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#### Review

# Chemical and biological aspects of octocorals from the Brazilian coast

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#### ABSTRACT

This review explores the chemical and biological aspects/results reported in the literature of the octocoral species collected at the Brazilian Coast. This article summarizes the biological activities (including pharmacological, antifouling and others related to chemical ecology) for the compounds and/or extracts described elsewhere. Data and references of compounds isolated from species belonging to the same genus, which have not been investigated in Brazil yet, are presented, emphasizing the importance for research in this area. © 2014 Sociedade Brasileira de Farmacognosia. Published by Elsevier Editora Ltda. All rights reserved.

Introduction

Octocorals or soft-corals (phylum Cnidaria, class Anthozoa, subclass Octocorallia = Alcyonaria) are soft-bodied invertebrates found throughout the world's oceans. The phylum Cnidaria, which includes mostly marine invertebrates with specialized cells called nematocysts, is divided into five classes: Anthozoa, Hydrozoa, Cubozoa, Staurozoa and Scyphozoa (Daly et al., 2007). From Class Anthozoa, we found colonial or solitary clonal animals, exclusively polypoid, separated into the Subclasses Hexacorallia (= Zoantharia) and Octocorallia (= Alcyonaria), each one further divided into multiples orders (Daly et al., 2007). Hexacorallia polyps have six tentacles and mesenteries or multiples thereof, and include black corals, sea anemones, tube anemones and stony corals, which comprise the main reef-building species (Daly et al., 2007). Octocorals are comprised by soft corals, sea pens and gorgonians, with eight tentacles and eight internal mesenteries that exhibit less variation in polyp morphology than hexacorals (Daly et al., 2007; McFadden et al., 2010).

Both groups can have endosymbiotic associations with dinoflagellates called zooxanthellae (Symbiodinium sp.). The host provides nitrogenous waste and receives photosynthetic products from the symbiont in return. Most zooxanthellate corals with obligate associates

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are restricted to shallow waters, such as some tropical scleractinians, and are the main reef-builders (Wells, 1956). Others can maintain facultative symbioses or survive without symbionts, being able to live in Polar Regions and deep-sea environments (Wells, 1956; Cairns, 1982; Huston, 1985; Cairns and Kitahara, 2012). Unlike stony corals (Hexacorallia, Scleractinia), most soft corals thrive in nutrient-rich waters with a less intense illumination. Almost all utilize symbiotic photosynthetic zooxanthella as a major energy source. However, most will readily eat, as passive suspensivorous feeders, any free-floating food, such as phytoplankton and zooplankton out of the water column (Lira et al., 2009; Gomes et al., 2012). They are integral members of the reef ecosystem and provide a habitat for fish, snails, algae and other marine species.

Octocorallia comprises approximately 3200 species of soft corals found in all marine environments. These are diverse on shallow tropical reefs and in deep-sea habitats, where they are often dominant space-occupiers and important structural components of the community (McFadden et al., 2010).

The Brazilian octocoral fauna, particularly deep-sea species, is still poorly known compared to the Caribbean fauna (Arantes et al., 2009; Castro et al., 2010). Around 107 species and/or morphotypes have been reported in Brazilian waters, some only recently. Fourteen of these species are endemic to the Brazilian coast (Arantes et al., 2006; Castro et al., 2010; Neves, 2010; Ofwegen and Haddad, 2011; Pérez et al., 2011; Neves and Pérez, 2012). Investigating the diversity and distribution of the Brazilian octocoral fauna is a complicated task, as the available literature is sparse and mainly found in gray literature, such as theses and dissertations (Castro et al., 2010). In contrast to deepwater species, shallow-water Octocorallia are well known on the Brazilian coast. According to a review published in early 2010 (Castro et al., 2010), seventeen reef species have been registered in Brazilian shallow waters, distributed from Amapá to Santa Catarina (Castro et al., 2010). The distribution of octocorals over large spatial areas is mainly regulated by substrate, temperature and salinity, while on smaller areas, food supply is one of the most important factors that control species distribution (Mortensen and Buhl-Mortensen, 2004; Arantes et al., 2006; 2009; Castro et al., 2010; Neves, 2010; Ofwegen and Haddad, 2011; Pérez et al., 2011; Neves and Pérez, 2012). The species distribution in deeper water may be related to water masses, as these influence food availability patterns (Clark et al., 2006).

Shallow-water samples from coral reefs are the usual targets of natural product chemists, mainly due to their abundance and easy collection. Nevertheless, in the past few years, deep-water species from less diverse environments, such as temperate and Antarctic seas, have also led to the discovery of some interesting compounds (Rodríguez Brasco et al., 2007). Octocorals from tropical and temperate waters have been a prolific source of novel secondary metabolites, most of them derived from the mevalonate pathway, such as terpenoid and steroidal derivatives (Blunt et al., 2005; Rocha et al., 2011; Leal et al., 2012). Notably, the families Gorgoniidae and Plexauridae, the most abundant in Brazil,

have been demonstrated to contain a wide variety of compounds including steroids, acetogenins, sesquiterpenes and diterpenes. This group of marine invertebrates is recognized as an extremely rich source of bioactive secondary metabolites: and since these animals lack physical defenses, these compounds are generally believed to function as chemical defenses. It has been reported that 50% of soft coral extracts exhibited ichthyotoxic activities (Sammarco and Coll, 1998). An encyclopedic review of the octocoral chemistry published by Coll (1992) reviews the natural products, chemotaxonomy, chemical ecology and biosynthetic derivation of octocoral metabolites. Many of cembranoid diterpenes, secondary metabolites from soft corals, may be involved in ecological interactions (Coll, 1992), while other metabolites have antimicrobial (Correa et al., 2011), cytotoxic (Wang and Duh, 2012), antiviral (Yeh et al., 2012) and anti-inflammatory activities (Reina et al., 2011). In a recent review, the order Alcyonacea was proven to be the most promising source of compounds for therapeutic use. In the case of isolated compounds, terpenoids proved to be the most auspicious. The greatest interest, for which the most studies have been carried out, is antitumor activity (Rocha et al., 2011).

Marine organisms are an important source of new bioactive molecules; thus the scientific community worldwide is focusing its efforts on the isolation and characterization of biologically active natural products. A relatively small number of marine organisms studied have already yielded thousands of new chemical compounds; Porifera (class Demospongiae) and Cnidaria (class Anthozoa) being two main sources of new molecules (Blunt et al., 2014). Moreover, research of species from unexplored geographical sites with a high biological diversity and endemisms, such as species found in tropical regions, can provide novel marine bioactive compounds (Leal et al., 2012).

Despite the great biodiversity present along the Brazilian coastline, an important source of potential biologically active compounds, chemical analysis of Brazilian marine organisms is still incipient. So far, the chemistry of marine natural products in Brazil has focused on sponges, tunicates and brown algae (Berlinck et al., 2004). Regarding the chemical studies on octocorals, of the approximately 107 species reported in Brazil, to date only twenty have been studied, from which thirteen have been studied by Brazilian research groups (Chart 1).

In this review we report the secondary metabolites isolated from octocorals present or collected in Brazil, specifically focusing on their structures and biological activities, as well as their importance in chemical ecology.

The reported results are organized and discussed in light of the currently accepted taxonomical classification, and the compounds found in each family are exemplified. The results obtained from species collected in Brazil are shown, highlighting the most representative compounds present. Also, the results obtained from species present in Brazil, but collected worldwide, are further discussed. In conclusion, octocorals represent a potential source of new bioactive molecules that could be exploited more productively in this country.

#### Subclass Octocorallia

The octocorals present on the Brazilian Coast, from which secondary metabolites have been isolated, or that are believed to be potential sources of bioactive compounds, belong to the orders Alcyonacea and Pennatulacea. The former consists of the families Clavulariidae (Carijoa riisei), Nephtheidae (Chromonephthea braziliensis and Neospongodes atlantica), Ellisellidae (Ellisella elongate and Nicella goreaui), Primnoidae (Convexella magelhaenica, Dasystenella acanthina, and Plumarella aculeata), Acanthogorgiidae (Acanthogorgia spp.), Gorgoniidae (Leptogorgia punicea, L. setacea, L. violacea and Phyllogorgia dilatata), Plexauridae (Bebryce spp., Heterogorgia uatumani, Muricea spp., Muriceides hirtus, Muriceopsis flavida, Paramuricea placomus, Placogorgia atlantica, Plexaurella dichotoma, Plexaurella regia and Swiftia exserta), Anthothelidae (Tripalea clavaria), Coralliidae (Corallium spp.), and Paragorgiidae (Paragorgia johnsoni). The order Pennatulacea consists of the families Anthoptilidae (Anthoptilum murrayi), Virgulariidae (Stylatula spp.and Virgularia presbytes) and Renillidae (Renilla reniformis and R. muelleri). The species or genera of greatest interest are presented below.

