

# Defensive strategies of Cladobranchia (Gastropoda, Opisthobranchia)

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The focus of this review lies on the evolution of defensive systems of an opisthobranch group, the Cladobranchia. These organisms completely lost the protective shell, and employ as alternative defence strategies toxic secondary metabolites or cnidocysts. Whereas the biochemistry of several opisthobranch groups is well studied (*e.g.* Doridoidea, Sacoglossa, Anaspidea, and to a lesser extent Cephalaspidea), the Cladobranchia are neglected in this respect. One group within the Cladobranchia, the Aeolidioidea, is of special interest since members of this group are known to employ either incorporated cnidocysts or secondary metabolites from their cnidarian prey for their own defence. Based on the reviewed literature, we discuss the impact of sequestration or *de novo* synthesis of secondary metabolites, and the incorporation of cnidocysts as key features for speciation within the Cladobranchia. 145 references are cited.

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## 1 Introduction

Most molluscs, such as bivalves, snails, polyplacophorans, and even primitive cephalopods such as *Nautilus*, have a shell to protect them from predators; its presence is without doubt the most important defensive strategy for these animals. Despite its protective function, a shell probably handicaps certain life-styles or actions like swimming, crawling on fragile substrates, or quick movements while pursuing potential prey. It also may hamper basic physiological processes, *e.g.* gas exchange through the epidermis. Loss of the shell has thus occurred in several molluscan groups. Whereas octopuses and squids gained much higher mobility and are able to escape potential predators by speed, this is not the case for the Gastropoda (snails and slugs). In marine gastropods, reduction or a complete loss of the shell has occurred in the Opisthobranchia, potentially facilitating the

occupation of new ecological niches and therefore supporting speciation within this group.<sup>1,2</sup> However, absence of a protective shell necessitates alternative defensive mechanisms such as the incorporation and use of cnidocysts from cnidarian prey<sup>3–5</sup> and the uptake or synthesis of biochemicals.<sup>6,7–11</sup> The sequestration of secondary metabolites from the prey, or even *de novo* synthesis, has been considered as a major driving force for speciation within Opisthobranchia.<sup>12–14</sup> In this review, we intend to shed light on the evolution of the defensive strategies of the Cladobranchia as an opisthobranch clade that completely lost the protective shell. The Cladobranchia are of special interest since the incorporation of cnidocysts is a unique feature in the animal kingdom, occurring exclusively within this group. In this context, we discuss the role of secondary metabolites and cnidocysts as key features for the evolutionary success of this enigmatic group. Tables 1, 2 and 3 summarize all chemical investigations on Cladobranchia, the presence of morphological structures probably related to the storage of defence chemicals, the uptake of cnidocysts, and information on the respective food organisms.

## 2 Cladobranchia

Opisthobranchia, often referred to as ‘butterflies of the sea’, show evolutionary reduction or a complete loss of the shell independently within many clades (Fig. 1A). The most important defence strategies which ensure protection against predators involve cryptic appearance by mimicking colouration and shape<sup>15,16</sup> of the food organism (Fig. 2A, B), formation of spicules<sup>17</sup> in epidermal tissue (Fig. 2C, D), and the uptake or synthesis of biochemicals encountered in many opisthobranch species (Fig. 2E–H). Defence by incorporation of toxic compounds has probably also led to the evolution of aposematism (warning colouration) in many groups<sup>15,16,18–21</sup> (Fig. 2E–G). Within the Opisthobranchia, the biochemistry of many groups is well studied,<sup>6,7–11,13,14</sup> whereas the Cladobranchia are neglected in this respect. Incorporation and use of

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cnidocysts from cnidarian prey (cleptocnides)<sup>3–5</sup> (Fig. 3C–F) occurs exclusively within this latter group, on which we focus here.

The Cladobranchia are divided into several well-defined clades (Fig. 1B), but their relationship to each other is not yet clarified.<sup>22,23</sup> Due to this uncertainty concerning the taxonomy of Cladobranchia, we use for the purpose of this review the traditional naming for the three main groups: Dendronotoidea, Arminoidea and Aeolidioidea (Tables 1–3). In general, the majority of cladobranch species feed on cnidarians, *i.e.* anthozoans (hexacorals and octocorals) and hydrozoans, whereas some members consume bryozoans (Fig. 1B). The food sources for Cladobranchia are summarized in more detail in Tables 1–3.



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### 3 Cleptocnides

The incorporation of cnidocysts from cnidarian prey ('cleptocnides') into special organs, *i.e.* the cnidosacs (Fig. 3D), is a unique feature of the cladobranch group Aeolidioidea, and not encountered elsewhere in the molluscs with one exception, the genus *Hancockia*<sup>24,25</sup> (Dendronotoidea).<sup>26</sup> Cnidocysts are complex structures emerging from the Golgi apparatus and stored in specialised cells of Cnidaria. The process of incorporation and maintaining these structures in a functional state inside of the slug's body is not yet understood. Interestingly, when considering the number of species within the different cladobranch groups, the Aeolidioidea, comprising about 600 species, by far outnumber the others. Dendronotoidea, as the second largest group within the Cladobranchia, only comprise about 250 species. Hence, a likely hypothesis is that incorporation of cleptocnides was an extremely successful strategy that enhanced speciation and radiation.<sup>27–29</sup>

