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1 **Biological activities associated to the chemodiversity of the brown algae**
2 **belonging to genus *Lobophora* (Dictyotales, Phaeophyceae)**

3

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27 **Running title** Bioactivity of natural products of the genus *Lobophora*

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31 **Abstract** Although *Lobophora* belongs to a marine algal family (Dictyotaceae)
32 that produces a large array of secondary metabolites, it has received little attention
33 compared to other genera, such as *Dictyota*, in terms of natural compounds isolation
34 and characterization. However, metabolites produced by *Lobophora* species have
35 been found to exhibit a wide array of bioactivities including pharmacological (e.g.
36 antibacterial, antiviral, antioxidant, antitumoral), pesticidal, and ecological. This
37 review aims to report the state-of-the-art of the natural products isolated from
38 *Lobophora* species (Dictyotales, Phaeophyceae) and their associated bioactivities. All
39 bioactivities documented in the literature are reported, therefore including studies for
40 which pure active substances were described, as well as studies limited to extracts or
41 fractions. From the early 1980s until today, 49 scientific works have been published
42 on *Lobophora* chemistry and bioactivity, among which 40 have reported bioactivities.
43 Only six studies, however, have identified, characterized and tested no less than 23
44 bioactive pure compounds (three C₂₁ polyunsaturated alcohols, three fatty-acids, a
45 macrolactone, 11 polyketides, a few sulfated polysaccharides, three sulfolipids, a
46 tocopherol derivative). The present review intends to raise awareness of chemists and
47 biologists given the recent significant taxonomic progress of this brown algal genus,
48 which holds a promising plethora of natural products yet to be discovered with
49 ecological and pharmacological properties.

50

51 **Keywords** Bioactivity · Brown algae · *Lobophora* · Natural products

52

53 **Abbreviations**

54	ACVr	Acyclovir-resistant
55	EC ₅₀	Half maximal Effective concentration
56	HCT-116	Human colon tumor
57	HEp-2	Human epithelial type 2
58	HIV	Human immunodeficiency virus
59	HL-60	Human promyelocytic leukemia cell line
60	HSV-1/2	Herpes simplex virus type 1 or 2
61	HT-29	Human colorectal adenocarcinoma cell line
62	IC ₅₀	Half maximal inhibitory concentration
63	LC ₅₀	Median lethal concentration
64	LD ₅₀	Median lethal dose
65	MCF-7	Human breast carcinoma cell line
66	MDCK	Madin-Darby canine kidney
67	MIC ₉₀	Minimal inhibitory concentration to inhibit the growth of 90%
68		of organisms
69	MZI	Mean zone of inhibition
70	RSV	Respiratory syncytial virus
71	SQDG	Sulfoquinovosyl diacylglycerol
72		

73 **Introduction**

74 The brown marine algal genus *Lobophora* J. Agardh (Dictyotales, Phaeophyceae) is
75 distributed worldwide in tropical to temperate waters and represents an important
76 algal component in coral reef ecosystems (Vieira et al. 2014; Bennett et al. 2010; De
77 Ruyter van Steveninck and Breeman 1987; Diaz-Pulido et al. 2009). *Lobophora*
78 belongs to the Dictyotaceae, a family which has proven to be a particularly rich and
79 diverse source of natural products and predominantly diterpenes (Maschek and Baker
80 2008; Vallim et al. 2005; Blunt et al. 2015). These natural products have been
81 particularly studied for their bioactivity for human health but also for their putative
82 ecological role in nature. The terpenoids isolated from the Dictyotaceae exhibit
83 various types of bioactivity such as feeding deterrence, antifungal, cytotoxic,
84 antibiotic, anti-inflammatory, insecticidal or antiviral activities. However, while some
85 genera have received much attention, notably *Dictyota* and *Dictyopteris* (Hay and
86 Steinberg 1992; Paul et al. 2006; Paul and Ritson-Williams 2008), others like
87 *Lobophora* raised less interest and a very limited number of natural products have
88 already been described from algae of this genus. This limited attention may be
89 explained by the taxonomic deficiency this genus has suffered from until recently.
90 Indeed, only three *Lobophora* species were recognized until the end of the last
91 century, with *Lobophora variegata* (Lamouroux) Womersley ex Oliveira being by far
92 the most commonly reported species, apparently distributed in the world's oceans.
93 This species has been cited in virtually all the chemical studies conducted on the
94 genus *Lobophora* (Table 1). However, recent DNA-based studies (Sun et al. 2012;
95 Vieira et al. 2014) have shed new light on *Lobophora* taxonomy. Today, 20 species
96 are taxonomically accepted (Guiry and Guiry 2015) and 80 more have been estimated
97 (Vieira 2015). The high genetic diversity recently unveiled within this genus
98 presupposes that a richer chemodiversity is yet to be discovered. This review aims to
99 report the state-of-the-art of the natural products isolated from *Lobophora* species
100 (Dictyotales, Phaeophyceae) and their associated bioactivities. All bioactivities
101 documented in the literature are reported in Table 1, therefore including studies for
102 which pure active substances were described, as well as studies limited to extracts
103 and/or fractions. The *Lobophora* natural products for which no bioactivity has yet
104 been reported are presented in Table 2. *Lobophora* bioactive natural products reported
105 here are presented in Figure 1.

106 Note that the recent taxonomic progress of the genus *Lobophora* naturally questions
107 the validity of what has been nearly always reported as *L. variegata* based on external
108 morphological criteria. Therefore, although referred to in the literature as *L. variegata*
109 or in only one instance as *L. papenfussii*, we will presently simply make reference to
110 the genus *Lobophora*.

111 Relevant literature was searched with the databases Marinlit, Google Scholar, ISI
112 Web of Science, JSTOR and PubMed. A targeted search of English literature (i.e.
113 papers with minimum an English title and abstract) was conducted using the key word
114 ‘*Lobophora*’ followed by the search terms [activity or allelopath* or anti* or
115 bioactiv* or chemi* or extract or metabolite or natural product]. An asterisk (*) is a
116 wildcard character that means “any character”, which allows the database or search
117 engine to look for multiple words that have different endings, e.g. bioactiv* captures
118 [bioactive AND bioactivity].

119 **Antimicrobial activities**

120 Antimicrobial (anti-bacterial, -viral, -fungal or -protozoal) activities of extracts,
121 fractions or compounds isolated from *Lobophora* species have been by far the most
122 explored type of bioactivities searched for this genus. Like other eukaryotes,
123 macroalgae harbor a large and diverse microbial community, which play important
124 roles for the host (Egan et al. 2013). The selection of associated or symbiotic bacteria
125 may be related to the production of specialized metabolites that play important
126 functions against harmful marine microorganisms (Egan et al. 2013) as well as against
127 some human pathogens.

