, 1157–1165. [CrossRef]
57. Brkljača, R.; Urban, S. HPLC–NMR and HPLC–MS investigation of antimicrobial constituents in Cystophora monilifera and Cystophora subfarcinata. Phytochemistry 2015, 117, 200–208. [CrossRef] [PubMed]
58. Laird, D.W.; Bennett, S.; Bian, B.; Suer, B.; Wright, K.; Hughes, V.; Van Altena, I.A. Chemical Investigation of seven Australasian Cystophora species: New chemistry and taxonomic insights. Biochem. Syst. Ecol. 2010, 38, 187–194. [CrossRef]
59. Kimura, J.; Makj, N. New Lolilolide derivatives from the brown alga Undaria pinnatifida. J. Nat. Prod. 2002, 65, 57–58. [CrossRef]
60. Peng, Y.; Huang, R.M.; Lin, X.P.; Liu, Y.H. Norisoprenoids from the Brown Alga Sargassum nazhouense Tseng et Lu. Molecules 2018, 23, 348. [CrossRef]
61. Masum, S.; Hossain, M.A.; Akamine, H.; Sakagami, J.-I.; Ishii, T.; Gima, S.; Kersaku, T.; Bhowmik, P. Isolation and characterization of allelopathic compounds from the indigenous rice variety ‘Boterswar’ and their biological activity against Echinocloa crus-galli L. Allelopath. J. 2018, 43, 31–42. [CrossRef]

62. Brkljača, R.; Urban, S. Chemical Profiling (HPLC-NMR & HPLC-MS), Isolation, and Identification of Bioactive Meroditerpenoids from the Southern Australian Marine Brown Alga Sargassum paradoxum. Mar. Drugs 2014, 13, 102–127.

63. Reddy, P.; Urban, S. Meroditerpenoids from the southern Australian marine brown alga Sargassum fallax. Phytochemistry 2009, 70, 250–255. [CrossRef] [PubMed]

64. Ovenden, S.P.; Nielson, J.L.; Liptrot, C.H.; Willis, R.H.; Wright, A.D.; Motti, C.A.; Tapiolas, D.M. Comosusols A-D and comosone A: Cytotoxic compounds from the brown alga Sporochmus comosus. J. Nat. Prod. 2011, 74, 739–743. [CrossRef] [PubMed]

65. Gunasekera, L.S.; Wright, A.E.; Gunasekera, S.P.; McCarthy, P.; Reed, J. Antimicrobial Constituent of the Brown Alga Sporochmus pedunculatus. Int. J. Pharmacogn. 1995, 33, 253–255. [CrossRef]

66. Rochfort, S.J.; Capon, R.J. A new sesquiterpene/phenol from the Australian marine brown alga Perithalia caudata. J. Nat. Prod. 1994, 6, 849–851. [CrossRef]

67. Blackman, A.J.; Rogers, G.I.; Volkman, J.K. A phenol from the brown alga Perithalia caudata. Phytochemistry 1988, 27, 3686–3687. [CrossRef]

68. Ravi, B.N.; Murphy, P.T.; Lidgard, R.O.; Warren, R.G.; Wells, R.J. C18 Terpenoid metabolites of the brown alga Cystophora moniliformis. Aust. J. Chem. 1982, 35, 171–182. [CrossRef]

69. El Hattab, M.; Culioli, G.; Valls, R.; Richou, M.; Piovetti, L. Apo-fucoxanthoids and loliolide from the brown alga Caulocystis cephalornithos linearifolium against malarial parasite Plasmodium falciparum. In vitro and in silico evaluation of fucosterol from Sargassum horridum as potential human acetylcholinesterase inhibitor. J. Biomol. Struct. Dyn. 2018, 36, 447–451. [CrossRef]

70. Van Altena, I.A. Terpenoids from the brown alga Cystophora moniliformis. Aust. J. Chem. 1988, 41, 49–56. [CrossRef]

71. Li, Y.; Li, W.; Li, Y. An Alternative Short Synthesis of 6, 10, 14-Trimethyl-5E, 9E-Pentadecadiene-2, 13-dione. Synth. Commun. 1994, 24, 117–121. [CrossRef]