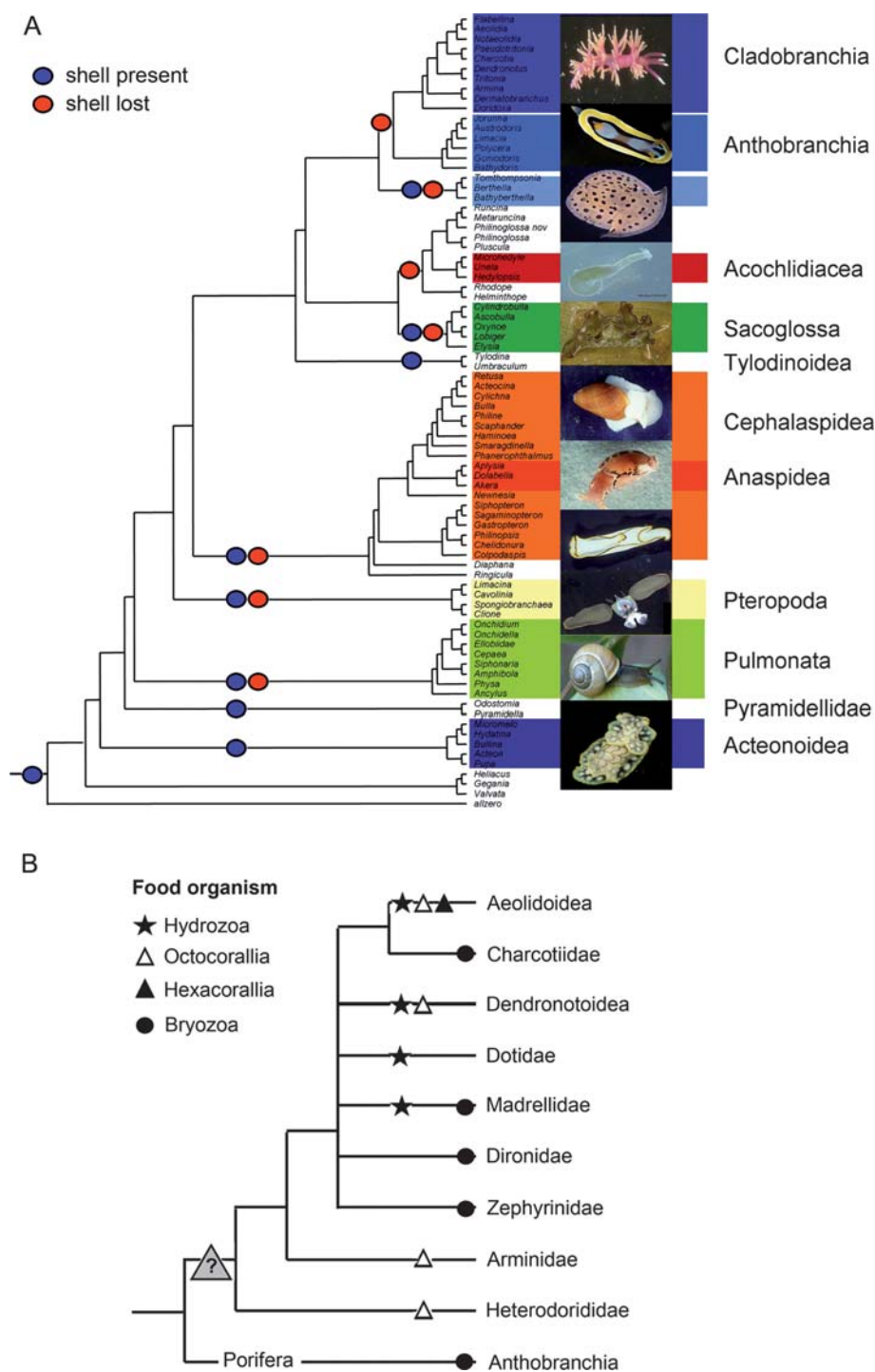
It is assumed that aeolidioideans defend themselves primarily by using these cleptocnides against potential predators. This was demonstrated by Frick<sup>30</sup> showing that *Flabellina verrucosa* modulates nematocyst incorporation in response to the presence of predators. During a study on defensive strategies in aeolidioideans on Guam (USA), the authors also experienced painful contact with *Pteraeolidia ianthina* (Fig. 3C), which incorporates nematocysts from the hydrozoan *Pennaria disticha* and an as-yet unidentified hydroid (Fig. 3E<sup>31,32</sup>).

On the other hand, members of the Aeolidioidea feeding on soft corals seem to be protected by compounds from their food, and do not rely on the incorporation of cnidocysts. The aeolidioidean genus *Phyllodesmium* exhibits cnidosacs, but functional cnidocysts are missing in the sacs of this genus.<sup>32–34</sup> *Phyllodesmium* species forage on octocorals with toxic metabolites, such as *Heteroxenia*, *Xenia*, *Briareum*, *Sarcophyton*, *Simularia*, *Clavularia*, or *Erythropodium*. These octocorals produce diterpenes and sesquiterpenes (see, for example, ref. 35 and other publications; Table 3). There is evidence that *Phestilla*, another genus lacking functional cnidocysts even though the cnidosac is still present,<sup>36</sup> obtains biochemicals from its prey.<sup>37</sup> Interestingly,