128 **Antibacterial activities**

129 Organic extracts of *Lobophora* species have shown a broad-spectrum of antibacterial
130 activities (Morrow et al. 2011; Engel et al. 2006; Manilal et al. 2012; Manilal et al.
131 2010a; Gutiérrez-Cepeda et al. 2015; Manilal et al. 2010b; Ballantine et al. 1987;
132 Sivakumar 2014). Engel et al. (2006) considered two morphotypes of *Lobophora*,
133 crustose and ruffled, which we strongly suspect to be two distinct species. Lipophilic
134 and hydrophilic parts of organic extracts from both morphotypes resulted in growth
135 inhibition of the bacteria *Pseudoalteromonas bacteriolytica*. However, the two
136 morphotypes extracts yielded contrasting IC₅₀ values: the lipophilic parts showed

137 volumetric IC_{50s} of 1 and 0.24 (unitless) for the crustose and ruffled types,
138 respectively, and the hydrophilic parts exhibited volumetric IC_{50s} of 0.51 and 0.67,
139 respectively. It would therefore appear that these two different morphotypes have
140 contrasting chemical production.

141 The chloroform-methanolic extract of Caribbean *Lobophora* presented antibacterial
142 activity against *Bacillus subtilis* (Ballantine et al. 1987). The organic extract of
143 *Lobophora* samples from India showed a strong inhibition against *Salmonella typhi*
144 and *Vibrio cholera* while being less active against *Klebsilla pneumonia* and *E.coli*
145 (Sivakumar 2014). Val et al. (2001) did not observed any antimicrobial activity of the
146 methanolic extract of *Lobophora* harvested in Canary Islands (Spain) against a panel
147 of pathogen bacterial strains. Manilal et al. (2010a), Manilal et al. (2010b) and
148 Manilal et al. (2012) showed that *Lobophora* methanolic extract exhibited a strong
149 antibacterial activity against a wide array of bacteria including the biofilm-forming
150 bacteria *Vibrio* sp., *Colwellia* sp. SW125 and *Pseudoalteromonas bacteriolytica*; the
151 pathogenic bacterial strains *Aeromonas hydrophila*, *Bacillus cereus*, *Escherichia coli*,
152 *Micrococcus luteus* and *Salmonella typhimurium*; the multiresistant human pathogens
153 *B. subtilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *S. epidermidis*; and the
154 shrimp pathogens *Vibrio parahaemolyticus*, *V. vulnificus*, *V. harveyi*, *V. alcaligenes*
155 and *V. alginolyticus*. Manilal et al. (2012) characterized by gas chromatography seven
156 fatty acids (palmitic, lauric, stearic, α -linolenic, oleic, myristic and hexadecatrienoic
157 acids) from an active *Lobophora* fraction, thus suggesting that the antibacterial
158 bioactivity could be attributed to the synergistic effects of these compounds. In fact,
159 fatty acids, such as oleic, lauric and palmitic acids have already demonstrated
160 antibacterial activity (Kabara et al. 1972). But while lauric and myristic acids
161 presented inhibitory effect on the 11 bacterial strains tested by the authors, the effect
162 of oleic acid was restricted to only one strain (*Streptococcus* group A) (Kabara et al.
163 1972). Morrow et al. (2011) showed that *Lobophora* organic extract induced a shift in
164 the assemblage of bacteria associated to corals. Gerwick Fenical (1982) tested the *in*
165 *vitro* antibacterial activity of a new aromatic polyketide identified from this species,
166 1-(2,4,6-trihydroxyphenyl)hexadecane-1-one (**1**), against a panel of six bacteria (*S.*
167 *aureus*, *B. subtilis*, *E. coli*, *Enterobacter aerogenes*, *P. aeruginosa*, *Vibrio*
168 *anguillarum*) but did not observe any effect. Similarly, Gutiérrez-Cepeda et al. (2015)
169 identified 10 new polyketides (**13-22**) and tested the antimicrobial effect of seven of

170 them (**13-15**, **17-19** and **22**) against *Enterococcus faecalis*, *E. coli*, and *S. aureus*. The
171 authors showed that the compounds **13** and **14** inhibited the growth of *S. aureus* by
172 $100 \pm 1\%$ (average \pm SD) and $65 \pm 2\%$, respectively at $100 \mu\text{g ml}^{-1}$ concentration.
173 The minimum inhibitory concentration (MIC_{90}) of lobophorol A (**13**) against *S.*
174 *aureus* was shown to be $25 \mu\text{g ml}^{-1}$.

175 Antiviral activities

176 *Lobophora* aqueous extracts presented interesting bioactivities against a wide range of
177 viruses. Some polysaccharides isolated from *Lobophora* exhibited antiviral activities
178 against the herpes simplex virus types 1 and 2 (EC_{50} 18.2 and $6.25 \mu\text{g ml}^{-1}$,
179 respectively), and a very low cytotoxicity to Vero, HEp-2, and MDCK cell lines as
180 well as a moderate activity against respiratory syncytial virus (RSV) (Wang et al.
181 2008a). *Lobophora* aqueous extract exhibited anti-HSV properties (EC_{50} 18.5 and
182 $9 \mu\text{g ml}^{-1}$ for HSV-1 and HSV-2, respectively) and a moderate anti-RSV activity
183 (Wang et al. 2008b). The organic extract strongly inhibited HSV-1-ACVr (92% of
184 inhibition) but did not inhibit at all HSV-2-ACVr (Soares et al. 2012). Queiroz et al.
185 (2008) showed that a sulfated polysaccharide isolated from *Lobophora* (a
186 galactofucan of 1400 kDa, with fucose, galactose, glucose and sulfate at molar ratio
187 of 1:2:3:0.5), exhibited antiretroviral effect by inhibiting reverse transcriptase activity
188 of human immunodeficiency virus. Kremb et al. (2014) showed that *Lobophora*
189 aqueous extracts also inhibited HIV-1 infection at the level of virus entry into cells.

190 Antifungal activities

191 Some *Lobophora* extracts showed antifungal activities against a broad spectrum of
192 fungi. The lipophilic part of an organic extract of the crustose type induced 100%
193 growth inhibition of *Dendryphiella salina* (ascomycete) and the fungi-like
194 *Halophytophthora spinosa* (oomycete), but no effect on *Lindra thalassiae*
195 (ascomycete). On the other hand, the lipophilic extract of the ruffled type did not
196 inhibit the growth of any of the three tested fungi. The hydrophilic extracts of both
197 *Lobophora* types resulted in the growth inhibition by ca. 70% of only the oomycete *H.*
198 *spinosa*. We notice here again that the different morphotypes of *Lobophora* have
199 contrasting bioactivities against different micro-organisms (Engel et al., 2006).
200 Gerwick Fenical (1982) tested the antifungal activity of the polyketide (**1**) against

201 *Candida albicans*, a causal agent of opportunistic oral and genital infections in
202 humans, but did not observe any effect. Some *Lobophora* organic extracts also failed
203 to inhibit the growth of *Aspergillus fumigatus*, *C. albicans* and *Saccharomyces*
204 *cerevisiae* (Val *et al.*, 2001). Kubanek *et al.* (2003) identified a macrolactone
205 polyketide named lobophorolide (**2**), which exhibited sub-micromolar activity against
206 pathogenic and saprophytic marine fungi (*Dendryphiella salina*, *Lindra thalassiae*
207 and *C. albicans*) with IC₅₀ values ranging from 0.034 to 1.3 µg ml⁻¹. Lobophorolide
208 is structurally related to tolytoxin, scytophycins, and swinholides, macrolides
209 previously isolated from terrestrial cyanobacteria, marine sponges and gastropods
210 (Kubanek *et al.* 2003). These structural similarities raise the question of its origin, and
211 the authors suggested that the molecule is more probably biosynthesized by
212 *Lobophora* associated-bacteria.