72. Reddy, P.; Urban, S. Linear and cyclic C18 terpenoids from the Southern Australian Marine Brown Alga Cystophora moniliformis. J. Nat. Prod. 2008, 71, 1441–1446. [CrossRef]

73. Chen, J.; Li, H.; Zhao, Z.; Xia, X.; Li, B.; Zhang, J.; Yan, X. Diterpenes from the marine algae of the genus Dictyota. Mar. Drugs 2018, 16, 159. [CrossRef] [PubMed]

74. Dunlop, R.W.; Ghisalberti, E.L.; Jeferies, P.R.; Skeltoni, B.W.; White, A.H. Structure of a new dolastane diterpene from Dictyota furcellata. Aust. J. Chem. 1989, 42, 315–319. [CrossRef]

75. Dang, T.T.; Bowyer, M.C.; Van Altena, I.A.; Scarlett, C.J. Comparison of chemical profile and antioxidant properties of the brown algae. Int. J. Food Sci. Technol. 2018, 53, 174–181. [CrossRef]

76. Aknin, M.; Dogbevi, K.; Samb, A.; Kornprobst, J.M.; Gaydou, E.M.; Miralles, J. Fatty acid and sterol composition of eight brown algae from the senegales coast. Comp. Biochem. Physiol. 1992, 102B, 841–843.

77. Castro-Silva, E.S.; Bello, M.; Hernandez-Rodriguez, M.; Correa-Basurto, J.; Murillo-Alvarez, J.L.; Rosales-Hernandez, M.C.; Munoz-Ochoa, M. In vitro and in silico evaluation of fucosterol from Sargassum horridum as potential human acetylcholinesterase inhibitor. J. Biomol. Struct. Dyn. 2018. [CrossRef]

78. Perumal, P.; Sowmiya, R.; Prasanna Kumar, S.; Ravi Kumar, S.; Deepak, P.; Balasubramani, G. Isolation, structural elucidation and antiplasmodial activity of fucosterol compound from brown seaweed, Sargassum linearifolium against malarial parasite Plasmodium falciparum. Nat. Prod. Res. 2017, 32, 1316–1319. [CrossRef]

79. Narkowicz, C.K.; Blackman, A.J. Further acetogenins from Tasmanian collections of Caulocystis cephalornithos demonstrating chemical variability. Biochem. Syst. Ecol. 2006, 34, 635–641. [CrossRef]

80. Gutiérrez-Cepeda, A.; Fernandez, J.J.; Norte, M.; Montalvaro, S.; Tammela, P.; Souto, M.L. Acetate-Derived Metabolites from the Brown Alga Lobophora variegata. J. Nat. Prod. 2015, 78, 1716–1722. [CrossRef]

81. Basha, S.; Jaiswar, S.; Jha, B. On the biosorption, by brown seaweed. Lobophora variegata, of Ni(II) from aqueous solutions: Equilibrium and thermodynamic studies. Biodegradation 2010, 21, 661–680.

82. Capon, R.J.; Barrow, R.A.; Skene, C.; Rochfort, S. The biomimetic synthesis of marine epoxylipsids: Bisepxeoids to tetrahydrofurans. Tetrahedron Lett. 1997, 38, 7609–7612. [CrossRef]

83. Kurihara, H.; Kagawa, Y.; Konno, R.; Kim, S.M.; Takashi, K. Lipoxygenase inhibitors derived from marine macroalgae. Bioorg. Med. Chem. Lett. 2014, 24, 1383–1385. [CrossRef] [PubMed]
84. Capon, R.J.; Barrow, R.A.; Rochfort, S.; Jobling, M.; Skene, C. Marine nematocides: Tetrahydrofurans from a Southern Australian brown alga, *Notheia Anomala*. *Tetrahedron* **1998**, *54*, 2227–2242. [CrossRef]