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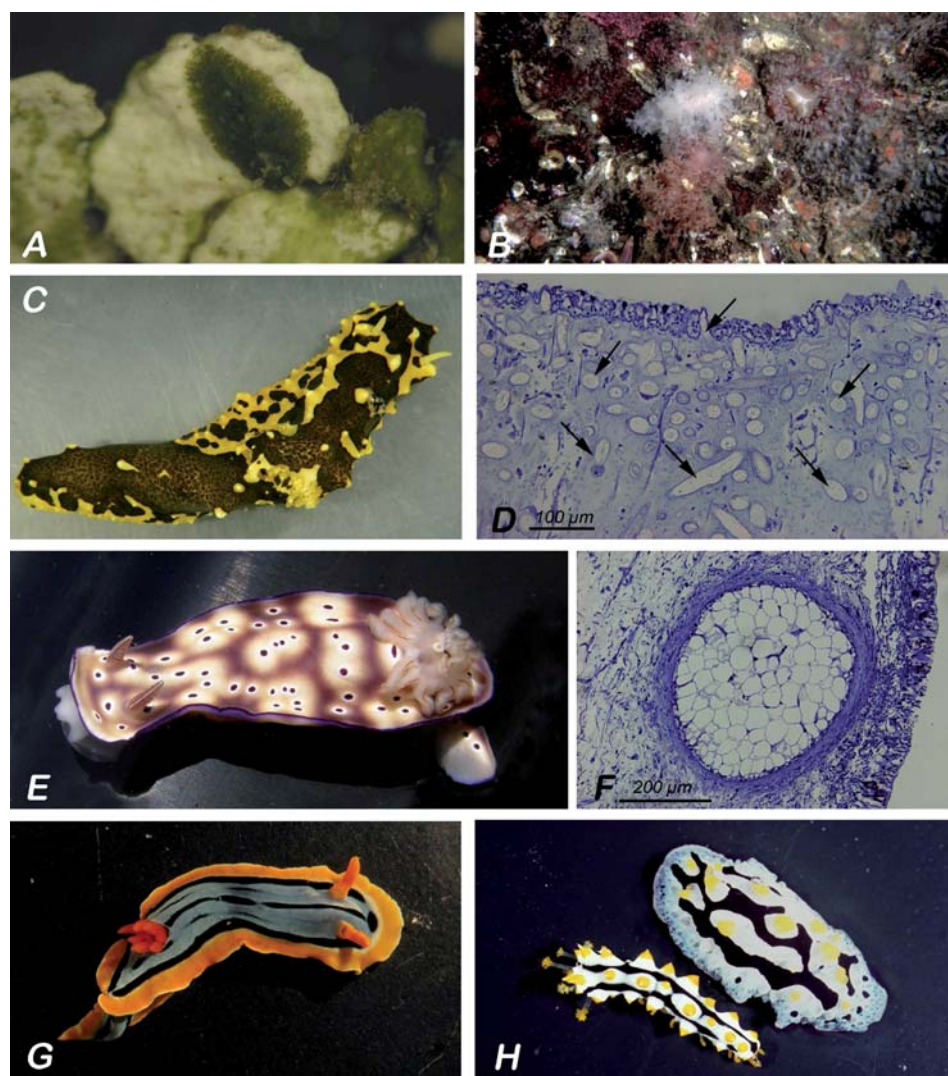


**Fig. 1** A. Information on phylogenetic relationships: A. Cladogram of the Opisthobranchia based on morphology and histology with information of shell loss within the different clades (after ref. 1). When both symbols (red and blue) are present in the same stemline, then at least the basal genera still have a shell. B. Phylogeny of Cladobranchia (after ref. 22,23). Main food organisms (higher taxa) are indicated with symbols on the respective stemline. According to the phylogeny, it seems likely that feeding on Octocorallia evolved in the stemline of the Cladobranchia (large triangle with question mark).

our own unpublished results on a juvenile *P. lugubris* reveal functional cleptocnides in the cnidosacs (see Table 3).

Preliminary observations indicate that especially those species protected exclusively by these compounds are rather cryptic in appearance (Fig. 3A, B), whereas others known to defend

themselves by cleptocnides are far more colourful (Fig. 3C, F, G). This leads to the following question – under which conditions are cleptocnides or biochemicals the better defence (the latter being much less obvious in the majority of aeolidoid species feeding on Hydrozoa<sup>38</sup>)?



**Fig. 2** Defensive mechanisms in opisthobranchs. A. Specimen of the sacoglossan *Elysia pusilla* on its food organism *Halimeda* (Lizard Island, Australia). B. Two specimens of *Dendronotus frondosus*, a white and a red form, in their natural habitat (Kungsfjord, Sweden, depth 10 m); size of animals about 3 cm. C. *Notodoris gardineri* (Lizard Island, Australia), a doridoidean feeding on sponges. D. Cross-section of notum (*Notodoris citrina*) showing many spicules in the tissue (arrows). E. *Risbecia tryoni* (Lizard Island, Australia); size of animal about 3 cm. F. *Risbecia tryoni*, mantle dermal formation in which natural products are usually stored. G. *Chromodoris elizabethina* (Lizard Island, Australia); size of animal about 2 cm; animal possesses mantle dermal formations with toxic compounds. H. *Phyllidia varicosa*, a sponge feeder known to incorporate toxic compounds. The warning colours of the slug are mimicked by juveniles of the holothurian *Pearsonathuria graeffei*.