213 Antiprotozoal activities

214 *Lobophora* extracts presented antiprotozoal activities against six protozoan parasites,
215 namely *Trichomonas vaginalis* (a common and worldwide parasite which infects the
216 urogenital tract of men and women), *Entamoeba histolytica* (parasite infecting
217 humans and other primates), *Giardia intestinalis* (responsible for enteric protozoan
218 infections), *Schizochytrium aggregatum* (marine protist), *Leishmania mexicana* (one
219 of the causative species of leishmaniasis) and *Trypanosoma cruzi* (causative species
220 of trypanomiasis). The organic extract exhibited anti-trichomonal activity with an IC₅₀
221 of 1.39 µg ml⁻¹ (Moo-Puc *et al.* 2008), an IC₅₀ of 3.2 µg ml⁻¹ against *Trichomonas*
222 *vaginalis* (Cantillo-Ciau *et al.* 2010), and anti-leishmanial *in vitro* properties against
223 *Leishmania mexicana* promastigote forms with a LC₅₀ value of 49.9 µg ml⁻¹ (Freile-
224 Pelegrin *et al.* 2008). The same extract exhibited a moderate *in vitro* antiprotozoal
225 activity against *Trypanosoma cruzi* with an IC₅₀ of 9.72 µg ml⁻¹ (León-Deniz *et al.*
226 2009). Cantillo-Ciau *et al.* (2010) identified three sulfoquinovosyldiacylglycerols
227 (SQDGs; 1-*O*-palmitoyl-2-*O*-myristoyl-3-*O*-(6'''-sulfo- α -*D*-
228 quinovopyranosyl)glycerol (**3**), 1,2-di-*O*-palmitoyl-3-*O*-(6'''-sulfo- α -*D*-
229 quinovopyranosyl)glycerol (**4**) and 1-*O*-palmitoyl-2-*O*-oleoyl-3-*O*-(6'''-sulfo- α -*D*-
230 quinovopyranosyl)glycerol (**5**) with antiprotozoal activity from a lipophilic fraction.
231 SQDGs were shown to exhibit an *in vitro* antiprotozoal activity against *Entamoeba*
232 *histolytica* with an IC₅₀ of 3.9 µg ml⁻¹, and a moderate activity against *T. vaginalis*

233 trophozoites with an IC₅₀ of 8 µg ml⁻¹. Engel et al. (2006) observed differences in the
234 antiprotozoal activities of both *Lobophora* types presented earlier. While both
235 hydrophilic and lipophilic parts of the organic extract of the crustose type inhibited
236 the growth of *Schizochytrium aggregatum*, only the lipophilic part of the ruffled type
237 showed a significant inhibition (Engel et al. 2006).

238 **Additional pharmacological bioactivities**

239 In addition to the antimicrobial activities presented above, *Lobophora* presented
240 several additional bioactivities with some pharmacological potential, including anti-
241 angiogenic, anticoagulant, anti-inflammatory antioxidant, cytotoxic (including
242 antitumoral) and hemagglutinating activities. *Lobophora* extracts and sulfated
243 polysaccharides were shown to exhibit anticoagulant (De Lara-Isassi et al. 2004;
244 Medeiros et al. 2008; Castro et al. 2014b), antioxidant (Zubia et al. 2007; Paiva et al.
245 2011; Castro et al. 2014b; Sathyaseelan et al. 2015), anti-inflammatory (Paiva et al.
246 2011; Siqueira et al. 2011; Medeiros et al. 2008; Castro et al. 2014b),
247 hemagglutinating (Lima Ainouz et al. 1992) as well as anti-angiogenic (Castro et al.
248 2014a) activities. *Lobophora* aqueous extract demonstrated low cytotoxic properties
249 on human breast carcinoma MCF-7 cell lines, at a concentration of 200 µg ml⁻¹
250 (Wang et al. 2008b), and against the human nasopharyngeal carcinoma (KB) cell
251 line (Moo-Puc *et al.* 2009). Semi-purified fractions of *Lobophora* also exhibited
252 potential cytotoxic activity on a cultured human melanoma cancer cell line (Rocha et
253 al. 2007). Lobophorolide (**2**) also showed antineoplastic activity (IC₅₀ 0.03 µg ml⁻¹)
254 on the human colon tumor cell line HCT-116 (Kubanek et al. 2003), and sulfated
255 polysaccharides presented anti-tumoral effects on human colon adenocarcinoma cell
256 line HT-29 (Castro et al. 2014b). Several organic *Lobophora* extracts were active
257 against P-388 lymphocytic leukemia and Ehrlich ascites tumor in mice (Kashiwagi *et*
258 *al.* 1980). Queiroz *et al.* (2006) showed a cytotoxic action of *Lobophora*
259 polysaccharides (a glucan and three galactofucans) on HL60 cells. The molecular
260 mechanism of the cytotoxic effect of these polymers has not been clearly defined but
261 this study suggested a possible involvement of phosphatases.

262 **Pesticidal activities**

263 Two studies assessed the pesticidal activities (i.e. pupicidal, nematicidal and
264 phytotoxic activities) of *Lobophora* (Manilal et al. 2012; Bianco et al. 2013).
265 *Lobophora* showed a larvicidal potential against the dengue mosquito *Aedes aegypti*
266 ($52 \pm 2.9\%$ larval mortality at 500 ppm concentration; Bianco et al. 2013), and
267 pupicidal potential against the urban mosquito *Culex quinquefasciatus* with a LD₅₀
268 value of 683 $\mu\text{g ml}^{-1}$ (Manilal et al. 2012). *Lobophora* methanolic extract presented a
269 nematicidal activity against the plant-pathogenic nematode *Meloidogyne javanica*
270 with a LD₅₀ value of 1.16 mg ml⁻¹; and a phytotoxic activities against several plant
271 seeds (*Cicer arietinum*, *Vigna radiate* and *Cajanus cajan*), with a no growth response
272 of *C. cajan*, *V. radiate* and *C. arietinum* at a seaweed extract concentration of 4, 6 and
273 8 mg ml⁻¹, respectively (Manilal et al. 2012). Manilal et al. (2012) have attributed
274 these pesticidal activities to a synergistic effect between the fatty acids they have
275 identified (see above).