#### **Order Alcyonacea**

The order Alcyonacea is comprised of soft corals (octocorals without a supporting skeletal axis) and gorgonians (octocorals with a supporting skeletal axis of scleroproteinous gorgonin and/or calcite). Families from the order Alcyonacea are primarily distinguished by their overall colony growth form, the presence or absence of a supporting skeletal axis and details of axial composition (Bayer, 1981). The order entails 31 families (McFadden et al., 2010) and 59 species from seventeen families are present in Brazil (Neves, 2010).

#### Family Clavulariidae

This family, widely distributed around the world, includes encrusting or branching colonies; the latter having primary polyps with lateral daughter polyps (Devictor and Morton, 2010).

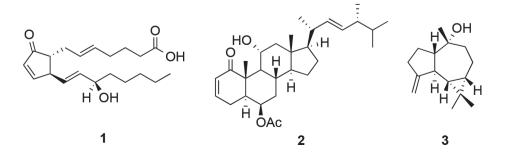
Many secondary metabolites have been isolated from species belonging to the Clavulariidae family, including prostanoids as claviridenone-A (1) (Kitagawa et al., 1985), steroids as yonarasterol A (2) (Iwashima et al., 2001), both from *Clavularia viridis*, and terpenoids as the aromadendrane-type sesquiterpenoid (3) from *Clavularia koelliker* (Iguchi et al., 2004).

#### Carijoa riisei (Duchassaing & Michelotti, 1860)

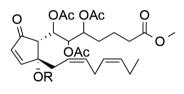
This species is an azooxanthellate octocoral commonly called "snowflake" or "branched pipe" coral. Its senior synonym Telesto riisei is still used in the literature. C. riisei commonly occurs from Florida (USA) to Santa Catarina state (Brazil) and across the Caribbean Sea (Pérez, 2002). C. riisei has also been reported on the Hawaiian coast and other sites in the Pacific Ocean (Zanzibar, Gulf of Sion, Singapore, Shanghai, Sumatra, Manila and Indonesia), as well as in the East Atlantic Ocean (Concepcion et al., 2008). In Brazil,, this species can be found from the mouth of the Amazon River (AP/PA) to Santa Catarina state, and at the Saint Peter and Saint Paul Archipelago. It is mainly found in shallow waters (< 30 m), but it can be found at depths of up to 95 meters (Bayer, 1959; Medeiros, 2005; Castro et al., 2010).

In general, pregnane-based steroids (Ciavatta et al., 2004; Diaz-Marrero et al., 2011), polyhydroxy steroids (Sung and Liu, 2010) and sterol glycosides (Liu et al., 2010) have been reported for the genus *Carijoa*. From *C. riisei* specimens collected in Hawaii, punaglandins (**4-11**) were isolated (Baker and Scheuer, 1994; Baker et al., 1985). These compounds, highly functionalized cyclopentadienone and cyclopentenone prostaglandins, are chlorinated at the endocyclic  $\alpha$ -carbon position and showed antiproliferative properties (Verbitski et al., 2004). Two acyl derivatives of  $\beta$ -phenylethylamine (**12** and **13**), and two tetrahydroxysterols (**14** and **15**), have been reported for *C. riisei* collected in Micronesia. All of them elicited mild toxicity to murine leukemia cells (P388) in culture (Liyanage and Schmitz, 1996).

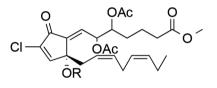
Concerning the species collected in Brazil, a polyhydroxy sterol (16) and sterol glycosides riiseins A and B (17 and 18) were isolated from the CH<sub>2</sub>Cl<sub>2</sub> crude extract of C. riisei collected in Rio de Janeiro. These compounds elicited in vitro cytotoxicity to HCT 116, a human colon adenocarcinoma cell line (Maia et al., 2000). Also, three  $C_{21}\Delta^{20}$  pregnanes and seven cholestane derivatives, ranging from steriods C26 to C29, were identified. The major component was found to be pregna-1,4,20-trien-3-one (19) (Maia et al., 1998). In 2007, Seleghim et al. (2007) reported the extract of Carijoa sp. from the São Paulo coastline elicit a high cytotoxic activity (against MC7- breast cancer cells, HCT8- colon cancer cells and B16- murine melanoma cancer cells), as well as having a growth inhibition effect on cancer cells growth of more than 75%. In the same year, Kossuga et al. (2007) reported the isolation of 18-acetoxypregna-1,4,20trien-3-one (20), previously isolated from C. riisei collected at Hawaii (Ross and Scheuer, 1979). This compound displayed mild cytotoxic activity against the cancer cell lines SF295,



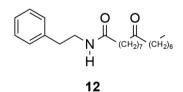
MDA-MB435, HCT8 and HL60. The steroid (18-acetoxypregna-1,4,20-trien-3-one) also displayed antileishmanial activity, with an  $IC_{50}$  value of 5.5 microg/ml against promastigotes and 16.88 microg/ml against intracellular amastigotes of *L.chagasi*; ,and showed mammalian cytotoxicity with an  $IC_{50}$  of 10.6 microg/ ml (Reimão et al., 2008). More recently, Almeida et al. (2012) described the antileishmanial activity against *L. braziliensis* of pregna-1,4, 20-trien-3-one (**19**), isolated from *C. riisei* collected in southern Brazil. Later on, Maia et al. (2013) studied the nature of carotenoids present in the same species collected at Rio de Janeiro.

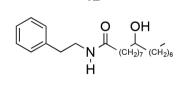


4 R=H 5 R=Ac 6 R=H 17,18-dihydro 7 R=Ac 17,18-dihydro

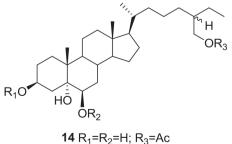


8 R=H 9 R=Ac 10 R=H 17,18-dihydro 11 R=Ac 17,18-dihydro

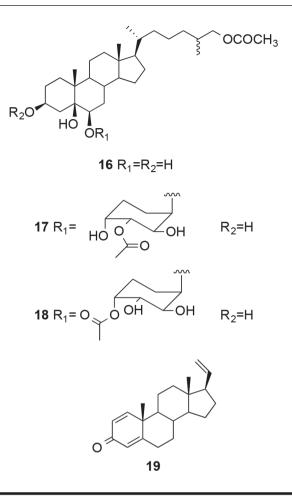








**15**  $R_1 = R_2 = R_3 = H$ 

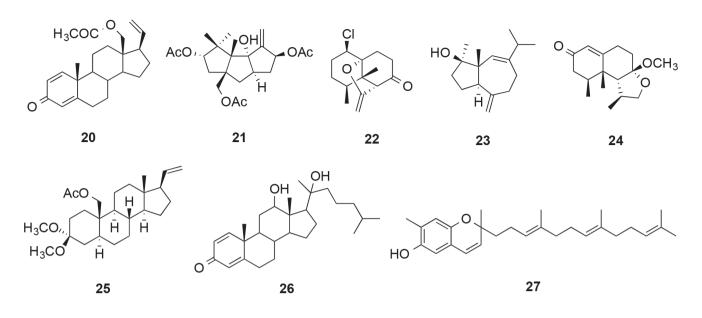


#### **Family Nephtheidae**

This family comprises twenty genera of azooxanthellate species, most of them arborescent, known as carnation corals, tree corals or colt corals. Two species of this family are found in Brazil (Daly et al., 2007; Castro et al., 2010). Numerous secondary metabolites have been isolated from these species, including steroids, diterpenoids, sesquiterpenoids and quinones; and many of them exhibit biological properties (Hu et al., 2011). Some examples of interesting compounds found in the family Nephtheidae are: acetoxycapnellene 2a,8β,13-triacetoxycapnell-9(12)-ene-10 $\alpha$ -ol (21) from Dendronephthya rebeola (Grote et al., 2007), paralemnolin A (22) from Paralemnalia thyrsoides (Huang et al., 2005), a guaiane-based sesquiterpene (23) from Nepthea chabrolii (Coll et al., 1985), flavalin E (24) from Lemnalia flava (Su et al., 2011), sclerosteroid J (25) from Scleronephthya gracillimum (Fang et al., 2013), polyoxygenated steroid cholesta-1,4-dien-12 $\beta$ ,16 $\beta$ , 20 $\alpha$ -triol-3-one from Chromonephthea sp. (26) (Geng et al., 2009) and tetraprenyl-benzoquinone derivatives from Nepthea sp. (27) (Coll et al., 1985).