#### 4 Secondary metabolites of Cladobranchia

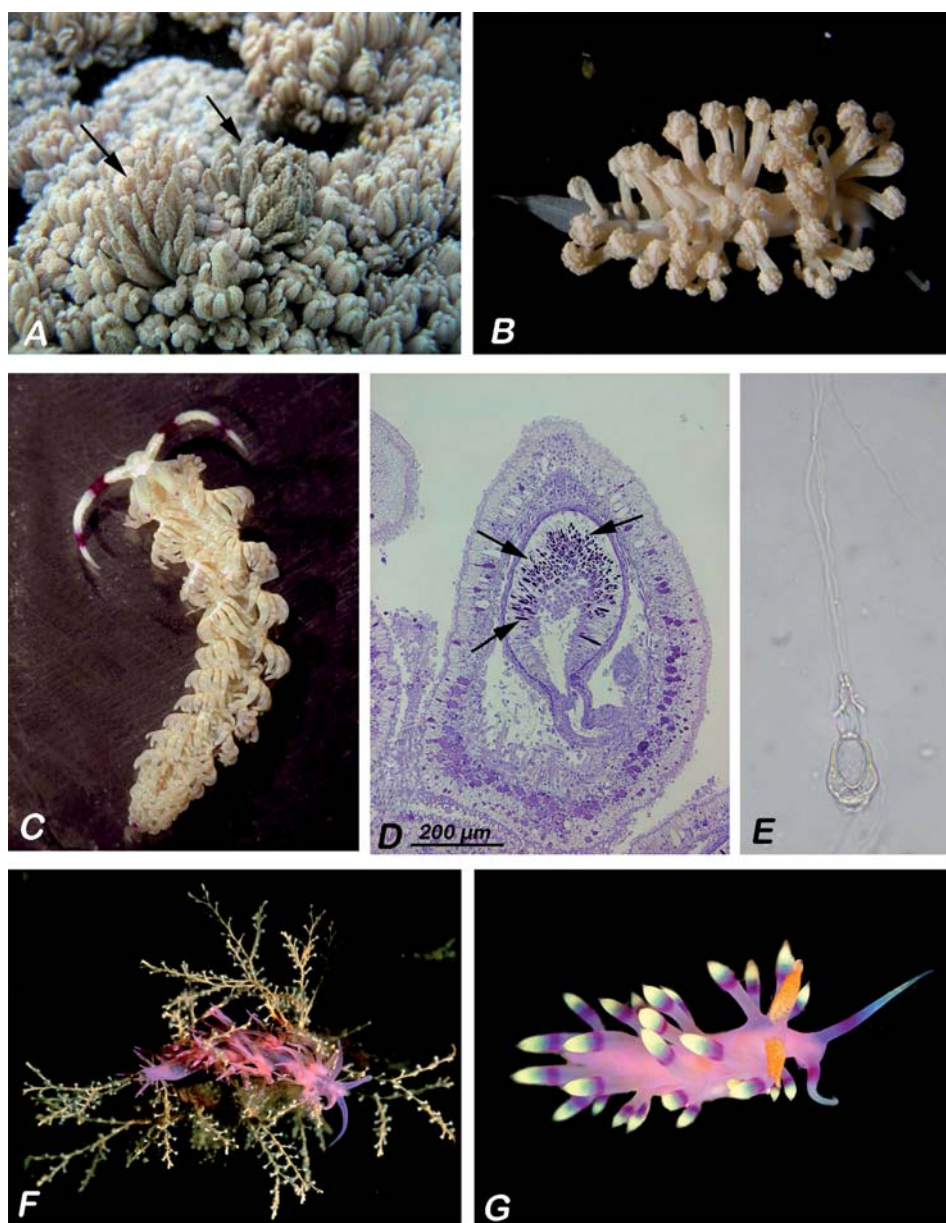
There is a tremendous wealth of information on the presence of secondary metabolites in opisthobranch groups closely related to the Cladobranchia<sup>39–46</sup> (reviewed, for example, in ref. 6). These slugs, called Anthobranchia, feed on Porifera (sponges) and to a lesser extent Bryozoa, as well as Tunicata<sup>47</sup> (Fig. 1A, B). In several of these studies, the feeding deterrence against predators was investigated and confirmed.<sup>48</sup> In contrast, the natural product chemistry of the Cladobranchia (Fig. 1B) has not been investigated extensively.<sup>49</sup>

In certain opisthobranch taxa, the occurrence of secondary metabolites seems to be related to characteristic morphological structures, the so-called mantle dermal formations (MDFs)<sup>49–53</sup> in which compounds are stored<sup>49</sup> (Fig. 2F). Histological

investigation of Cladobranchia revealed no MDFs, but special cells in the epidermis of many members of the Dendronotoidea<sup>49</sup> and the so-called marginal sacs in the Arminidae<sup>54,55</sup> (Table 1), which have a similar distribution as the MDFs and indicate the possible storage of toxic chemicals. However, neither the contents nor the function of these structures have been investigated. From aeolidoidean species, no comparable structures are currently known.

##### 4.1 Dendronotoidea

Of the Dendronotoidea, comprising about 250 species, information is available from organisms belonging to the families Tritoniidae, Dotidae and Tethydidae. These animals usually feed on Octocorallia or Hydrozoa (Fig. 1B, Table 1).

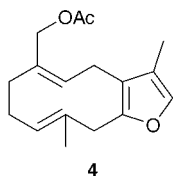
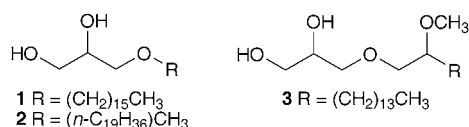


**Fig. 3** Defensive mechanisms in Cladobranchia: A. Two specimens of *Phylloidesmium lizardensis* (arrows) *in situ* on their sole food organisms, *Heteroxenia* sp. (Lizard Island, Australia). B. Isolated specimen of *Phylloidesmium lizardensis*; size of animal about 3 cm. C. *Pteraeolidia ianthina*; note the many cerata along the back, each of which contains a cnidosac at the end. D. Cnidosac of *Aeolidia papillosa* with cleptocnides (arrows). E. Isolated cnidocyst of *Pteraeolidia ianthina*. F. *Flabellina pedata* (North Sea); size of animal 1 cm. G. *Flabellina exoptata* (Lizard Island, Australia), size of animal 1.5 cm.