276 **Bromophenols production**

277 *Lobophora* have been shown to produce bromophenols, a group of key flavor
278 compounds in seafood. Chung et al. (2003) found four bromophenols in *Lobophora*
279 namely 4-bromophenol (**9**), 2,4-dibromophenol (**10**), 2,6-dibromophenol (**11**), and
280 2,4,6-tribromophenol (**12**). These authors also showed that comparatively to two other
281 brown algae, *Padina arborescens* and *Sargassum siliquastrum*, *Lobophora* presented
282 the highest amount of bromophenols. Bromophenols have demonstrated a variety of
283 biological activities including antioxidant, antimicrobial, anticancer, anti-diabetic, and
284 anti-thrombotic effects (Liu et al. 2011). Nevertheless, to our knowledge no study has
285 yet shown bioactivities for any of the four bromophenols isolated from *Lobophora*.
286 Chkhikvishvili Ramazanov (2000) reported that the total phenolic substances content
287 in *Lobophora* represent 1.2% of dry weight.

288 **Edibility, nutritional and nutraceutical values**

289 Widely consumed in some Asian countries (Zaneveld 1959), marine algae are well-
290 known as a functional food for their richness in carotenoids, dietary fibers, essential
291 fatty acids, lipids, minerals, polysaccharides, proteins and vitamins (Holdt and Kraan
292 2011; Plaza et al. 2008; Ito and Hori 1989; Dawczynski et al. 2007; Burtin 2003).
293 However, only a handful of studies have been interested in testing the edibility and

294 nutritional value of *Lobophora*. Gerwick Fenical (1982) isolated one form of vitamin
295 E (γ -tocopherol (6)) from *Lobophora*, which has distinct properties from the more
296 common α -tocopherol (Jiang et al. 2001), the form of vitamin E that is preferentially
297 absorbed and accumulated in humans (Rigotti 2007). Sousa et al. (2008) measured the
298 content in β -carotene, retinol equivalent (vitamin A) and γ -tocopherol in *Lobophora*:
299 $4.185 \pm 1.559 \mu\text{g g}^{-1}$ fresh weight of β -carotene, $0.697 \pm 0.260 \mu\text{g g}^{-1}$ of retinol
300 equivalent and $4.722 \pm 2.062 \mu\text{g g}^{-1}$ of γ -tocopherol. *Lobophora* presented the lowest
301 γ -tocopherol concentration amongst other Phaeophyceae (i.e. *Dictyopteris delicatula*,
302 *Dictyota dichotoma*, *Padina gymnospora* and *Sargassum cymosum*). Hegazi (2002)
303 analyzed the pigment composition of *Lobophora* from the Red Sea and fourteen
304 compounds were reported: chlorophylls a, a', c₁ and c₂, fucoxanthin, violaxanthin,
305 flavoxanthin, fucoxanthol, antheraxanthin, 9-cis-neoxanthin, diatoxanthin, zeaxanthin,
306 β -carotene and phaeophytin a. fucoxanthin, flavoxanthin, diatoxanthin and zeaxanthin
307 are typical xanthophylls of Chromophyta, while chlorophyll c₁ and chlorophyll c₂ are
308 the characteristic chlorophylls of this algal group. In *Lobophora* chlorophyll a is the
309 most important (0.27 mg g^{-1}), followed by chlorophylls c₁ and c₂ (0.001 mg g^{-1} each).
310 Among the carotenoids, fucoxanthin was the dominant pigment (0.12 mg g^{-1}),
311 followed by β -carotene (0.06 mg g^{-1}) and violaxanthin (0.04 mg g^{-1}). Carotenoids
312 such as fucoxanthin, β -carotene and violaxanthin have demonstrated the ability to act
313 as antioxidants, and to prevent the development of different degenerative diseases and
314 health conditions in humans, including age-related macular degeneration, cataract,
315 certain cancers, rheumatoid arthritis, muscular dystrophy and cardiovascular problems
316 (Kim and Pangestuti 2011; Ibañez and Cifuentes 2013; Ahmed et al. 2013).
317 Thennarasan (2015) analyzed the biochemistry of *Lobophora*, i.e. the composition in
318 fatty acids, minerals, sterols, total carbohydrates, total lipids, total proteins and
319 vitamins (Table 2). Results of this study showed that *Lobophora* presents a high
320 content of total protein ($23.13 \pm 0.05\%$ of total content) and total carbohydrate
321 ($19.34 \pm 0.10\%$), and a low content of total lipid ($0.27 \pm 0.5\%$). While *Lobophora* has
322 a high fatty acid to total lipid ratio (58%), it has a low total lipid content ($<50 \text{ mg g}^{-1}$
323 dry weight) in comparison with other Dictyotales species (*Dictyota bartayresii*,
324 *Dictyota dichotoma*, and *Spatoglossum macrodontum*; total lipid content $>100 \text{ mg g}^{-1}$
325 dry weight) (Gosch et al. 2012). *Lobophora* is also rich in vitamins (especially
326 vitamin C, $23.430 \pm 0.152 \text{ mg } 100\text{g}^{-1}$), fatty acids (omega fatty acid), and minerals

327 (calcium, 135.4 ± 0.20 mg 100g⁻¹). de Alencar et al. (2011) have not found histamine
328 and tyramine, amines that can cause intoxication symptoms, in quantities high enough
329 to cause pharmacological actions in *Lobophora*. *Lobophora* appears to be a source of
330 carbonyl compounds (e.g. aldehydes and ketones) (Mota da Silva et al. 2006). While
331 many aldehydes and ketones are used as food flavorings (e.g. propanal, propanone)
332 and preservatives (e.g. formaldehyde), some aldehydes can also act as mutagens and
333 carcinogens (Leikauf 1992; Goldschmidt 1984). For instance, formaldehyde is
334 classified as a “probable human carcinogen” (Thrasher and Kilburn 2001), and
335 acetaldehyde can induce nasal carcinomas (Miyake and Shibamoto 1995).

336 **Ecological roles**

337 Fewer are the studies targeted towards understanding the ecological roles of
338 *Lobophora* metabolites. Three main ecological roles have been investigated, namely
339 antifouling, feeding deterrence, and effects on benthic competitors.

340 Antifouling

341 As an evolutionary response to the ecological disadvantages of epibiosis, most if not
342 all macroalgae have developed antifouling chemical defenses. However, these
343 antifouling defenses are not equally efficient across different algal taxa, and some
344 may harbor a significant community of epiphytes. Such is the case of *Lobophora*,
345 which blades act as an important living substratum (Fricke et al. 2011). Yet, the
346 upper-side blade surface is generally less epiphytized than the underside surface. Two
347 studies have been performed to assess the antifouling properties of compounds
348 produced by *Lobophora* against mussels, barnacles and bacterial biofilm (Manilal et
349 al. 2010a; Da Gama et al. 2008). The methanolic extracts showed considerable
350 antifouling activity against biofilm forming bacteria, i.e. *Vibrio* sp. (11 ± 2.5 mm zone
351 of inhibition (MZI)), *Colwellia* sp. SW125 (6 ± 2.1 mm MZI) and *Pseudoalteromonas*
352 sp. SW124 (9 ± 1.5 mm MZI) (Manilal et al. 2010a). On the other hand, some
353 *Lobophora* extract stimulated the attachment to the algal surface of the brown mussel
354 *Perna perna*, and apparently did not show significant activity against the barnacle
355 *Balanus amphitrite* and mussel *Mytilus edulis* attachment (data not presented; Manilal
356 et al. 2010a). Although not clearly demonstrated, antifouling activities might be

357 attributable to phlorotannins, a class of molecules present in *Lobophora*, that have
358 been reported to present antifouling activity (Amsler and Fairhead 2005).