#### Chromonephthea braziliensis van Ofwegen, 2005

Ferreira (2003) reported in the state of Rio de Janeiro this species as Stereonephthya aff. curvata (8-10 m) and in 2005 Ofwegen (Ofwegen, 2005) identified the same specimens as a new species of Chromonephthea. Ferreira noted that it was probably an invasive species possibly introduced to Brazil



by an oil platform, in the same way as the scleractinian *Tubastraea* (Ofwegen, 2005; Castro et al., 2010). *C. braziliensis* holds potential chemical activity which has been proposed by its allelopathic effect against the gorgonian *Phyllogorgia dilatata* (Ofwegen, 2005; Lages et al., 2006). The *n*-hexane extract of *C. braziliensis* collected in Rio de Janeiro exhibited potent feeding-deterrent properties against a natural assemblage of fish at the natural concentration, and led to the isolation of the compound 23-keto-cladiellin-A (**28**) (Fleury et al., 2008).

Polyenes belonging to the class of parrodienes were also characterized in this species (Maia et al., 2011b). Recent investigations show that extracts of *C. braziliensis* are genotoxic when evaluated by micronucleus formation and DNA breakage (Carpes et al., 2013). From *Chromonephthea* sp. collected in the South China Sea, some sterols were isolated (Geng et al., 2009), including polyhydroxysteroids (Zhang et al., 2010).

#### Neospongodes atlantica Kükenthal, 1903

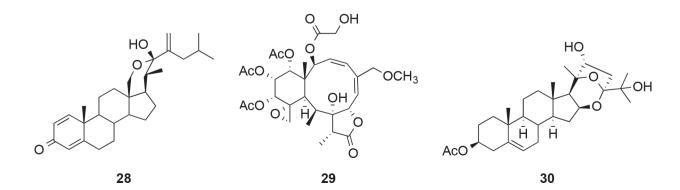
This is an endemic species found off the coasts of northeastern and eastern Brazil (Castro et al. 2010). The feeding deterrence property of the crude extract of N. *atlantica* collected from the National Marine Park of Abrolhos (Bahia state), was investigated; however it had no apparent effect over this property. In fact, it seemed to stimulate feeding (Epifanio et al., 1999).

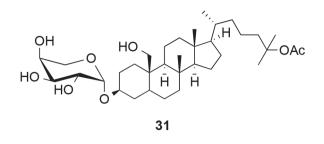
#### Family Ellisellidae

The family Ellisellidae is represented by four genera and is found mainly at shelf depths, although they can also occur at depths of up to 819 meters. Species of this family are characterized by the presence of sclerites, consisting of double heads and spindles or rods (Cairns, 2007). For the soft corals of the family Ellisellidae, mainly briarane-type diterpenoids were reported, such as gemmacolide A (29), and polyoxygenated steroids such as suberoretisteroid A (30) from *Verrucella umbraculum* and glycosides of steroids such as Junceelloside C (31) from *Dichotella gemmacea* (Jiang et al., 2013; Sun et al., 2010; Li et al., 2013a). Five species of this family are found in Brazil.

#### Ellisella elongata (Pallas, 1766)

Occurs in the western Atlantic, Florida, the Gulf of Mexico, the Caribbean, the northern coast of South America, and Brazil, where it can be found from Amapá to Santa Catarina (9-706 m) and at some submarine banks in the southeastern region (Deichmann, 1936; Bayer, 1959; Bayer, 1961; Medeiros, 2005). Bayer (1959) previously reported two species from Brazilian waters: E. elongata and E. barbadensis. However Castro et al. (2010) analyzed several Brazilian





specimens and opted to classify them as a single species. There are no chemical studies on *Ellisella elongata*, but many briarane-type diterpenes have been reported for the genera (Sung et al., 2008), including chlorinated compounds, mostly isolated from Ellisella robusta (Wang et al., 2010; Chang et al., 2010). 11,20-Epoxybriaranes were found to be a chemical marker for gorgonians belonging to the family Ellisellidae (Su et al., 2007).

#### Nicella goreaui Bayer, 1973

This species forms delicate colonies that distribute in the waters of the Bahamas, the southern Caribbean, and the state of Maranhão (Brazil) at depths ranging from 45 to 146 m (Cairns, 2007). Crude extract of *N. goreau* collected in the Caribbean showed feeding deterrence activity (O'Neal and Pawlik, 2002). 56276900 ext22710

#### **Family Primnoidae**

Among the Octocorallia, Primnoidae is the fourth largest family in terms of species richness, and it has worldwide distribution. It is found at depths from 8 to 5,850 m, although there are few records in shallower waters. Some primnoids are very abundant in deep waters, providing a habitat for fish and invertebrates (Cairns and Bayer, 2009). Six species of this family are found in Brazil (Medeiros, 2005; Neves, 2010). The family Primnoidae is typical of environments that are difficult to access, with low water temperatures and strong currents, which may explain the lack of chemical information on these species. Previous chemical investigations on soft corals of the family Primnoidae led to the isolation of polyoxynated steroid (24R, 22E)-24-hydroxycholest-4,22-dien-3-one (**32**) (Mellado et al., 2004) and the diterpenoids plumarellide (**33**) (Stonik et al., 2002) and ainigmaptilone A (**34**) (Iken and Baker, 2003).

#### Convexella magelhaenica (Studer, 1879)

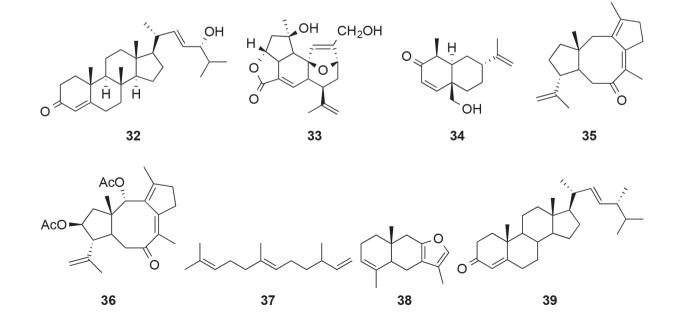
This sea whip has an amphiamerican subantarctic distribution, recorded in southern Chile and Argentina, as well as the Malvinas Islands, Burdwood Bank, and South Orkney Islands (Bayer, 1996). In Brazilian waters, *C. magelhaenica* has been reported in the state of Rio Grande do Sul (Bemvenuti, 1998).

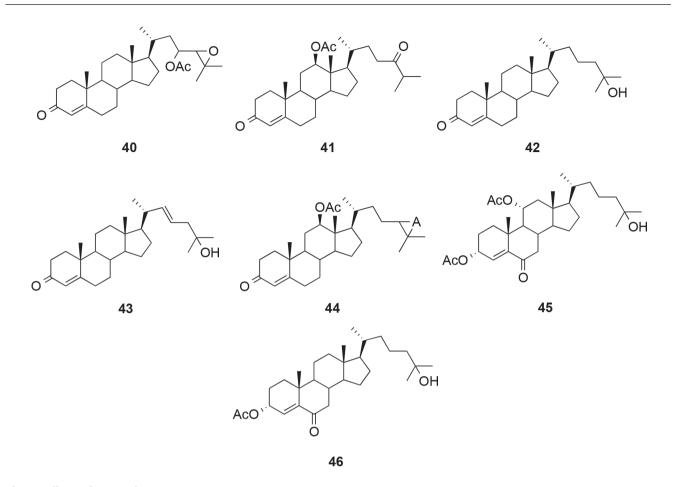
Almeida et al. (2010) isolated two new bioactive dolabellane diterpenoids (**35** and **36**) from *C. magelhaenica* collected in Argentina at a depth of 100m. Both compounds were cytotoxic against a human pancreatic adenocarcinoma cell line at micromolar concentrations.