85. Roy, S.; Spilling, C.D. An expeditious total synthesis of both diastereoisomeric lipid dihydroxytetrahydrofurans from *Notheia anomala*. *Org. Lett.* **2012**, *14*, 2230–2233. [CrossRef] [PubMed]

86. Barrow, R.A.; Capon, R.J. Epoxy lipids from the Australian epiphytic brown alga *Notheia anomala*. *Aust. J. Chem.* **1990**, *43*, 895–911. [CrossRef]

87. Kazlauskas, R.; Mulder, J.; Murphy, P.T.; Wells, R.J. New metabolites from the brown alga *Caulocystis cephalarinthis*. *Aust. J. Chem.* **1980**, *33*, 2097–2101. [CrossRef]

88. Rochfort, S.; Murray, L.; Capon, R.J. The chemistry of *notheia anomala*, III: Two new methylene-interrupted trisepoxylips. *J. Nat. Prod.* **1992**, *55*, 1332–1335. [CrossRef]

89. Murray, L.M.; Barrow, R.A.; Capon, R.J. Epoxy lipids from the Australian epiphytic brown alga *Notheia anomala*. *II. Aust. J. Chem.* **1991**, *44*, 843–854. [CrossRef]

90. Womersley, H.B.S. The morphology and taxonomy of *Cystophora* and related genera (Phaeophyta). *Aust. J. Bot.* **1964**, *12*, 53–110. [CrossRef]

91. Brkljača, R.; Gker, E.S.; Urban, S. Dereplication and chemotaxonomical studies of marine algae of the Ochrophyta and Rhodophyta phyla. *Mar. Drugs* **2015**, *13*, 2714–2731. [CrossRef]

92. Kazlauskas, R.; King, L.; Murphy, P.T.; Warren, R.G.; Wells, R.J. New metabolites from the brown algal genus *Cystophora*. *Aust. J. Chem.* **1981**, *34*, 439–447. [CrossRef]

93. Zhang, H.; Xiao, X.; Conte, M.M.; Khalil, Z.; Capon, R.J. Spiralisones A-D: Acylphloroglucinol hemiketals from an Australian marine brown alga, *Zonaria spiralis*. *Org. Biomol. Chem.* **2012**, *10*, 9671–9676. [CrossRef] [PubMed]

94. Blackman, A.J.; Rogers, G.I. Phloroglucinol derivatives from three Australian marine algae of the genus *Zonaria*. *J. Nat. Prod.* **1988**, *51*, 158–160. [CrossRef]

95. Gerwick, W.; Fenical, W. Phenolic lipids from related marine algae of the order Dictyotales. *Phytochemistry* **1982**, *21*, 633–637. [CrossRef]

96. Choukchou-Braham, N.; Asakawa, Y.; Lepoittevin, J.P. Isolation, Structure determination and synthesis of new dihydroisocoumarins from *Ginkgo biloba*. *Tetrahedron Lett.* **1994**, *35*, 3949–3952. [CrossRef]

97. Zhu, Y.; Conklin, D.R.; Chen, H.; Wang, L.; Sang, S. 5-alk(en)ylresorcinols as the major active components in wheat bran inhibit human colon cancer cell growth. *Bioorg. Med. Chem.* **2015**, *23*, 3773–3780. [CrossRef]

98. Wang, K.-W.; Zhang, T.-T.; Zhang, L. Chemical Constituents and Biological Activities of *Grevillea robusta*. *Chem. Biol. Drug Des.* **2016**, *88*, 293–301. [CrossRef]

99. Guan, Y.F.; Song, X.; Qiu, M.H.; Luo, S.H.; Wang, B.J.; Van Hung, N.; Cuong, N.M.; Soejarto, D.D.; Fong, H.H.; Franzblau, S.G.; et al. Bioassay-Guided Isolation and Structural Modification of the Anti-TB Resorcinols from *Ardisia gigantifolia*. *Org. Biomol. Chem.* **2018**, *16*, 3973–3982. [CrossRef]