359 Effects on benthic competitors

360 As a consequence of natural or anthropogenic perturbations of their environmental
361 conditions, some coral reefs have shifted from a coral- to a macroalgal-dominance.
362 *Lobophora* has been reported in such events and allelopathy has been suggested as a
363 possible mechanism allowing the alga to outcompete corals in damaged reefs by
364 causing bleaching and suppressing photosynthetic efficiency. Some authors (e.g.
365 Longo and Hay 2014; Vieira et al. 2015; Antonius and Ballesteros 1998) observed
366 that *Lobophora* contacting some corals (e.g. *Agaricia*, *Porites*, *Seriatopora*) was
367 associated with more or less important bleaching. While an allelopathic mechanism
368 has been suggested in the late 1990s (Antonius and Ballesteros 1998), it has only
369 recently been experimentally tested (Rasher and Hay 2010b; Slattery and Lesser
370 2014; Vieira et al. in revision). Those latter studies clearly demonstrated that
371 *Lobophora* possesses potentially adverse chemicals to several corals (*Porites*
372 *cylindrica*, *Porites porites*, *Montastrea cavernosa*, *Acropora muricata*, *Stylophora*
373 *pistillata* and *Montipora hirsuta*), although their actual efficiency *in situ* remains to be
374 proven (Vieira et al. in revision). Slattery Lesser (2014) and Vieira et al. (in revision)
375 identified four molecules with bleaching properties: SQDG (**3**) identified by Cantillo-
376 Ciau et al. (2010) (Slattery and Lesser 2014), and three new C₂₁ polyunsaturated
377 alcohols (**6-8**) (Vieira et al. in revision). Slattery Lesser (2014) experimentally
378 showed that **3** presented bleaching activity against the coral *M. cavernosa*, and Vieira
379 et al. (in revision) showed that the all lobophorenols (**6-8**) exhibited bleaching
380 activities against the coral *A. muricata*. In Vieira et al. (in revision) a significant
381 number of semi-purified fractions also exhibited a more or less significant activity
382 against corals.

383 *Lobophora* natural compounds adversity towards corals may be indirect, by affecting
384 the coral-associated bacterial community and notably by causing community shifts on
385 *Montastraea faveolata* and *Porites astreoides* colonies (Morrow et al. 2012), and also
386 causing a sublethal stress. No compounds with such effects have yet been identified,
387 but only the aqueous extract has been found to show ecological effects.

388 Effects on coral larval recruitment

389 *Lobophora* has contrasting effects on coral larval recruitment. Birrell et al. (2008)
390 showed that *Lobophora* is able to enhance larvae settlement of *Acropora millepora* by
391 40%. On the contrary, Kuffner et al. (2006) showed that *Lobophora* causes either
392 recruitment inhibition or avoidance behavior in *P. astreoides* larvae. Diaz-Pulido et al.
393 (2010) also showed that *Lobophora* presented either no effect on 2-days-old larvae or
394 inhibitory effects on settlement of coral larvae. Similarly, Baird Morse (2004) showed
395 that *Lobophora* inhibited metamorphosis in coral larvae. Morse et al. (1996) found
396 that larvae of several Acroporids species did not settle in assays that included
397 *Lobophora* plants. Nevertheless, no compound, either acting as enhancers or
398 inhibitors, has already been identified.

399 Deterrence function

400 *Lobophora* has been the subject of contradictory observations in terms of
401 susceptibility to herbivory. For example, while De Lara-Isassi et al. (2000) showed
402 ichthyotoxicity (from ethanol and acetone extracts) against the goldfish *Carassius*
403 *auratus*, Slattery Lesser (2014) concluded that *Lobophora* chemical defenses
404 (*Lobophora* crude extract and a purified SQDG) were inactive against the omnivorous
405 pufferfish (*Canthigaster rostrata*). The experiment of De Lara-Isassi et al. (2000),
406 which aimed at testing the ichthyotoxicity of phlorotannins, is nonetheless
407 ecologically poorly relevant since the goldfish is a freshwater fish. *Lobophora* feeding
408 deterrence potential was suggested based on the presence of phlorotannins and
409 terpenes (Targett and Arnold 1998; Amsler and Fairhead 2005), which may cause the
410 precipitation of proteins (Stern et al. 1996). Stern et al. (1996) isolated phlorotannins
411 from *Lobophora* and suggested several explanations for why the biological activity of
412 phlorotannins may vary as a function of the gut environment of marine herbivores. In
413 addition, Bolser Hay (1996) concluded that the greater consumption of temperate
414 (North Carolina) versus tropical (the Bahamas) *Lobophora* by the sea urchin *Arbacia*
415 *punctulata* was likely due to the higher concentrations of secondary metabolites such
416 as phlorotannins in *Lobophora* from the temperate regions than in tropical regions.
417 Weidner et al. (2004) showed that while *Lobophora* exhibited inducible defenses
418 following direct consumption by amphipods, the repulsive effects of the non-polar
419 extracts were overridden by counteracting effects of non-extracted chemicals, making
420 live plants more nutritive. Nevertheless, toxicity of *Lobophora* extracts towards fish

421 has only been suggested, but not rigorously tested (De Lara-Isassi et al. 2000).
422 Cetrulo Hay (2000) investigated the activation of chemical defenses in 42 species of
423 seaweeds including *Lobophora*, but the latter, together with other Dictyotacean
424 species, failed to show activation following damage by the spottail finfish *Diplodus*
425 *holbrooki*, and the sea urchin *Lytechinus variegatus*.

426 **Conclusion and prospects**

427 The chemical content and associated bioactivities of *Lobophora* species started to be
428 explored in the early 1980s. *Lobophora* exhibits a wide array of bioactivities such as
429 pharmacological (e.g. antibacterial, antiviral, antioxidant, antitumoral), pesticidal, and
430 ecological. The limited number of studies conducted on the subject showed that this
431 alga is a promising functional food.

432 Most studies were performed with extracts and mainly focused on their
433 pharmacological potential, whereas only few chemical compounds have been
434 characterized. Only six studies have identified, characterized and tested no less than
435 23 bioactive compounds (three C₂₁ polyunsaturated alcohols, three fatty-acids, a
436 polyketide macrolactone, 11 polyketides, a few sulfated polysaccharides, three
437 sulfolipids, a tocopherol derivative). Additional chemical studies are urgently required
438 in order to fully characterize the compounds responsible for the large array of
439 biological activities encountered. Furthermore, recent major progress in the taxonomy
440 of this brown algal genus, suggests that a plethora of natural compounds is yet to be
441 discovered within the 110 estimated species (Vieira 2015).