#### Dasystenella acanthina (Wright & Studer, 1889)

D. acanthina has been reported in the southwestern Atlantic as well as in Brazilian waters, off the coast of the state of Rio Grande do Sul (8,101 m) (Medeiros, 2005).

Two furanosesquiterpenoids; trans- $\beta$ -farnesene (37) and isofuranodiene (38) (Gavagnin et al., 2003), and polyoxygenated steroids (39-46) (Mellado et al., 2004), have been isolated from the Patagonian gorgonian *D. acanthina*.





#### Plumarella aculeata Cairns & Bayer, 2004

This species is commonly found in the Western Atlantic, on the coasts of Florida (USA), the Bahamas (Caribbean) and the state of São Paulo (Brazil) at depths of 400 to 900 m (Medeiros, 2005; Cairns, 2007). There are no chemical studies on P. aculeata. Two cytotoxic diterpenoids, plumarellide and the ethyl ester of plumarellic acid were isolated from *Plumarella* sp., found in the Russian Kuril Islands (Stonik et al., 2002).

#### Family Acanthogorgiidae

This family is distributed over the Atlantic Ocean and the Mediterranean Sea, it is subdivided in eight genera, of which only one has been reported in Brazil, represented by two species, (Acanthogorgia aspera and Acanthogorgia schrammi), and yet no chemical studies have been published. For other species of the family Acanthogorgiidae, 9,10-secosterols isolated from methanolic extract of a gorgonian octocoral collected in Japan was lethal to Artemia salina, (LD<sub>50</sub> values ranging from 1.0 to 10 ppm) and inhibited insect growth in the silkworm, Bombyx mori (Ochi et al., 1990). From species of the family Acanthogorgiidae, steroids as Acanthovagasteroid A (47) (Zhang et al., 2004) and a diversity of terpenes such as eunicellin diterpenes from Muricella subogae (48) (Li et al., 2013b), xenicane norditerpenes and diterpenes from Acalycigorgia inermis, such as 9-deoxy-xeniolide-A (49) (Rho et al., 2001), and guaiazulene-based terpenoids (50, 51) (Seo et al., 1996; Chen et al., 2012a,b) were isolated.

The steroids acanthovagasteroids A-D were isolated from the gorgonian *Acanthogorgia vagae* from the South China Sea. This was the first report of the 19-hydroxy steroid from a gorgonian, and the suggested biosynthetic route between 19-nor and 19-hydroxy steroids (Zhang et al., 2004). Besides steroids, the authors have isolated lindenene, lindestrene, bebryazulene, furanodiene (Zhang et al., 2003), germacrone, 15-acetoxyfuranodiene, (1R,2E,4Z,7E,11E)-cembra-2,4,7,11-tetraene, thunbergol and its 4-epimer (Zhang et al., 2005). It also has been described a xenicane-based norditerpene, isoacalycixeniolide-A, from the gorgonian *Acanthogorgia turgida*, found in the coasts of India. Other xenicane norditerpenes from the genus were reported previously (Manzo et al., 2009).

#### Family Gorgoniidae

The family Gorgoniidae is one of the most abundant and diverse in the Atlantic Ocean. It is characterized by its high morphological plasticity, among other morphological traits, which often complicate taxonomic classification. The polyps are retractable and the stems have an axis of gorgonin surrounding a narrow, hollow, cross-chambered central core. Ten species of this family are found in Brazil (Castro et al., 2010; Neves, 2010). The features that separate the members of the different genera include the presence of furanocembranolides, as pukalide (52) and lophotoxin (53) (Missakian et al., 1973; Fenical et al., 1981), the branching pattern, and the morphology of the whole colony. There is an increase in complexity from unbranched whip forms to open branched forms, reticulate forms, and leafy frond forms. The most common natural products from gorgonians are diterpenes (Berrue and Kerr, 2009).

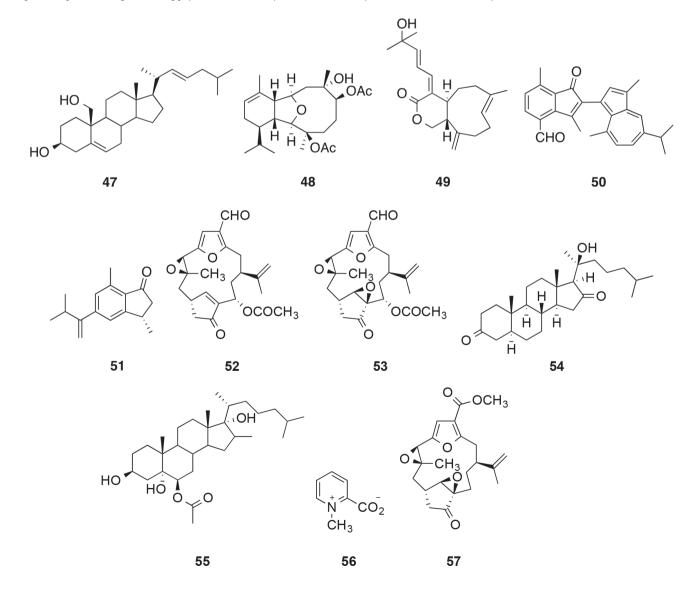
The genus *Leptogorgia* is, in general, chemically well studied. Initial works isolated some cembrene diterpenoids like lophotoxin (53), a neurotoxin originally isolated from the Pacific Ocean gorgonians *L. rigida*, *L. alba* and *L.cuspidata* (Fenical et al., 1981). In addition to the diterpenoids, some species present cytotoxic polyoxygenated steroids, such as compound 54, isolated from *L. sarmentosa* collected in the Strait of Gibraltar (Garrido et al., 2000).

#### Leptogorgia punicea (Milne Edwards & Haime, 1857)

Recorded for shallow waters on the Brazilian coast (up to 22 m depth), it can also be found in deeper waters (72 m depth on Florida, USA) (Bayer, 1961; Medeiros, 2005). From *L. punicea*, collected in southeastern Brazil, hydroquinone, common C26 to C29 cholestane sterols, and an uncommon polyhydroxylated sterol, punicin (55), which possess a C-17 hydroxyl group, were isolated (Epifanio et al., 1998). Pigments related to the carotenoid astaxanthin were also characterized in the same species by Raman spectroscopy (Maia et al., 2013).

#### Leptogorgia setacea (Pallas, 1766)

The species distributes from Chesapeake Bay (USA) to Uruguay at depths up to 60 m (Deichmann, 1936; Bayer, 1961; Medeiros, 2005). Targett et al. (1983) showed that homarine (N-methyl-2-carboxypyridine) (56) isolated from L. setacea inhibits the growth of the fouling diatom, N. salinicola, by 50-60%. A furanocembranolide, 11β,12β-epoxypukalide (57), was isolated from the gorgonian L. setacea, collected in Texas (Ksebati et al., 1984). L. virgulata (= L. setacea) extract inhibits the settlement of the barnacle Balanus amphitrite, activity was attributed to the diterpenoids pukalide (52) and epoxypukalide 57 (Gerhart et al., 1988). Gerhart and Coll (1993) demonstrated that pukalide (52), which comprises as much as 0.1-0.5% of the wet tissue weight of L. virgulata, induces vomiting in fish and may function as a defensive toxin by inducing emesis and learned aversion in potential octocoral predators. Further, the reported antimicrobial activity of extract of L. virgulata was attributed to the compound homarine 56 (Shapo et al., 2007). Conjugated polyenals were also investigated in L. setacea from Brazil (Maia et al., 2011b; 2013).