100. Usov, A.I.; Smirnova, G.P.; Kamenarska, Z.; Dimitrova-Konaklieva, S.; Stefanov, K.L.; Popov, S.S. Polar constituents of brown seaweed *Colpomenia peregrina* (Sauv.) Hamel from the Black Sea. *Russ. J. Bioorg. Chem.* **2004**, *30*, 161–167. [CrossRef]

101. Dasyam, N.; Munkacsi, A.B.; Fadzilah, N.H.; Senanayake, D.S.; O’Toole, R.F.; Keyzers, R.A. Identification and bioactivity of 3-epi-xestoaminol C isolated from the New Zealand brown alga *Xiphophora chondrophylla* (Phaeophyceae). *Eur. J. Biochem.* **1997**, *252*, 734–744. [CrossRef]

102. Boland, W. The chemistry of gamete attraction: Chemical structures, biosynthesis, and (a)biotic degradation of algal pheromones. *Proc. Natl. Acad. Sci. USA* **1995**, *92*, 37–43. [CrossRef] [PubMed]

103. Boland, W.; Marner, F.J.; Jaenicke, L.; Muller, D.G.; Folster, E. Comparative receptor study in gamete chemotaxis of the seaweeds *Ectocarpus siliculosis* and *Cutleria multifida*. *Eur. J. Biochem.* **1983**, *134*, 97–103. [CrossRef] [PubMed]

104. Schotten, T.; Boland, W.; Jaenicke, L. Synthesis of enantiomerically pure pheromones of south-pacific brown algae: Hormosirene and dictyopterene A. *Helv. Chim. Acta.* **1985**, *68*, 1186–1192. [CrossRef]