442 This review is written in this pivotal moment in the chemical knowledge of
443 *Lobophora*, and aims at triggering the interest of chemists, biologists and
444 pharmacologists in exploring this mine of natural compounds still largely under-
445 explored.

446

447 **Compliance with ethical standards**

448 **Conflicts of interest** The authors state no conflict of interest and have received no
449 payment for the preparation of this manuscript.

450

451 Table 1. *Lobophora* natural products and associated bioactivities.

Bioactivity	Species	Biological target	Molecule	Type of extract	Reference
Antimicrobial activities					
Antibacterial	<i>L. variegata</i>	<i>Enterococcus faecalis</i> , <i>Escherichia coli</i> , <i>Staphylococcus aureus</i>	Lobophorols A-C, lobophopyranones A and B, lobophorones A-E	-	Gutiérrez-Cepeda et al. (2015)
Antibacterial	<i>L. variegata</i>	<i>Escherichia coli</i> , <i>Salmonella typhi</i> , <i>Klebsiella pneumonia</i> , <i>Vibrio cholera</i>	-	CHCl ₃ /MeOH	Sivakumar (2014)
Antibacterial	<i>L. variegata</i>	<i>Bacillus cereus</i> , <i>Micrococcus luteus</i> , <i>Salmonella typhimurium</i> , <i>Aeromonas hydrophila</i> , <i>Escherichia coli</i>	Mixture of fatty acids	MeOH	Manilal et al. (2012)
Antibacterial	<i>L. variegata</i>	Marine bacteria isolated from Caribbean macroalgae and corals	-	EtOAc/MeOH and then MeOH/H ₂ O	Morrow et al. (2011)
Antibacterial	<i>L. variegata</i>	Biofilm-forming bacteria	-	MeOH	Manilal et al. (2010a)
Antibacterial	<i>L. variegata</i>	<i>Vibrio parahaemolyticus</i> , <i>Vibrio vulnificus</i> , <i>Vibrio harveyi</i> , <i>Vibrio alcaligenes</i> , <i>Vibrio alginolyticus</i> , <i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , <i>Bacillus subtilis</i> , <i>Klebsiella pneumoniae</i> , <i>Staphylococcus epidermidis</i>	-	MeOH	Manilal et al. (2010b)
Antibacterial	<i>L. variegata</i>	<i>Pseudoalteromonas bacteriolytica</i>	-	CH ₂ Cl ₂ /MeOH [divided into lipophilic (EtOAc) and hydrophilic (H ₂ O) parts]	Engel et al. (2006)
Antibacterial	<i>L. variegata</i>	<i>Bacillus subtilis</i> , <i>Enterococcus faecium</i> , <i>Mycobacterium smegmatis</i> , <i>Pseudomonas aeruginosa</i> , <i>Serratia marcescens</i> , <i>Staphylococcus aureus</i>	-	MeOH	Val et al. (2001)
Antibacterial	<i>L. variegata</i>	<i>Bacillus subtilis</i> , <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Candida albicans</i>	-	CHCl ₃ /MeOH	Ballantine et al. (1987)
Antibacterial	<i>L. papenfussii</i>	<i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Escherichia coli</i> , <i>Enterobacter aerogenes</i> , <i>Pseudomonas aeruginosa</i> , <i>Candida albicans</i> , <i>Vibrio anguillarum</i>	2-(1'-Oxohexadecyl)-1,3,5-trihydroxybenzene	-	Gerwick Fenical (1982)
Antiviral	<i>L. variegata</i>	HIV	-	H ₂ O	Kremb et al. (2014)
Antiviral	<i>L. variegata</i>	HSV-1	-	CH ₂ Cl ₂ /MeOH	Soares et al. (2012)
Antiviral	<i>L. variegata</i>	HIV	Polysaccharide (galactofucan)	-	Queiroz et al. (2008)

Antiviral	<i>L. variegata</i>	Herpes simplex virus type 1 and 2 (HSV-1 and -2), respiratory syncytial virus (RSV)		H ₂ O	Wang et al. (2008b)
Antifungal	<i>L. variegata</i>	<i>Dendryphiella salina</i> , <i>Halophytophthora spinosa</i>	-	CH ₂ Cl ₂ /MeOH [divided into lipophilic (EtOAc) and hydrophilic (H ₂ O) parts]	Engel et al. (2006)
Antifungal	<i>L. variegata</i>	<i>Dendryphiella salina</i> , <i>Lindra thalassiae</i> , <i>Candida albicans</i>	Lobophorolide	-	Kubaneck et al. (2003)
Antifungal	<i>L. variegata</i>	<i>Aspergillus fumigatus</i> , <i>Candida albicans</i> , <i>Saccharomyces cerevisiae</i>	-	MeOH	Val et al. (2001)
Antiprotozoal	<i>L. variegata</i>	<i>Trichomonas vaginalis</i> , <i>Entamoeba histolytica</i> , <i>Giardia intestinalis</i>	Mixture of sulfoquinovosyl-diacylglycerols (SQDGs)	CH ₂ Cl ₂ /MeOH	Cantillo-Ciau et al. (2010)
Antiprotozoal	<i>L. variegata</i>	<i>Trypanosoma cruzi</i>	-	CH ₂ Cl ₂ /MeOH	León-Deniz et al. (2009)
Antiprotozoal	<i>L. variegata</i>	<i>Trichomonas vaginalis</i>	-	CH ₂ Cl ₂ /MeOH	Moo-Puc et al. (2008)
Antiprotozoal	<i>L. variegata</i>	<i>Leishmania mexicana</i>	-	CH ₂ Cl ₂ /MeOH	Freile-Pelegrin et al. (2008)
Antiprotozoal	<i>L. variegata</i>	<i>Schizochytrium aggregatum</i>	-	CH ₂ Cl ₂ /MeOH [divided into lipophilic (EtOAc) and hydrophilic (H ₂ O) parts]	Engel et al. (2006)

Other pharmacological activities

Anti-angiogenic	<i>L. variegata</i>	Embryonated chicken eggs	Sulfated polysaccharides (fucans)	-	Castro et al. (2014a)
Anticoagulant	<i>L. variegata</i>	Human plasma	Sulfated polysaccharides (fucans)	-	Castro et al. (2014b)
Anticoagulant	<i>L. variegata</i>	Human plasma	Sulfated polysaccharide (fucoidan)	-	Medeiros et al. (2008)
Anticoagulant	<i>L. variegata</i>	Human plasma	-	H ₂ O (Phosphate buffer)	De Lara-Isassi et al. (2004)
Anti-inflammatory	<i>L. variegata</i>	Male Swiss-Webster mice	Sulfated polysaccharides (fucans)	-	Castro et al. (2014b)
Anti-inflammatory	<i>L. variegata</i>	Wistar rats	Sulfated polysaccharides (fucans)	-	Paiva et al. (2011)
Anti-inflammatory	<i>L. variegata</i>	Wistar rats	Sulfated polysaccharide (fucan)	-	Siqueira et al. (2011)
Anti-inflammatory	<i>L. variegata</i>	Wistar rats	Sulfated polysaccharide (fucoidan)	-	Medeiros et al. (2008)
Antioxidant	<i>L. variegata</i>	Chemical test	3-(2-methoxy-4-((2,5,6,8a-tetramethyl-1,4,8,8a-tetrahydronaphthalen-1-yl)methyl)phenyl)propanoate	H ₂ O/MeOH	Sathyaseelan et al. (2015)
Antioxidant	<i>L. variegata</i>	Wistar rats	-	-	Paiva et al. (2011)
Antioxidant	<i>L. variegata</i>	Chemical test	-	CH ₂ Cl ₂ /MeOH	Zubia et al. (2007)