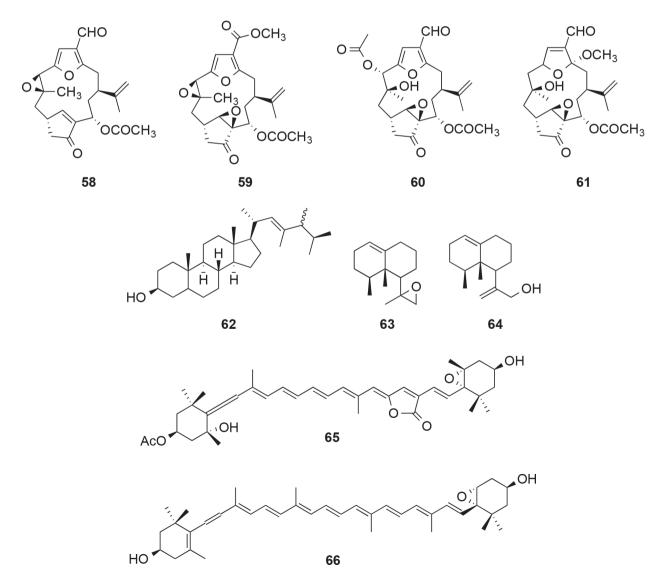
#### Leptogorgia violacea (Pallas, 1766)

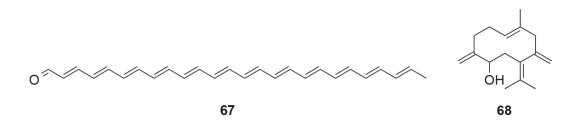
Endemic to the Brazilian coast, *Leptogorgia violacea* is found at Espírito Santo state and Rio de Janeiro (3-60 m) (Medeiros, 2005). A complex mixture of furanocembranolides from *L. violacea* was found to be responsible for feeding deterrence of generalist fish. The most potent feeding deterrent identified was lophotoxin (53), followed by deoxylophotoxin (58), and 13-acetoxy-11 $\beta$ ,12 $\beta$ epoxypukalide (59), as well as the furanocembranolides 7-acetoxy-8-hydroxylophotoxin (60) and 3-methoxy-8-hydroxylophotoxin (61) (Epifanio et al, 2000). Polyenals such as parrodienes were also identified in the same species (Maia et al., 2011b).

#### Phyllogorgia dilatata (Esper, 1806)

This genus Phyllogorgia is endemic to Brazil and can be found from Fortaleza (Ceará) to Cabo Frio (Rio de Janeiro), Rocas Atoll, Fernando de Noronha and Trindade Island (Castro et al., 2010; Bayer, 1961). The first chemical study of P. dilatata, collected in the state of Rio de Janeiro, revealed the presence of  $23,24\xi$ -dimethylcholesta-5,22-dien-3 $\beta$ -ol (62) (Kelecom et al., 1980). Moreover, nardosinane sesquiterpenes, 11,12-epoxynardosin-1(10)-ene (**63**) and 12-hydroxynardosin-1(10),11(13)-diene (**64**), were isolated from the same species (Kelecom et al., 1990; Fernandes and Kelecom, 1995). Further investigation isolated the symbiotic pigment peridinin, a C37 carotenoid with an allenic-lactonic group (**65**) (Martins and Epifanio, 1998), diadinoxanthin (**66**) (Maia et al., 2013) and characterized long-chain polyenal pigments, such as compound **67** (Maia et al., 2011a).

The icthyodeterrent diterpene  $11\beta$ ,  $12\beta$ -epoxypukalide (57), isolated previously from L. setacea, and the sesquiterpene (E)-germacra-1(10), 4(15), 7(11)-trien-5-ol-8-one (68) were found in P. dilatata (Martins and Epifanio, 1998). The diterpene  $11\beta$ ,  $12\beta$ -epoxypukalide (57) was proven to to be used as a chemical defensive strategy against natural generalist fish predators (Lages et al., 2006). Also, the compound displayed antifouling property when tested on Perna perna (Epifanio et al., 2006). In another study, the crude organic extract of P. dilatata elicited antifouling activity, inhibiting the settlement of barnacles (Pereira et al., 2002). A novel antimicrobial peptide was recently reported for this species, which was able to control the growth of K. pneumoniae, S. flexineri and S. aureus (de Lima et al., 2013).







The Plexauridae is a highly diverse family, widely distributed around the world. Currently it comprises the ancient family Paramuriceidae as a subfamily. Twenty-six species of this family are found in Brazil (Castro et al., 2010; Neves, 2010).

A recent review of the natural products of the family Plexauridae describes substances already isolated from several species; the most common are terpenoids, mainly guaiane-type diterpenes (69) and other classes of diterpenes like eunicellin (70) and clerodane (71). Moreover, alkaloids as nuttingin A for *Euplexaura nuttingi* (72), and polyoxygenated steroids such as bebrycoside from *Bebryce indica* (73) were also isolated (Wang et al., 2012).

#### Bebryce spp.

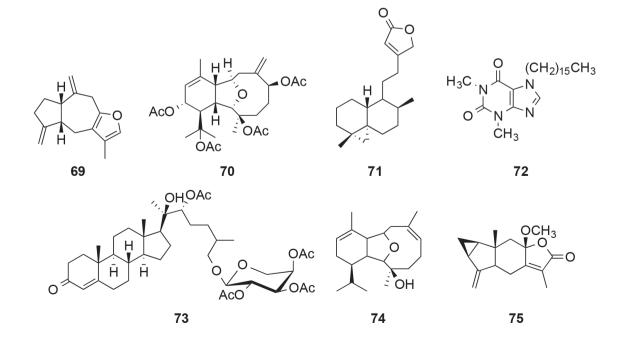
Two species of this genus have been reported in Brazil: B. *cinerea* Deichmann, 1936 and B. *parastellata* Deichmann, 1936 (Jiang et al., 2013). There are no chemical studies on this species, but for other species of Bebryce, the presence of a guaiane sesquiterpene (Aknin et al., 1998), a steroidal glycoside (Yang et al., 2007), and polyhydroxysterols (Sung and Liu, 2010) have been reported.

#### Heterogorgia uatumani Barreira e Castro, 1990

Registered in the Caribbean and Brazil, this is the only record of the genus on the Atlantic Ocean (Breedy and Guzman, 2011), found mainly in shallow waters (< 50 m) (Medeiros, 2005). In Brazil, this species has been recorded at the states of Amapá, Bahia, Espírito Santo, Rio de Janeiro, São Paulo and Santa Catarina at depths up to 68 m (Medeiros, 2005; Castro et al., 2010). Studies of the Brazilian gorgonian H. *uatumani* have resulted in the discovery of two metabolites, the eunicellane diterpenoid, (6E)- $2\alpha$ , $9\alpha$ -epoxyeunicella-6,11(12)-dien- $3\beta$ -ol (74) and the sesquiterpene lactone heterogorgiolide (75), which inhibit fish feeding under natural conditions (Maia et al., 1999).

#### Muricea spp.

Four species from the genus Muricea have been registered in Brazil, Muricea atlantica (Kukenthal, 1911), M. flamma (Marques and Castro, 1995; Breedy and Guzman, 2011), M. laxa Verrill, 1864 and M. midas Bayer, 1959 (Bayer, 1959). Several compounds have been reported for Muricea species: hydrocarbons and eicosanoids (Camacho et al., 2011), tyramine derivatives, sesquiterpenoids, steroidal pregnane glycosides (Murillo-Alvarez and Encarnacion-Dimayuga, 2003; Gutierrez et al, 2006), norsteroid (Popov et al., 1983), 24(28)-epoxide sterol (Lorenzo et al., 2006), degraded pregnanes (Ortega et al., 2002), and saponins (Bandurraga and Fenical, 1985; Gutierrez et al., 2004). Regarding the species collected in Brazil, astaxanthin and polyenals have been identified in M. atlantica and M. flamma, respectively (Maia et al., 2013).



#### Muriceides hirtus (Pourtalès, 1868)

The species occurs in the western Atlantic off the coasts of Florida (USA), the Caribbean and Brazil, where it has been reported in Amapá (off Amazon River mouth, 234 m) and Rio Grande do Sul (Bayer, 1996; Medeiros, 2005). The only chemical study of the genera describes the presence of common sterols and nucleosides from *Muriceides collaris* from China (Shi et al., 2009).