105. Muller, D.G. Cystophorene and Hormosirene, Sperm Attractants in Australian Brown Algae. *Naturwissenschaften* **1985**, *72*, 97–99. [CrossRef]
107. Green, D.; Kashman, Y. Colpol, a new cytotoxic C6-C4-C6 metabolite from the alga Colpomenia sinuosa. J. Nat. Prod. 1993, 56, 1201–1202. [CrossRef]
108. Martin, L.J. Fucoxanthin and Its Metabolite Fucoxanthinol in Cancer Prevention and Treatment. Mar. Drugs 2015, 13, 4783–4798. [CrossRef]
109. Zorofchian Moghadamtousi, S.; Karimian, H.; Khanabdali, R.; Razavi, M.; Firoozinia, M.; Zandi, K.; Abdul Kadir, H. Anticancer and antitumor potential of fucoidan and fucoxanthin, two main metabolites isolated from brown algae. Sci. World J. 2014, 2014, 768323. [CrossRef]
110. Hussain, E.; Wang, L.-J.; Jiang, B.; Riaz, S.; Butt, G.Y.; Shi, D.-Y. A review of the components of brown seaweeds as potential candidates in cancer therapy. RSC Adv. 2016, 6, 12592–12610. [CrossRef]
111. Mori, K.; Ooi, T.; Hiraoka, M.; Oka, N.; Hamada, H.; Tamura, M.; Kusumi, T. Fucoxanthin and its metabolites in edible brown algae cultivated in deep seawater. Mar. Drugs 2004, 2, 63–72. [CrossRef]
112. Muller, M.; Hogg, M.; Ulms, K.; Vetter, W. Concentrations, stability, and Isolation of the furan fatty acid 9-(3-methyl-5-pentylfuran-2-yl)-nonanoic acid from disposable latex gloves. J. Agric. Food Chem. 2017, 65, 7919–7925. [CrossRef]
113. Kubanek, J.; Jensen, P.R.; Keifer, P.A.; Sullards, M.C.; Collins, D.O.; Fenical, W. Seaweed resistance to microbial attack: A targeted chemical defense against marine fungi. Proc. Natl. Acad. Sci. USA 2003, 100, 6916–6921. [CrossRef]
114. Wirth, D.; Boland, W. Absolute configuration and synthesis of (+)-Caufoxine, the gamete-releasing and gamete-attracting pheromone of the brown alga Perithalia caudata (Phaeophyceae). Helv. Chim. Acta. 1992, 75, 751–758. [CrossRef]
115. Muller, D.G. Sexual pheromones in Cladostepus (Sphacelariaceae, Phaeophyceae). Naturwissenschaften 1986, 73, 99–100. [CrossRef]
116. Kazlauskas, R.; Murphy, P.T.; Wells, R.J.; Gregson, P. Two new furans from the brown alga Acrocarpia paniculata: The Use of 4-Phenyl-4H-1, 2, 4-triazolina-3, 5-dione to Determine the Substitution pattern of a Furan. Aust. J. Chem. 1982, 35, 165–170. [CrossRef]
117. Norton, R.S.; Warren, R.G.; Wells, R.J. Three new polyhalogenated monoterpenes from Plocamium species. Tetrahedron Lett. 1977, 44, 3909–3908. [CrossRef]
118. Dias, D.; Urban, S. Phytochemical analysis of the Southern Australian marine alga, Plocamium mertensii using HPLC-NMR. Phytochem. Anal. 2008, 19, 453–470. [CrossRef]
119. San-martin, A.; Negrette, R.; Rovirosa, J. Insecticide and acaricide activities of polyhalogenated monoterpenes from chilean Plocamium cartilagineum. Phytochemistry 1991, 30, 2165–2169. [CrossRef]
120. Argandona, V.H.; Rovirosa, J.; San-Martin, A.; Riquelme, A.; Diaz-Marrero, A.R.; Cueto, M.; Darias, J.; Santana, O.; Guadano, A.; Gonzalez-Coloma, A. Antifeedant effects of marine halogenated monoterpenes. J. Agric. Food Chem. 2002, 50, 7029–7033. [CrossRef]
121. Konig, G.M.; Wright, A.D.; Linden, A. Plocamium hamatum and its monoterpenes: Chemical and biological investigations of the tropical marine red alga. Phytochemistry 1999, 52, 1047–1053. [CrossRef]
122. Timmers, M.A.; Dias, D.A.; Urban, S. Application of HPLC-NMR in the Identification of Plocamene and Isoplocamene from the marine red alga Plocamium angustum. Mar. Drugs 2012, 10, 2089–2102. [CrossRef]
123. Stierle, D.B.; Wing, R.M.; Sims, J.J. Marine natural products XI Costatone and Costatolide, new halogenated monoterpenes from the red seaweed, Plocamium costatum. Tetrahedron Lett. 1976, 49, 4455–4458. [CrossRef]
124. Kazlauskas, R.; Murphy, P.T.; Quinn, R.J.; Wells, R.J.; Schönhlzer, P.; F-Konzern, J.S.; Hoffmann-La Roche, F. Two polyhalogenated monoterpenes from the red alga Plocamium costatum. Tetrahedron Lett. 1976, 49, 4451–4454. [CrossRef]
125. Motti, C.A.; Thomas-Hall, P.; Hagiwara, K.A.; Simmons, C.J.; Willis, R.; Wright, A.D. Accelerated identification of halogenated monoterpenes from Australian specimens of the red alga Plocamium hamatum and Plocamium costatum. J. Nat. Prod. 2014, 77, 1193–1200. [CrossRef] [PubMed]
126. Sakata, K.; Iwase, Y.; Ina, K.; Fujita, D. Halogenated terpenes isolated from the red alga Plocamium leptophyllum as feeding inhibitors for marine herbivores. Nippon Suisan Gakk. 1991, 57, 743–746. [CrossRef]
127. Rochfort, S.J.; Capon, R.J. Paraguereines revisited: New brominated diterpenes from the Southern Australian marine red alga Laurencia filiformis. Aust. J. Chem. 1996, 49, 19–26. [CrossRef]
128. Huang, X.-C.; Sun, Y.-L.; Salim, A.A.; Chen, Z.-S.; Capon, R.J. Paraguereines: Marine red alga bromoditerpenes as inhibitors of P-glycoprotein (ABCB1) in multidrug resistant human cancer cells. Biochem. Pharmacol. 2013, 85, 1257–1268. [CrossRef] [PubMed]
129. Takeda, S.; Kurosawa, E.; Komiyama, K.; Suzuki, T. The structures of cytotoxic diterpenes containing bromine from the marine red alga *Laurencia obtusa* (Hudson) Lamouroux. *Bull. Chem. Soc. Jpn.* 1990, 63, 3066–3072. [CrossRef]