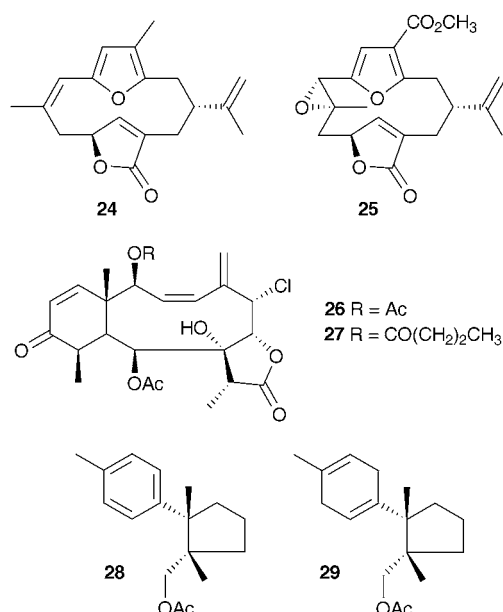
Only a few members of the Dendronotoidea, particularly animals of the family Tritoniidae which forage on octocorals, have been studied in detail concerning their secondary metabolites. Three glycerol ethers **1–3** were detected in *Tritoniella belli* from Antarctic waters, primarily 1-*O*-hexadecyl glycerol (chimyl alcohol, **1**). Chimyl alcohol **1** was also detected after gradient flash chromatography and reversed-phase HPLC purification in the tissues of *Clavularia frankliniana*, a stoloniferan octocoral, the most common prey of *Tritoniella belli*.<sup>56</sup> The feeding deterrence of these compounds was confirmed in feeding experiments against the common omnivorous predatory Antarctic sea star *Odontaster validus* and fish.<sup>56</sup> A close relative from the Caribbean

waters, *Tritonia hamnerorum*, specializes on the sea fan *Gorgonia ventalina* as a food source and sequesters the furano-germacrene julieannafuran **4** from its host; this compound effectively protects the nudibranch from consumption by the common predatory reef fish *Thalassoma bifasciatum*.<sup>57</sup> The methanolic extract of *Tritonia* sp. (presumably *T. wellsi*) collected on its prey, the punaglandin-containing octocoral *Telesto riisei*, revealed that punaglandins **5–23** are sequestered by the predator.<sup>58</sup> Punaglandins are chlorinated prostaglandins and show cytotoxic effects.<sup>59</sup> Finally, Kennedy and Vevers<sup>60</sup> reported that “the upper integument” of a further *Tritonia* species, *Tritonia* (formerly *Duvaucelia*) *plebeia* yields a uroporphyrin pigment. *Tochuina*

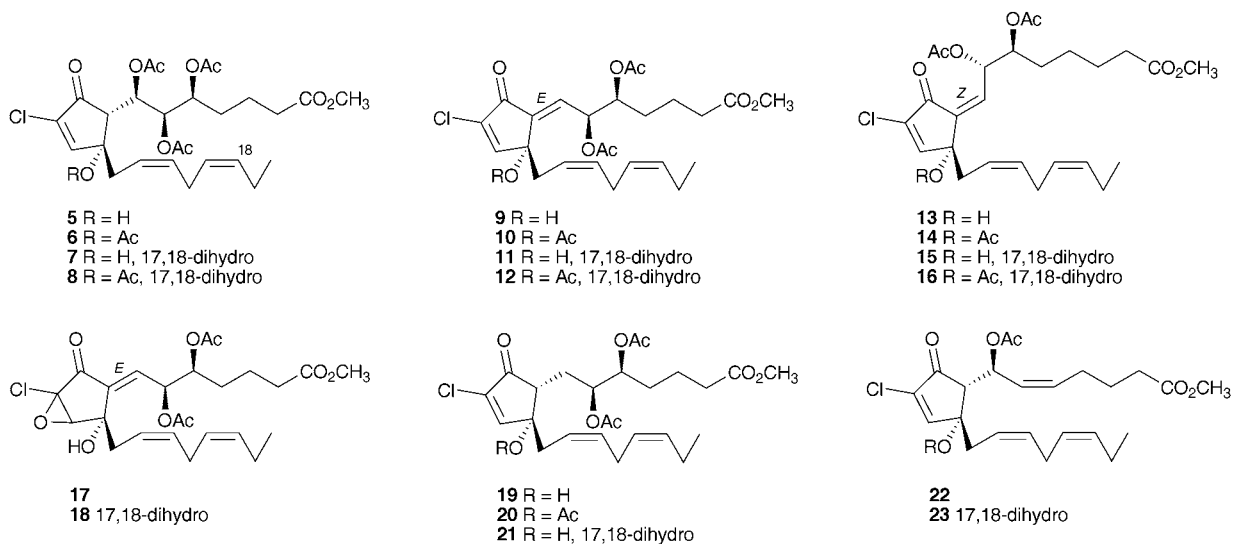
*tetraquetra* sampled in British Columbia yielded the previously known cembrane diterpenoids rubifolide **24** and pukalide **25**, the briarein-type diterpenoid ptilosarconone **26** along with a new butanoate analogue **27**, and the two new cuparane sesquiterpenoids, tochuinyl acetate **28** and dihydrotochuinyl acetate **29**.<sup>61</sup> The two latter compounds **28–29** and rubifolide **24** are metabolites of the soft coral *Gersemia rubiformis*,<sup>62</sup> one of the preferred dietary organisms of *T. tetraquetra*. The toxin ptilosarconone **26** was described as a major natural product of the sea pen *Ptilosarcus gurneyi*<sup>63</sup> commonly encountered in the habitat of the nudibranch. However, despite extensive studies, pukalide **25** and the butanoate analogue **27** could be attributed neither to *G. rubiformis* nor to *P. gurneyi*. It thus remains an open question as to whether these metabolites are accumulated from yet another food source, or are present in undetectable trace amounts in the food, or result from chemical transformations carried out by the nudibranch.<sup>64</sup>