#### Muriceopsis flavida (Lamarck, 1815)

Recently recorded in Brazilian waters, Muriceopsis flavida can be distinguished by its pinnate colonies with sparse branches. Previously registered for the Caribbean, it can also be found off the coasts of the states of Maranhão, Pernambuco and Alagoas (Brazil) (Pérez et al., 2011; Bayer, 1961). The first chemical study on M. flavida reported the presence of sterols, 76-82, including  $4\alpha$ -Me sterols 83-87, the biosynthesis of which is normally attributed to the dinoflagellate symbionts in zooxanthellated octocorals (Kokke et al., 1982). From M. flavida collected in the China Sea, two antimicrobial sesquiterpenes, menverins C (88) and D (89) (Liu et al., 2012), as well as five epidioxy sterols, like 90-94 (Liu et al., 2011), were isolated. More recently, three new polyhydroxysterols, named muriflasteroids A-C (95-97), together with sixteen known analogs, were isolated also and exhibited different levels of growth inhibition activity against A549 and MG63 cell lines. Some can significantly induce apoptosis in A549 cells. The same study suggests that the acetylation on 3-OH and the appearance of D7 may decrease the apoptotic activity, while the substitution of 1-OH and the nature of the side chain may also play an important role in the activity (Liu et al., 2013).

#### Paramuricea placomus (Linnaeus, 1758)

Reported in Europe, North America, the Mediterranean Sea and Brazil, where it can be found in the states of Bahia and Espírito Santo (665 to 935 m) (Medeiros, 2005). There are no chemical studies on this species, but from the genus *Paramuricea*, cytotoxic linderazulenes (Reddy et al., 2005), caffeine (Imre et al., 1987), linderazulene (Imre et al., 1981), and simple indole derivatives in *P. chamaeleon* (Cimino and De Stefano, 1978) have been isolated.

#### Placogorgia atlantica Wright & Studer, 1889

Occurs in Barbados (Caribbean), Amapá, Saint Peter and Saint Paul Archipelago and Bahia at depths up to 1,700 m (Medeiros, 2005). There are no chemical studies on this species, but a guaianolide yellow pigment was isolated from *Placogorgia* sp. from Hawaiian waters (Li and Scheuer, 1984).

#### Plexaurella dichotoma (Esper, 1791)

Found in Bermuda, Florida, Bahamas, the Antilles (Caribbean) and Parcel Manuel Luiz, Rocas Atoll, and Fernando de Noronha (Brazil) (Bayer, 1961; Castro et al., 2010). The species has considerable morphological variability, which may explain the high number of synonymies (Castro et al., 2010). The first chemical studies on P. dichotoma, and also the first study on octocorals in Brazil, identified cetyl palmitate in its wax (Sharapin, 1968; Rodríguez et al., 1983). Furthermore, Weinheimer et al. (1967) showed that P. dichotoma from Jamaica contained (+)- $\alpha$ -muurolene (98) and (+)- $\beta$ -bisabolene (99). These sesquiterpenes isolated from gorgonians were enantiomers of those commonly found in terrestrial plants. Di Marzo (1996) presented evidence in P. dichotoma for the presence of 11-R-hydroxy-5Z,8Z,12E,14Z-eicosatetraenoic acid (100), as well as the enzyme responsible for its biosynthesis.

#### Plexaurella regia Castro, 1986

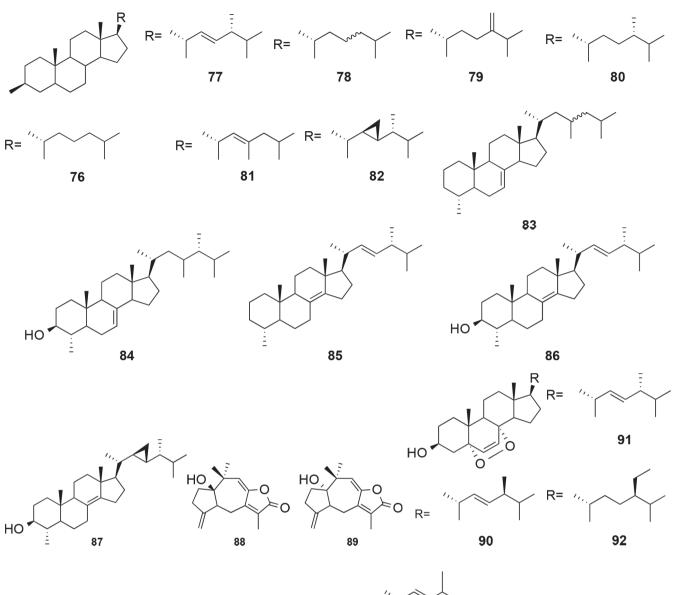
This endemic species is found off the coast of the southern parts of Bahia, Brazil. Typical of shallow waters, Castro et al. (2010) pointed out that this species seems to be restricted to reefs located more than 5 km from the coast.

Epifanio (1999) studied the potential chemical defenses of the crude extract of P. regia, collected at the National Marine Park of Abrolhos (state of Bahia), and found that it appeared to stimulate feeding, presenting no feeding deterrence property. Octocorals of the genus Plexaurella are known to be the source of a diverse array of sesquiterpenes. A study involving an examination of the terpene chemistry of five of the six known species of this genus to identify links between sesquiterpene composition and species, location, and depth, indicated a high level of variability of sesquiterpene content and essentially no correlation between species and sesquiterpene chemistry, concluding that Plexaurella spp. is a chemically indistinguishable species with respect to terpene chemistry (Frenz-Ross and Kerr, 2009). In addition, gorgonians from the Plexaurella genera are known to contain prostaglandinlike compounds, as well as other products of arachidonic acid lipoxygenation, and the formation of the latter has been suggested as representing the first step in prostaglandin biosynthesis. PGA2 and its ester derivatives comprise as much as 8% of the wet tissue weight of some octocoral species, such as Plexaura homomalla. These high levels of prostaglandins, although initially palatable to fish, may function as defensive toxins by inducing emesis and learned aversions in potential predators (Gerhart and Emesis, 1991). For Plexaurella spp. sesquiterpenes and sterols have been reported (Jeffs and Lytle, 1974; Gopichand et al., 1980; Pruna et al., 1982; Rueda et al., 2001a,b; Bashyal et al., 2006).

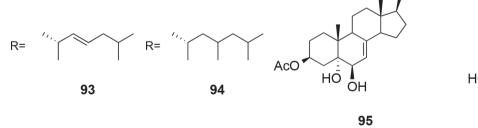
#### Swiftia exserta (Ellis & Solander, 1786)

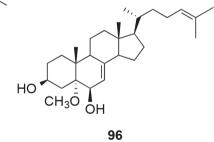
Distributed in the western Atlantic along the coast of Florida (USA), the Gulf of Mexico, the eastern Caribbean and Brazil, this species has been seen in the states of Pará (110 m), Maranhão (110 m) and Rio de Janeiro (50 m) (Deichmann, 1936; Goldberg, 2001; Medeiros, 2005). It distributes mainly in deep water, but can also be found in shallower environments (Goldberg, 2001).

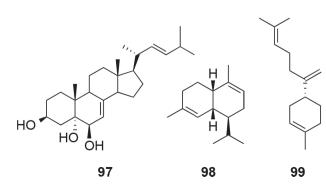
Two patents exist for S. *exserta*: one relating to its source of terpenes, obtained through direct culture of microbial populations derived from coral homogenates (Kerr and Brueck, 2007) and the other related to an antiproliferative glycosylated pregnene (Wright et al., 2004), swiftiapregnene (**101**).

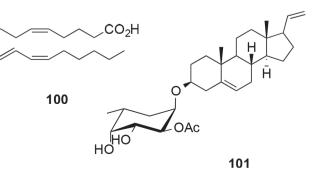


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#### Family Anthothelidae

The family is composed of species with a ring of longitudinal boundary canals separating the medulla from the cortex (Bayer, 1961). There are thirteen genera, of which four occur in Brazilian waters. Previous studies have reported a tricyclic sesquiterpene and its dimer, named alertenone (**102** and **103**) from Alertigorgia sp. collected in Australia, and secosteroids (**104-110**) from Tripalea clavaria (Rodríguez Brasco et al., 2007; Bokesch et al., 1999).

#### Tripalea clavaria (Studer, 1878)

This species is a colonial octocoral adapted to different environments. It is distributed across South America, from the coast of Bahia (Brazil) to Argentina (Bayer, 1961; Pérez and Neves, 2007). Seven  $\Delta^5$ , 9,11-secosteroid with a 22S hydroxyl **104-110** were isolated from *T. clavaria* collected in Argentina (Rodríguez Brasco et al., 2007). Some of them presented antimicrobial activities.