130. Kurata, K.; Taniguchi, K.; Agatsuma, Y.; Suzuki, M. Diterpenoid feeding-deterrents from *Laurencia saitoi*. *Phytochemistry* 1998, 47, 363–369. [CrossRef]

131. Awad, N.E. Bioactive brominated diterpenes from the marine red alga *Jania rubens* (L.) Lamx. *Phytother. Res.* 2004, 18, 275–279. [CrossRef]

132. Sims, J.J.; Lin, G.H.Y.; Wing, M. Marine natural products elatol, a halogenated sesquiterpene alcohol from the red alga *Laurencia elata*. *Tetrahedron Lett.* 1974, 39, 3487–3490. [CrossRef]

133. Dias, D.A.; Urban, S. Phytochemical studies of the southern Australian marine alga, *Laurencia elata*. *Phytochemistry* 2011, 72, 2081–2089. [CrossRef] [PubMed]

134. Dias, T.; Brito, I.; Moujir, L.; Paiz, N.; Darias, J.; Cueto, M. Cytotoxic sesquiterpenes from *Aplysia dactylomela*. *J. Nat. Prod.* 2005, 68, 1677–1679. [CrossRef] [PubMed]

135. Davyt, D.; Fernandez, R.; Suescun, L.; Mombru, A.W.; Saldana, J.; Domínguez, L.; Coll, J.; Fujii, M.T.; Manta, E. New Sesquiterpene derivatives from the red alga *Laurencia scoparia*. Isolation, structure determination, and anthelintic activity. *J. Nat. Prod.* 2001, 64, 1552–1555. [CrossRef] [PubMed]

136. Vairappan, C.S.; Anangdan, S.P.; Tan, K.L.; Matsunaga, S. Role of secondary metabolites as defense chemicals against ice-ice disease bacteria in biofouler at carrageenophyte farms. *J. Appl. Phycol.* 2009, 22, 305–311. [CrossRef]

137. Nocchi, N.; Soares, A.R.; Souto, M.L.; Fernandez, J.J.; Martin, M.N.; Pereira, R.C. Detection of a chemical cue from the host seaweed *Laurencia dendroidea* by the associated mollusc *Aplysia brasiliana*. *PLoS ONE* 2017, 12, 1–15. [CrossRef]

138. Jongaramruong, J.; Blackman, A.J.; Skelton, B.W.; White, A.H. Chemical relationships between the sea hare *Aplysia parvula* and the red seaweed *Laurencia filiformis* from Tasmania. *Aust. J. Chem.* 2002, 55, 275–280. [CrossRef]

139. Thomas, S.G.; Beveridge, A.A. The novel marine natural product plocamadiene A causes histamine release from mast cells of the guinea-pig and *rat in vitro*. *Clin. Exp. Pharmacol.* 1993, 20, 223–229. [CrossRef]

140. Dunlop, R.W.; Murphy, P.T.; Wells, R.J. A new polyhalogenated monoterpane from the red alga *Plocamium angustum*. *Aust. J. Chem.* 1979, 32, 2735–2739. [CrossRef]

141. Brownlee, R.T.C.; Hall, J.G.; Reiss, J.A. An application of the INEPT pulse sequence to the NMR assignment and absolute configuration. *Aust. J. Chem.* 1977, 30, 2679–2687. [CrossRef]

142. Antunes, B.L.; Fleury, B.G.; Fujii, M.T.; Teixeira, V.L. Sesquiterpenes of the Brazilian marine red alga *Laurencia filiformis* (Rhodophyta, Ceramiales). *Nat. Prod. Commun.* 2008, 3, 1653–1654. [CrossRef]