Members of the family Tethydidae lack jaws and a radula, and are characterized by a peculiar mode of feeding not encountered elsewhere in opisthobranchs, *i.e.* animals capture crustaceans and turbellarians with their hood-shaped head and swallow their prey whole. *Melibe* and *Tethys* are the two single genera within this family, both being well-investigated with regard to their chemistry. For *Melibe leonina*, it was reported that the primary defence is an odoriferous substance secreted by specialized



glands in the body wall. This substance was identified as 2,6-dimethyl-5-heptenal **30**<sup>64</sup> acquired by *de novo* biosynthesis, which was proven by applying stable isotope feeding studies using [1,2-<sup>13</sup>C<sub>2</sub>]-sodium acetate.<sup>65</sup> However, deterrent activity could not be demonstrated due to the volatile nature of this compound.<sup>64</sup> Chemical studies of the Mediterranean *Tethys fimbria* led to the characterization of many prostaglandin-1,15-lactones<sup>66,67</sup> (PGLs) such as **31–36** which have been shown to be produced *de novo* by injecting tritiated arachidonic acid, prostaglandin-E<sub>2</sub> and prostaglandin-F<sub>2α</sub>.<sup>68,69</sup> Anatomical investigations revealed that PGE **31–32** and PGA lactones **33–34** were present in the cerata, PGF **35–36** lactones dominated in the mantle and, as fatty acid esters, in hermaphroditic glands and egg masses.<sup>70,71</sup> A double defensive role was suggested for the PGE lactones. On one hand they act as ichthyotoxins, while, as the PG



free acids (but not the PG-1,15-lactones), they contract mammalian smooth muscle.<sup>72</sup> The authors speculated that PG free acids derived from opening of PG-1,15-lactones of the E series following detachment of the slug's back appendages, *i.e.* the cerata,<sup>71</sup> are used *in vivo* to contract ceratal tissue. If this proves right, PG-1,15-lactones of the E series would participate in the defensive mechanisms at two different levels: directly by

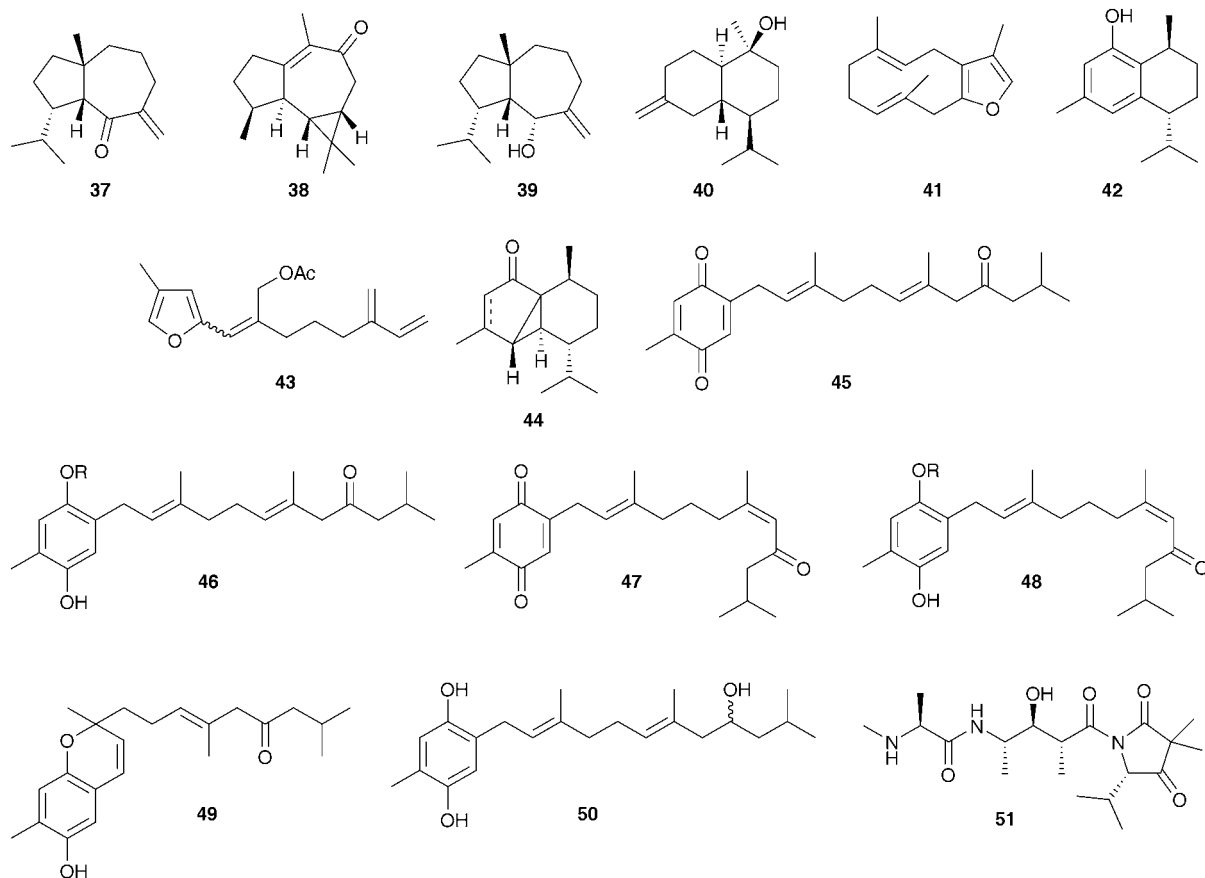
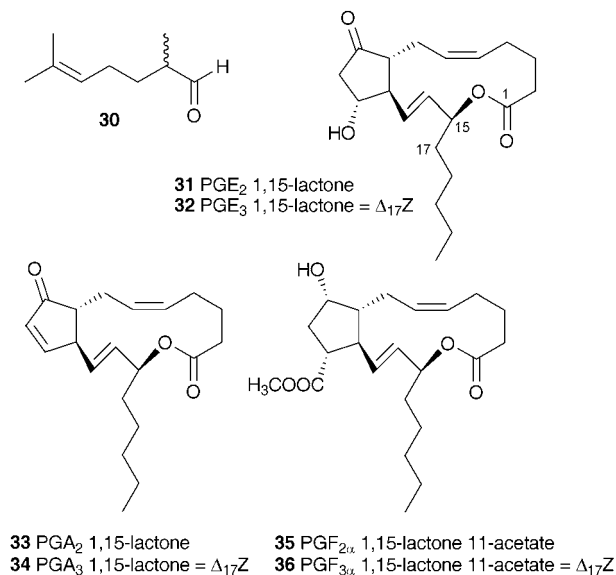
ceratal secretion and indirectly as precursors of bioactive PGs which contract the ceratal tissue, probably facilitating the secretion of lactones.<sup>70</sup>