Antioxidant	<i>L. variegata</i>	Chemical test	Sulfated polysaccharides (fucans)	-	Castro et al. (2014b)
Cytotoxic	<i>L. variegata</i>	Human nasopharyngeal carcinoma (KB) cell line	-	CH ₂ Cl ₂ /MeOH	Moo-Puc et al. (2009)
Cytotoxic	<i>L. variegata</i>	C32 human melanoma cells	-	Acetone and H ₂ O	Rocha et al. (2007)
Cytotoxic	<i>L. variegata</i>	Human promyelocytic leukemia HL-60 cells	Polysaccharides (a glucan and three galactofucans)	-	Queiroz et al. (2006)
Cytotoxic	<i>L. variegata</i>	Human colon tumor cell line HCT-116	Lobophorolide	-	Kubaneck et al. (2003)
Cytotoxic	<i>L. variegata</i>	Murine P-388 lymphocytic leukemia, Ehrlich ascites tumor cells	-	<i>n</i> -Hexane, CHCl ₃ and then ButOH	Kashiwagi et al. (1980)
Cytotoxic	<i>L. variegata</i>	Vero, HEp-2 and MDCK cells	-	H ₂ O	Wang et al. (2008a)
Cytotoxic	<i>L. variegata</i>	Human breast carcinoma MCF-7 cells	-	H ₂ O	Wang et al. (2008a)
Cytotoxic	<i>L. variegata</i>	Human colon tumor cell line HT-29	Sulfated polysaccharides (fucans)	-	Castro et al. (2014b)
Hemagglutinating	<i>L. variegata</i>	Chicken, goat, pig, rabbit and human erythrocytes	-	H ₂ O (NaCl)	Lima Ainouz et al. (1992)
<i>Pesticidal activities</i>					
Pupicidal	<i>L. variegata</i>	<i>Culex quinquefasciatus</i>			
Nematicidal	<i>L. variegata</i>	<i>Meloidogyne javanica</i>	Fatty acids	MeOH	Manilal et al. (2012)
Phytotoxic	<i>L. variegata</i>	<i>Cicer arietinum</i> , <i>Vigna radiate</i> and <i>Cajanus cajan</i> seeds			
Larvicidal	<i>L. variegata</i>	<i>Aedes aegypti</i>	-	CH ₂ Cl ₂ /MeOH	Bianco et al. (2013)
<i>Ecological roles</i>					
Antifouling	<i>L. variegata</i>	<i>Perna perna</i>	-	CH ₂ Cl ₂ /MeOH or CH ₂ Cl ₂	Da Gama et al. (2008)
Antifouling	<i>L. variegata</i>	<i>Balanus amphitrite</i> , <i>Mytilus edulis</i>	-	MeOH	Manilal et al. (2010a)
Bleaching	<i>L. variegata</i>	<i>Porites cylindrica</i>	-	MeOH [Lipophilic (EtOAc) part]	Rasher Hay (2010a)
Bleaching	<i>L. variegata</i>	<i>Montastrea cavernosa</i>	SQDG	CH ₂ Cl ₂ /MeOH	Slattery Lesser (2014)
Cell lysis	<i>L. variegata</i>	<i>Agelas clathrodes</i>	SQDG	CH ₂ Cl ₂ /MeOH	Slattery Lesser (2014)
Ichthyotoxic	<i>L. variegata</i>	-	Phlorotannins	-	Stern et al. (1996)
Ichthyotoxic	<i>L. variegata</i>	<i>Carassius auratus</i>	-	Acetone, EtOH and H ₂ O	De Lara-Isassi et al. (2000)
Ichthyotoxic	<i>L. variegata</i>	<i>Lytechinus variegatus</i> , <i>Diplodus holbrooki</i>	-	CH ₂ Cl ₂ /MeOH	Cetrulo Hay (2000)
Settlement enhancement	<i>L. variegata</i>	<i>Acropora millepora</i>	-	Seawater (waterborne extract)	Birrell et al. (2008)

Shift of coral-associated bacteria	<i>L. variegata</i>	<i>Montastraea faveolata</i> , <i>Porites astreoides</i>	-	EtOAc/MeOH and then EtOH/H ₂ O	Morrow et al. (2012)
Sublethal stress response	<i>L. variegata</i>	<i>Montastraea faveolata</i> , <i>Porites astreoides</i>	-	EtOAc/MeOH and then EtOH/H ₂ O	Morrow et al. (2012)