#### **Family Coralliidae**

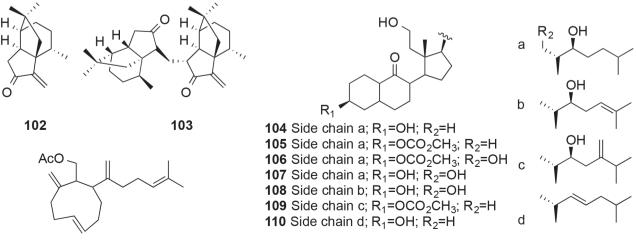
Two species of the family are recorded in Brazil, Corallium medea Bayer, 1964 and C. niobe Bayer, 1964 (Medeiros, 2005), but there are no chemical studies. The only compounds reported for this family were isolated from Corallium sp. and Corallium rubrum. The diterpenes, corabohcin (111) and the coraxeniolides A (112), B (113) and the epimers C and C' (114 and 115) were isolated from the Hawaiian deep sea gorgonian Corallium sp. (Schwartz et al., 1981). Corallium rubrum, another species from the Mediterranean Sea, has been widely studied for its polyconjugated pigments. Initial works proposed that canthaxanthin (116) is the main carotenoid in this species (Cvejic et al., 2007), however, recent studies have demonstrated that the nature of the pigments is probably demethylated polyenes (Brambilla et al., 2012).

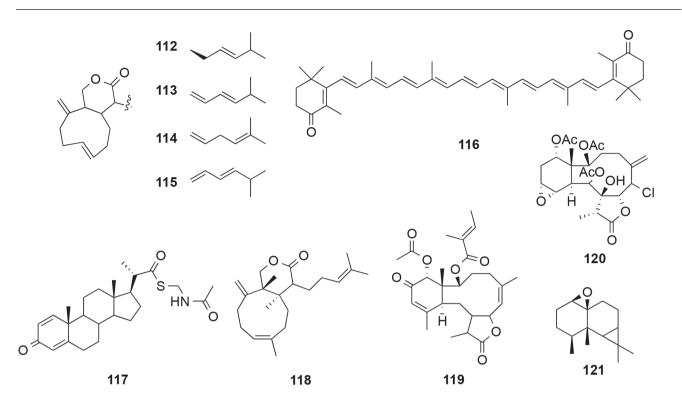
#### Family Paragorgiidae

Also known as bubblegum octocorals, the species of this family are abundant and widely distributed in deep waters all over the world. They have unfused sclerites instead of the calcified or corneous skeletons found on most octocorals, and they are extremely important as they provide a three-dimensional habitat for many deep-sea communities of species (Herrera et al., 2010). The family is comprised by two genera, one of them present in Brazilian waters. The only isolated compounds reported are those from species of *Paragorgia* genus.

#### Paragorgia johnsoni Gray, 1862

This species has been reported off the coast of Florida, central Atlantic Ocean, the Mediterranean Sea and the coasts of Brazil, from Bahia (up to 750 m) to Rio de Janeiro (up to 1,059 m) (Medeiros, 2005). There are no chemical studies for Paragorgia johnsoni, but some compounds have been reported for the genera. The first natural steroid bearing a C22 thioester in its side chain, parathiosteroids A (117), was isolated from the 2-propanol extract of Paragorgia sp. collected in Madagascar. These compounds displayed cytotoxicity against three human tumor cell lines at micromolar level, and its structureactivity relationship has been investigated (Poza et al., 2008). In P. arborea, joastaxanthin and canthaxanthin-like carotenoids were identified (Elde et al., 2012). Also, it was shown that lipophilic compounds at high concentrations stimulate defensive responses in red-colored P. arborea, while in white coral colonies it did not produce significant defensive behavioral responses in fish (Bright-Diaz et al., 2011). For the same species, diterpenes of the xeniane series (118) (D'Ambrosio et al., 1984; Stonik et al., 1990) and tetracosapentaenoic acid (Vysotskii et al., 1990) have been reported.





#### **Order Pennatulacea**

The order includes sea pens and sea pansies, which are distributed throughout all oceans in polar and tropical regions, at depths up to 6,100 meters. The majority is adapted to soft sediments, and has a peduncle, which they use to anchor onto sand or mud. Since these corals do not depend on hard substrate, they can frequently distribute over large areas (Williams, 2011). Pennatulaceans are a highly specialized group of octocorals that differ markedly from other soft corals with reference to their colonial structure and habitat utilization. Morphologically, they are highly diverse, with perhaps 300 or more valid species within 35 genera of fourteen families (McFadden et al., 2010), seven of them reported for Brazil, represented by seventeen species/morphotypes (Neves, 2010; Neves and Pérez, 2012). Regarding chemical studies, briarane-type diterpenes predominate among Pennatulacea (Sung et al., 2008; 2011).

#### Family Anthoptilidae

This family, comprised of only two species classified as a single genus, seems to be cosmopolitan, occurring from shelf to abyssal environments.

#### Anthoptilum murrayi Kölliker, 1880

This deepwater species is found in southern Brazil, in the Campos Basin at depths of 1,059 to 1,114 meters (Arantes et al., 2009). There are no chemical studies on this species, but briarane-type diterpenes, as anthoptilide A, have been isolated from the Australian A. *kukenthai* (**119**) (Pham et al., 2000).

#### Family Virgulariidae

This family has colonies with bilateral symmetry and autozooids arranged in leaves (Devictor and Morton, 2010). Five species of this family are found in Brazil (Neves, 2010). Chemical studies report their terpenoid content, mainly briarane diterpenoids (120), sesquiterpenoids (121) and steroids (122) (Do and Erickson, 1983).

#### Stylatula spp.

Three species have been identified in Brazil: Stylatula brasiliensis Gray, 1870, S. darwini Kölliker, 1870 and S. diadema Bayer, 1959 (Neves, 2010). There are no chemical studies on these species, but the diterpene toxin stylatulide, as well as other briaranes, have been isolated from Stylatula sp. collected in shallow waters of Baja California, and Mexico (Wratten et al., 1977; Wratten and Faulkner, 1979).

#### Virgularia presbytes Bayer, 1955

This sea whip is distributed along the east coast of America from Florida to Rio de Janeiro, Brazil (Neves, 2010). There are no chemical studies regarding this species, however, fatty acids, sterols, sesquiterpenes and diterpenes have been reported for *V. juncea*, collected in shallow-waters located on the west coast of Taiwan (Chen et al., 2001).

#### **Family Renillidae**

This family includes only the genus *Renilla*, known as "sea pansy". It is distinguished by its heart-shaped colonies containing a primary polyp that is broad and flattened, with siphonozooids and autozooids on the upper surface (Devictor and Morton, 2010). Anthozoan octocorals belonging to the genus *Renilla* are members of sublittoral soft-bottom communities, ranging from nearshore (2 m) to deeper (128 m) waters (Clavico et al., 2007). Five species of this family are found in Brazil (Zamponi et al., 1997; Neves, 2010). The only compounds reported are those isolated from *R. reniformis*, *R.muelleri* and *R. octadentata*.

Two conjugated polyunsaturated fatty acids, renillenoic acids, were isolated from the Patagonian species *Renilla* octodentata. These compounds showed both anti-feeding properties against the generalist fish predator Pagrus pagrus, and anti-settlement activity against cypris larvae of the barnacle Amphibalanus amphitrite (Garcia-Matucheski et al., 2012).

Regarding the species found in Brazil, recent chemical and ecological studies were performed on R. *muelleri* and R. *reniformis* collected at Rio de Janeiro: polyenals were characterized by Raman spectroscopy in R. *muelleri* (Maia et al., 2013) and both species were investigated for their potential chemical and physical defenses against fishes in field feeding assays (Clavico et al., 2013). On the other hand, briaranetype diterpenoids are the main active secondary metabolites isolated from R. *reniformis* species.