143. Kazlauskas, R.; Murphy, P.T.; Quinn, R.J.; Wells, R.J. New Laurene derivatives from *Laurencia filiformis*. *Aust. J. Chem.* 1976, 29, 2533–2539. [CrossRef]

144. Kazlauskas, R.; Murphy, P.T.; Wells, R.J.; Daly, J.J.; Oberhansli, W.E. Heterocladol, a halogenated selinana sesquiterpene of biosynthetic significance from the red alga *Laurencia filiformis*: Its isolation, crystal structure and absolute configuration. *Aust. J. Chem.* 1977, 30, 2679–2687. [CrossRef]

145. Dias, D.A.; White, J.M.; Urban, S. *Laurencia filiformis*: Phytochemical profiling by conventional and HPLC-NMR approaches. *Nat. Prod. Commun.* 2009, 4, 157–172. [CrossRef] [PubMed]

146. Kladi, M.; Xenaki, H.; Vagias, C.; Papazafiri, P.; Roussis, V. New cytotoxic sesquiterpenes from the red algae *Laurencia obtusa* and *Laurencia microcladia*. *Tetrahedron* 2006, 62, 182–189. [CrossRef]

147. Vairappan, C.S.; Kawamoto, T.; Miwa, H.; Suzuki, M. Potent antibacterial activity of halogenated compounds against antibiotic resistant bacteria. *Planta Med.* 2004, 70, 1087–1090. [CrossRef]

148. Konig, G.M.; Wright, A.D.; Franzblau, S.G. Assessment of antimycobacterial activity of a series of mainly marine derived natural products. *Planta Med.* 2000, 66, 337–342. [CrossRef]

149. Brennan, M.R.; Erickson, K.L. Austradiol acetate and austradiol diacetate, 4, 6- dihydroxy- (+)- selinane derivatives from an Australian *Laurencia* sp. *J. Org. Chem.* 1982, 47, 3917–3921. [CrossRef]

150. Capon, R.J.; Ghisalberti, E.L.; Jefferies, P.R.; Skelton, B.W.; White, A.H. Sesquiterpene metabolites from *Laurencia filiformis*. *Tetrahedron* 1981, 38, 1613–1621. [CrossRef]
152. Barbero, H.; Diez-Poza, C.; Barbero, A. The Oxepane Motif in Marine Drugs. *Mar. Drugs* 2017, 15, 361. [CrossRef]

153. Pettit, G.R.; Herald, C.L.; Allen, M.S.; Von Dreele, R.B.; Vanell, L.D.; Kao, J.P.Y.; Blake, W. Antineoplastic agents. 48. The isolation and structure of aplysistatin. *J. Am. Chem. Soc.* 1977, 99, 262–263. [CrossRef] [PubMed]

154. Hall, J.G.; Reiss, J.A. Elatenyne- a Pyrano[3, 2-b]pyranyl vinyl acetylene from the red alga *Laurencia elata*. *Aust. J. Chem.* 1986, 39, 1401–1409. [CrossRef]

155. Dyson, B.S.; Burton, J.W.; Sohn, T.-I.; Kim, B.; Bae, H.; Kim, D. Total Synthesis and Structure Confirmation of Elatenyne: Success of Computational Methods for NMR Prediction with Highly Flexible Diastereomers. *J. Am. Chem. Soc.* 2012, 134, 11781–11790. [CrossRef]

156. Snyder, S.A.; Brucks, A.P.; Treitler, D.S.; Moga, I. Concise synthetic approaches for the determination of the Absolute Configuration of the Pseudo-Symmetric Natural Product Elatenyne by the Crystalline Sponge Method. *Angew. Chem. Int. Ed. Engl.* 2016, 55, 2678–2682. [CrossRef]

157. Iliopoulou, D.; Vagias, C.; Harvala, C.; Roussis, V. C15 Acetogenins from the red alga *Laurencia snackeyi* (Weber-van Bosse) Masuda in LPS-stimulated RAW 264.7 macrophages. *J. Am. Chem. Soc.* 2013, 25, 1805–1813. [CrossRef]