## 4.2 Arminoidea

Investigation into the Arminoidea, which comprises about 150 species (assigned to the families Charcotiidae, Madrellidae, Dironidae, Zephyrinidae and Arminidae; Fig. 1B), is also scarce and only covers members of a few families (Table 2).

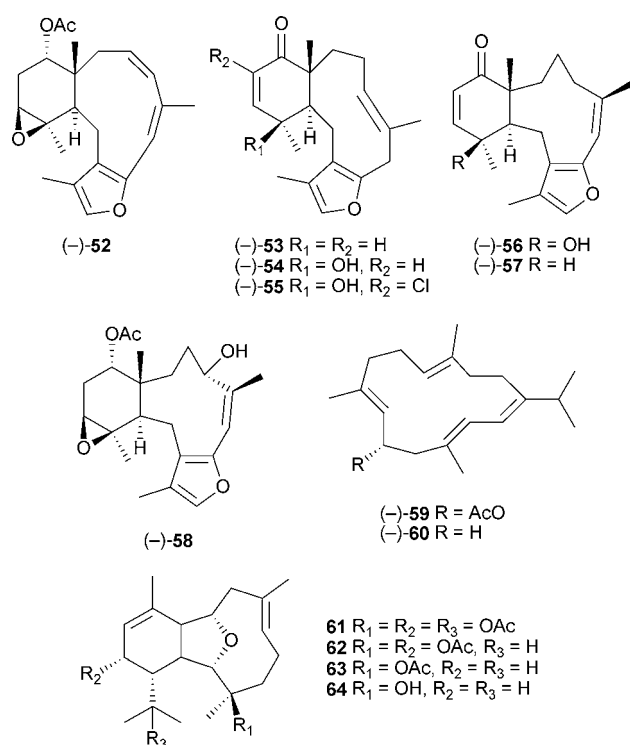
The dietary habits of members of the family Charcotiidae are not clear, with *Leminda millecra* being the only species from this family that has been investigated chemically. Pika and Faulkner<sup>73</sup> identified four new sesquiterpenes, the antimicrobially active millecrones A **37** and B **38**, and millecrols A **39** and B **40**, resembling metabolites typically found in soft corals. Investigation of the nudibranch's digestive gland revealed the presence of spicules from soft corals.<sup>73</sup> McPhail *et al.*<sup>74</sup> subsequently isolated further compounds in addition to the previously described sesquiterpenes, *i.e.* isofuranodiene **41**, (+)-8-hydroxycalamenene **42**, algoafuran **43**, cubebenone **44** and a series of prenylquinones and hydroquinones **45–50**. Furthermore, the source of millecra A **37** was identified as the soft coral *Alcyonium fauri*, while millecra B **38** and cubebenone **44** were found in the gorgonian *Leptogorgia palma*, the food source of *L. millecra*.

Sodano and Spinella<sup>75</sup> investigated *Janolus cristatus* of the family Zephyrinidae, and found a nitrogen-containing compound, the toxic tripeptide janolusimide **51**. Since the



nudibranch's diet was not analysed, it is not clear if this compound is food-derived. Janolidae feed on Bryozoa,<sup>47</sup> of which many species exhibit elaborate chemical protection (see, for example, ref. 76,77).

Members of the Arminidae feed on octocorals (Fig. 1B, Table 1). Guerrero *et al.*<sup>78–80</sup> identified briarane (verecynarmins A–G **52–58**) and cembrane (preverecynarmin **59**, cembrene C **60**) diterpenoids in *Armina maculata* and its prey organism, the pennatulacean octocoral *Veretillum cynomorium*. In *Dermatobranchus ornatus*, another representative of the family Arminidae distributed in the tropical Indo–West Pacific region, four diterpenoids from the eunicellin class could be identified, namely ophirin **61**, calcicophirin B **62**, 13-deacetoxycalcicophirin B **63**, and 13-deacetoxy-3-deacetylcalcicophirin B **64**.<sup>81</sup> Calcicophirin B **62** and 13-deacetoxycalcicophirin B **63** were also present in the octocoral *Muricella sinensis*, the possible prey organism,<sup>81</sup> and