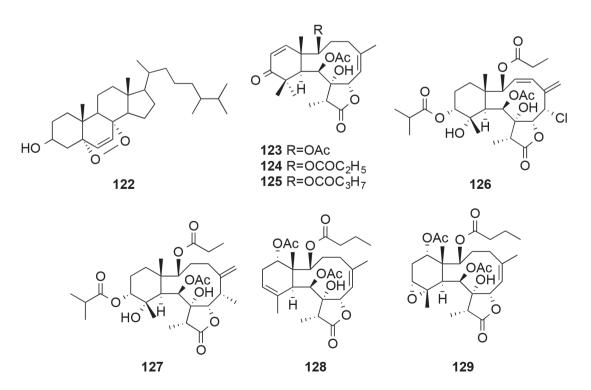
#### Renilla reniformis (Pallas, 1766)

This species has been reported in the USA, the Caribbean, Brazil and Argentina. In Brazilian waters, it can be found on Ceará, the Campos Basin, São Paulo, Paraná and Rio Grande do Sul

(Medeiros, 2005; Castro et al., 2010; Da Silveira and Morandini, 2011). R. reniformis is capable of exhibiting bioluminescence when disturbed, due to the interplay between a luciferase and a Green Fluorescent Protein. The Renilla genus is widely studied in relation to those molecules that have become extremely important for modern biological science (Loening et al., 2007). However there are few reports regarding the secondary metabolites of this species. Prior studies on the chemistry of a North Carolina population of R. reniformis resulted in the isolation of antifouling briarane diterpenoids, renillafoulins A-C (123-125), which inhibit the settlement of the larvae of the barnacle Balanus amphitrite, indicating a promising use of those compounds as a method of inhibiting fouling by these organisms, thus providing an alternative to the current toxic materials used in coatings, which cause serious environmental problems (Keifer et al., 1986). From the sea pansy collected in shallow waters of Georgia, renillins A-D (126-129) were isolated and it was demonstrated that they deterred feeding of the predatory lesser blue crab, Callinectes similis, as well as of the predatory mummichog fish, Fundulus heteroclitus (Barsby and Kubanek, 2005).

#### **Concluding remarks**

Notwithstanding the extensive Brazilian coastline (ca. 8.000 km), and the distribution of octocorals in most tropical and subtropical marine habitats, only a limited number of these organisms has been described for this region so far. Regarding their chemical or biological activities, from the ca. 107 species of occurrence in Brazil, only twenty species have been studied, thirteen by Brazilian research groups. Among the studied species, 20% are endemic to this country and most belong to families Gorgoniidae (20%) and Plexauridae (35%); some of the richest sources of bioactive



#### Chart 1

Biological activities of extracts and/or compounds reported for octocorals recorded in Brazil.

Species	Extracts/Compounds	Biological activities	References
Carijoa riisei <sup>a</sup>	polyoxygenated steroids, sterol glycosides	cytotoxicity	Maia et al., 2000
	punaglandins	antiproliferative	Baker and Scheuer, 1994; Baker et al., 1994; Verbitski et al., 2004
	pregnanes	antileishmanial	Maia et al., 1998; Almeida et al., 2012
	amides, polyoxygenated steroids	cytotoxicity	Liyanage and Schmitz, 1996
	18-acetoxypregna-1,4,20-trien-3- one	cytotoxicity, antileishmanial	Seleghim et al., 2007; Kossuga et al., 2007; Ross and Scheuer, 1979; Reimão et al., 2008
	carotenoids		Maia et al., 2013
Chromonephthea braziliensis	23-ketocladiellin-A	feeding deterrent	Fleury et al., 2008
	polyenes	-	Maia et al., 2011b
	extract	feeding deterrent	Lages et al., 2006
	extracts	genotoxicity	Carpes et al., 2013
Convexella magelhaenica	dolabellane diterpenoids	cytotoxicity	Almeida et al., 2010
Dasystenella acanthina	sesquiterpenoids, polyoxygenated steroids	-	Mellado et al., 2004; Gavagnin et al., 2003
Heterogorgia uatumani <sup>a</sup>	eunicellane diterpenoid, sesquiterpene lactone, heterogorgiolide	feeding inhibition	Maia et al., 1999
Leptogorgia puniceaª	hidroquinone, steroids, punicin		Epifanio et al., 1998
	carotenoids	-	Maia et al., 2013
Leptogorgia setacea	pukalide 11β,12β-epoxypukalide	antifouling, feeding deterrent	Ksebati et al., 1984; Gerhart et al., 1988; Gerhart et al., 1993
	homarine	antifouling, antimicrobial	Targett et al., 1983; Shapo et al., 2007
	polyenals	-	Maia et al., 2013
Leptogorgia violacea (E)ª	lophotoxin, deoxylophotoxin, 13-acetoxy-11β,12β-epoxypukalide, furanocembranolides	feeding deterrent	Epifanio et al., 2000
	polyenals	-	Maia et al., 2011b
Muricea atlântica	carotenoids	-	Maia et al., 2013
Muricea flamma	polyenals	-	Maia et al., 2013
Muriceopsis flavida	steroids, sesquiterpenes	antimicrobial	Kokke et al., 1982; Liu et al., 2012; 2011
	steroids	antiproliferative	Liu et al., 2013
Neospongodes atlantica (E)ª	crude extract	feeding stimulation	Epifanio et al., 1999
Nicela goreauii	crude extract	feeding deterrent	O'Neal and Pawlik, 2002
Phyllogorgia dilatata (E) <sup>a</sup>	steroids	-	Kelecom et al., 1980
	diterpene epoxypukalide,		
	germacrane sesquiterpene	antipredatory, antifouling	Epifanio et al, 1999; 2006; Martins and Epifanio, 1998
	nardosinane sesquiterpene	-	Kelecom et al., 1980; Fernandes and Kelecom, 1995
	crude extract	antifouling	Pereira et al., 2002
	polyenals, carotenoids	-	Maia et al., 2011a; 2013
	peptide	antimicrobial	De Lima et al., 2013
Plexaurella dichotomaª	cetylpalmitate	-	Rodríguez et al., 1983
	eicosatetraenoic acid	-	Di Marzo et al., 1996
	muurolene sesquiterpene, bisbolene	-	Weinheimer et al., 1967

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Species	Extracts/Compounds	<b>Biological activities</b>	References
Renilla reniformis	briarane-type diterpenes	antifouling, feeding deterrent	Rueda et al., 2001; Barsby and Kubanek, 2005
	extracts	feeding deterrent	Clavico et al., 2013
Renilla muelleri	polyenals	-	Maia et al., 2013
	extracts	feeding deterrent	Clavico et al., 2013
Swiftia exerta	glycosylated pregnene	-	Wright et al., 2004
Tripalea clavaria	secosteroids	antimicrobial	Rodríguez Brasco et al., 2007

compounds in Phylum Cnidaria. A total of 106 compounds were isolated from these twenty species, consisting mostly of steroids (ca. 58%), diterpenes (ca. 15%), sesquiterpenes (ca. 8%) and prostaglandins (ca. 8%), with 3% amines and ca. 6% other compounds from diverse classes. In addition, 9% of the isolated substances are halogenated. The most frequently reported biological activities were antimicrobial, antiproliferative, antipredatory, antifouling, cytotoxic and antiprotozoal.

As pointed out by Leal and co-authors (2012), research strategies focused on less explored taxonomical groups or geographical regions help improve the chances of finding new bioactive molecules. Thus, research on octocorals collected on the Brazilian coasts could represent an interesting source of investigation. This review provides data and references for further chemical and biological research on octocorals, and highlights the great richness of Octocorallia as an important source of new bioactive compounds, with the aim to stimulate research on this promising and abundant class of organisms, which could be better exploited in Brazil.

#### Authors' contributions

MTRA (Postdoctoral student) contributed with the concept, design, and arrangement of the present review article, including data collection, selection of papers and writing of the sections related to natural products. MIGM (PhD student) contributed with data collection, writing of the sections related to natural products and formatting of the manuscript. KCCC (PhD student) contributed with data collection, selection of papers and thesis and writing of the sections related to taxonomical aspects. CDP contributed with expertise related to taxonomic aspects and critical reading of the draft manuscript. EPS supervised the process of drafting and contributed in finalizing the article through critical reading of the draft manuscript. All the authors have read the final manuscript and approved submission. MTRA, MIGM and KCCC contributed equally to this work.

#### **Conflicts of interest**

The authors declare no conflicts of interest.

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