452 Table 2. *Lobophora* natural products for which bioactivity has not been tested in
 453 the study.

Molecule	Species	Reference
Volatile carbonyl compounds		
Acetaldehyde	<i>Lobophora variegata</i>	Mota da Silva et al. (2006)
Butanal	<i>Id.</i>	<i>Id.</i>
Formaldehyde	<i>Id.</i>	<i>Id.</i>
Hexanal	<i>Id.</i>	<i>Id.</i>
Pentanal	<i>Id.</i>	<i>Id.</i>
Propanal	<i>Id.</i>	<i>Id.</i>
Propanone	<i>Id.</i>	<i>Id.</i>
Fatty acids		
Docosahexaenoic acid (DHA)	<i>Lobophora variegata</i>	Thennarasan (2015)
Eicosapentaenoic acid (EPA)	<i>Id.</i>	<i>Id.</i>
Hexadecatrienoic acid	<i>Id.</i>	Manilal et al. (2012)
Lauric acid	<i>Id.</i>	<i>Id.</i>
Linoleic acid	<i>Id.</i>	Thennarasan (2015)
Margaric acid	<i>Id.</i>	<i>Id.</i>
Myristic acid	<i>Id.</i>	Manilal et al. (2012)
Oleic acid	<i>Id.</i>	Thennarasan (2015), Manilal et al. (2012)
Palmitic acid	<i>Id.</i>	<i>Id.</i>
Stearic acid	<i>Id.</i>	<i>Id.</i>
Stearidonic (moroticic) acid	<i>Id.</i>	Thennarasan (2015)
α -Linolenic acid	<i>Id.</i>	Thennarasan (2015), Manilal et al. (2012)
Phenols		
Phenolic substances	<i>Lobophora variegata</i>	Chkhikvishvili Ramazanov (2000)
4-Bromophenol	<i>Lobophora</i> sp.	Chung et al. (2003)
2,4,6-Tribromophenol	<i>Id.</i>	<i>Id.</i>
2,4-Dibromophenol	<i>Id.</i>	<i>Id.</i>
2,6-Dibromophenol	<i>Id.</i>	<i>Id.</i>
Polyphenols	<i>Lobophora variegata</i>	(Rao and Untawale 1991)
Photosynthetic pigment		
9'- <i>Cis</i> -Neoxanthin	<i>Lobophora variegata</i>	(Hegazi 2002)
Antheraxanthin	<i>Id.</i>	<i>Id.</i>
Chlorophyll <i>a</i>	<i>Id.</i>	<i>Id.</i>
Chlorophyll <i>a</i> '	<i>Id.</i>	<i>Id.</i>
Chlorophyll c1	<i>Id.</i>	<i>Id.</i>
Chlorophyll c2	<i>Id.</i>	<i>Id.</i>
Diatoxanthin	<i>Id.</i>	<i>Id.</i>
Flavoxanthin	<i>Id.</i>	<i>Id.</i>
Fucoxanthin	<i>Id.</i>	<i>Id.</i>
Fucoxanthol	<i>Id.</i>	<i>Id.</i>
Phaeophytin <i>a</i>	<i>Id.</i>	<i>Id.</i>
Violaxanthin	<i>Id.</i>	<i>Id.</i>
Zeaxanthin	<i>Id.</i>	<i>Id.</i>
β -carotene	<i>Id.</i>	Sousa et al. (2008), (Hegazi 2002)
Vitamins		
Vitamin A	<i>Lobophora variegata</i>	Thennarasan (2015), Sousa et al. (2008)

Vitamin B1	<i>Id.</i>	Thennarasan (2015)
Vitamin B2	<i>Id.</i>	<i>Id.</i>
Vitamin B3 (niacinamide)	<i>Id.</i>	<i>Id.</i>
Vitamin B5 (calcium pantothenate)	<i>Id.</i>	<i>Id.</i>
Vitamin B6	<i>Id.</i>	<i>Id.</i>
Vitamin B9 (folic acid)	<i>Id.</i>	<i>Id.</i>
Vitamin B12	<i>Id.</i>	<i>Id.</i>
Vitamin C	<i>Id.</i>	<i>Id.</i>
Vitamin D	<i>Id.</i>	<i>Id.</i>
Vitamin E	<i>Id.</i>	<i>Id.</i>
γ -Tocopherol	<i>Lobophora papenfussii, L. variegata</i>	Gerwick Fenical (1982), Sousa et al. (2008)
Sterols		
Campesterol	<i>Lobophora variegata</i>	Thennarasan (2015)
Stigmastanol (sitostanol)	<i>Id.</i>	<i>Id.</i>
β -sitosterol	<i>Id.</i>	<i>Id.</i>

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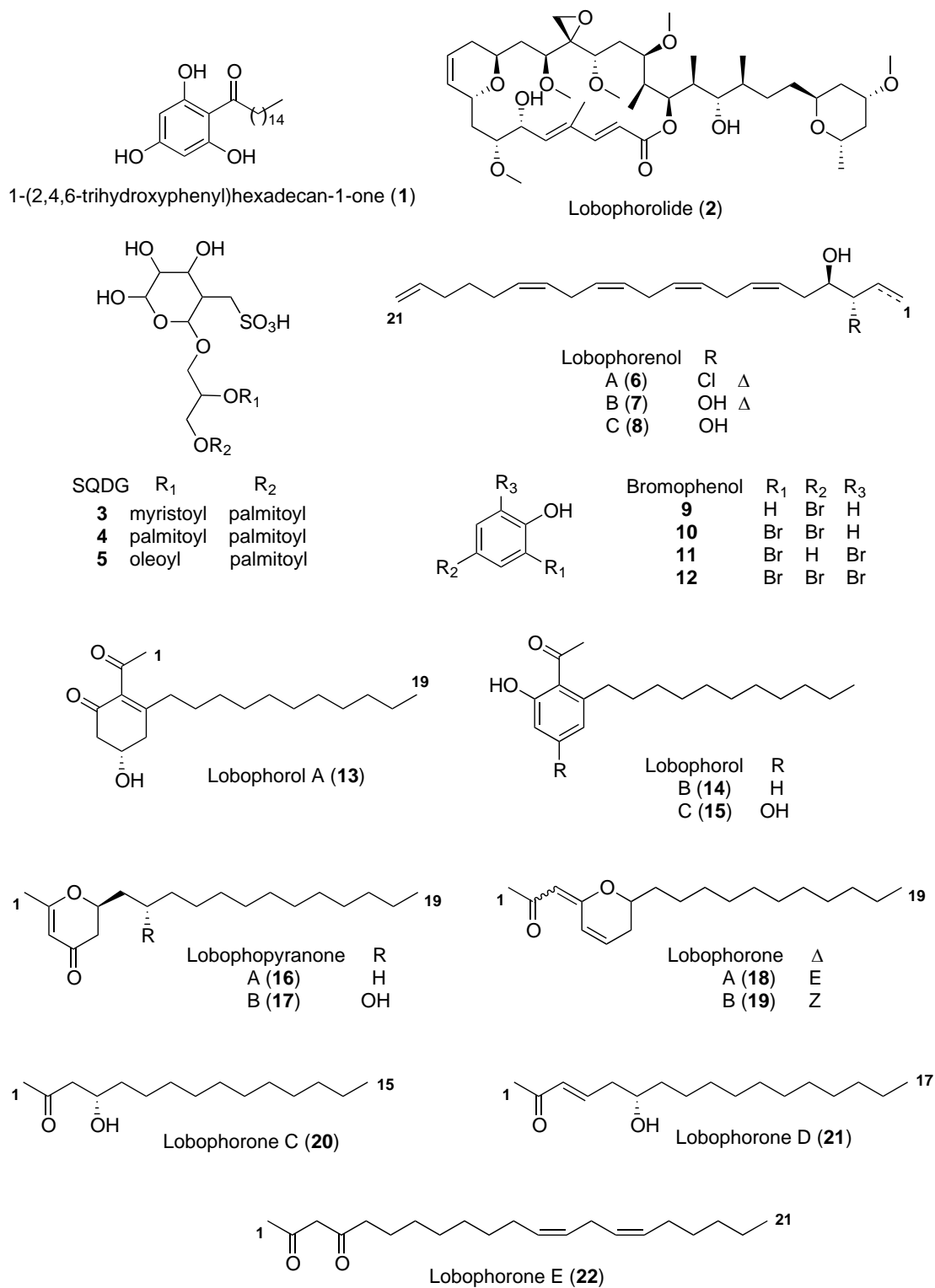
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722 **Fig. 1** Chemical structure of the natural products isolated from different species of *Lobophora*
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 724 Kubanek et al. 2003; Vieira et al. in revision).

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