158. Urban, S.; Brkljaca, R.; Hoshino, M.; Lee, S.; Fujita, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

159. Poulsen, L.; Craig, R.; Capon, R.J.; Ghisalberti, E.L.; Mori, T.A.; Jeppesen, P. Sesquiterpenes from *Rhodophyllis membranacea* harvey. *J. Nat. Prod.* 2013, 76, 1805–1813. [CrossRef]

160. Pettit, G.R.; Herald, C.L.; Allen, M.S.; Von Dreele, R.B.; Vanell, L.D.; Kao, J.P.Y.; Blake, W. Antineoplastic agents. 48. The isolation and structure of aplysistatin. *J. Am. Chem. Soc.* 1977, 99, 262–263. [CrossRef] [PubMed]

161. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

162. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

163. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

164. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

165. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

166. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

167. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

168. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

169. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]

170. Woolner, V.H.; Jones, C.M.; Field, J.J.; Fadzilah, N.H.; Munkacsi, A.B.; Miller, J.H.; Keyzers, R.A.; Stallard, M.O.; Fuji, M. Determination of the Absolute Configuration of the trans-fused polycyclic systems: Asymmetric total synthesis of (+)-Aplysistatin, (+)-Palisadin A, (+)-Palisadin B, (+)-12-hydroxy-palisadin B, and the AB ring system of adociasulfate-2 and toxicol A. *Chemistry* 2004, 10, 3822–3835. [PubMed]
173. Patterson, G.W. The Distribution of Sterols in Algae. *Lipids* 1971, 6, 120–127. [CrossRef]

174. de Nys, R.; Steinberg, P.D.; Rogers, C.N.; Charlton, T.S.; Duncan, M.W. Quantitative variation of secondary metabolites in the sea hare *Aplysia parvula* and its host plant, *Delisea pulchra*. *Mar. Ecol. Prog. Ser.* 1996, 130, 135–146. [CrossRef]

175. Konig, G.M.; Wright, A.D. Determination of the absolute configuration of a series of halogenated furanones from the marine alga *Delisea pulchra*. *Helv. Chim. Acta.* 1995, 78, 758–764. [CrossRef]

176. Andrade, P.B.; Barbosa, M.; Matos, R.P.; Lopes, G.; Vinholes, J.; Mouga, T.; Valentao, P. Valuable compounds in macroalgae extracts. *Food Chem.* 2013, 138, 1819–1828. [CrossRef]

177. Shin, J.; Paul, V.J.; Fenical, W. New macrocyclic alpha- and gamma-pyrones from the marine red alga *Phacelocarpus labillardieri*. *Tetrahedron Lett.* 1986, 27, 5189–5192. [CrossRef]

178. Nozaki, H.; Minohara, K.; Miyazaki, I.; Kondo, H.; Shirane, F.; Nakayama, M. Two new pyrogallols from the marine alga, *Grateloupia filicina* (Wulfen) J. Agardh. *Agric. Biol. Chem.* 1988, 52, 3229–3230.

179. Arnesen, U.; Hallenstvet, M.; Liaaen-jensen, S. More about the carotenoids of red algae. *Biochem. Syst. Ecol.* 1979, 7, 87–89. [CrossRef]

180. Urban, S.; Timmers, M. HPLC-NMR Chemical profiling and dereplication studies of the marine brown alga, *Cystophora torulosa*. *Nat. Prod. Commun.* 2013, 8, 715–719. [CrossRef]
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Title:
Natural Products of Marine Macroalgae from South Eastern Australia, with Emphasis on the Port Phillip Bay and Heads Regions of Victoria.

Date:
2020-02-28

Citation:
Lever, J., Brkljaa, R., Kraft, G. & Urban, S. (2020). Natural Products of Marine Macroalgae from South Eastern Australia, with Emphasis on the Port Phillip Bay and Heads Regions of Victoria.. Marine Drugs, 18 (3), pp.142-142. https://doi.org/10.3390/md18030142.

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