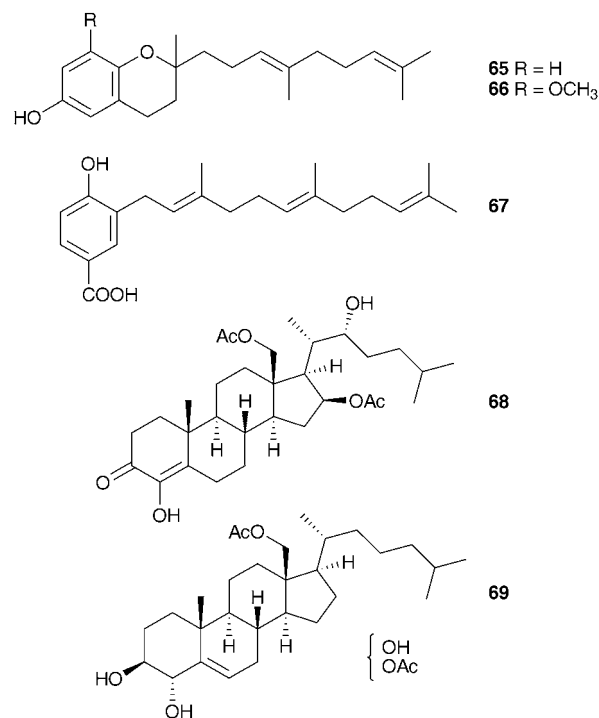


13-deacetoxy-3-deacetylcalcicophirin B **64** was found in an unidentified Pacific soft coral.<sup>82</sup> Ophirin **61** has previously been isolated from *Muricella* spp. and showed significant brine shrimp lethality and moderate cytotoxicity.<sup>83</sup>

### 4.3 Aeolidioidea

The Aeolidioidea comprise about 600 species. Some information is available for animals of the families Flabellinidae, Fionidae, Facelinidae, Aeolidiidae, and Tergipedidae. As illustrated in Table 3 and Fig. 1B, these animals use various cnidarian food sources, *i.e.* hydrozoans, hexacorals and octocorals.

Two prenylchromanols, **65–66**, prenyl-*p*-hydroxy acid **67**, as well as polyhydroxylated steroids **68–69**, have been isolated from *Cratena peregrina* (Flabellinidae).<sup>84–86</sup> Whereas the steroids **68–69** were also found in the nudibranch's diet (the Mediterranean hydroid *Eudendrium racemosum*<sup>84,86</sup>), prenylchromanols **65–66**

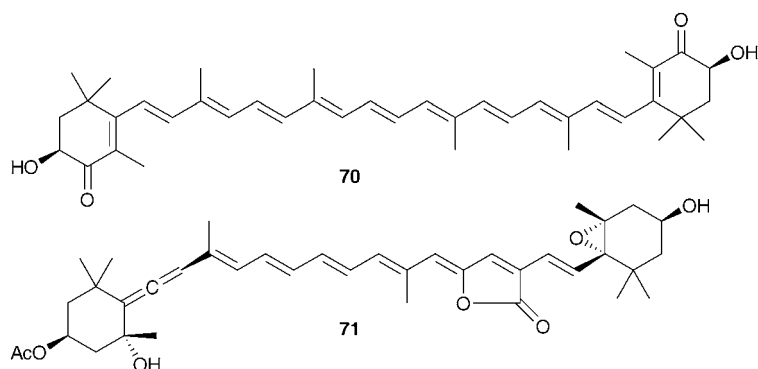


and the prenyl-*p*-hydroxy acid **67** were completely absent from its prey.<sup>85</sup> Steroids **68–69** were also identified in further flabellinid species, namely *Flabellina affinis* and *Flabellina* (formerly *Coryphella*) *lineata*, and their food sources, Mediterranean *Eudendrium* species.<sup>84,86</sup> McBeth<sup>87</sup> identified the pigment of *Flabellina iodinea* as astaxanthin **70** and quantified carotenoids in different body parts of the animal.

A pigment was also found in *Fiona marina* belonging to the family Fionidae. In this case the blue pigment was acquired from the siphonophoran *Veleva spirans*.<sup>88</sup> When feeding on the crustacean *Lepas anatifera* instead, *F. marina* sequesters a pink pigment from the prey.<sup>89</sup> The pigments were not further characterized in either of these studies.

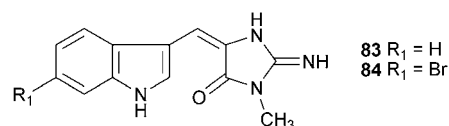
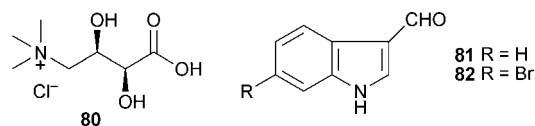
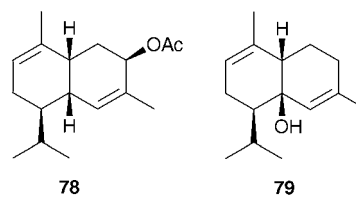
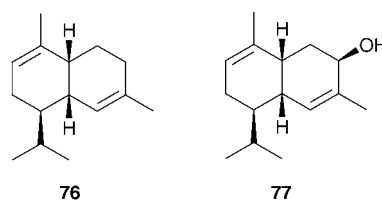
Members of the family Facelinidae include so-called “solar-powered sea slugs” that obtain symbiotic zooxanthellae from their food and nurture these in ducts of the digestive gland, both in the cerata and the body wall.<sup>90</sup> *Pteraeolidia ianthina* (Fig. 3C) feeds on various hydrozoans.<sup>31</sup> No defensive chemistry was detected in this species (König *et al.*, unpublished). The carotenoids identified in *P. ianthina*, with peridinin **71** being the major metabolite, were shown to be produced by the cladobranch's zooxanthellate symbionts *via* analysis of unialgal, host-free cultures.<sup>91</sup> The source of the zooxanthellae remains an open question.<sup>31</sup> *Phylloidesmium guamensis* sequesters the diterpene 11 $\beta$ -acetoxy-pukalide **72** selectively within various body parts, with levels highest in the cerata, and moderate to nonexistent



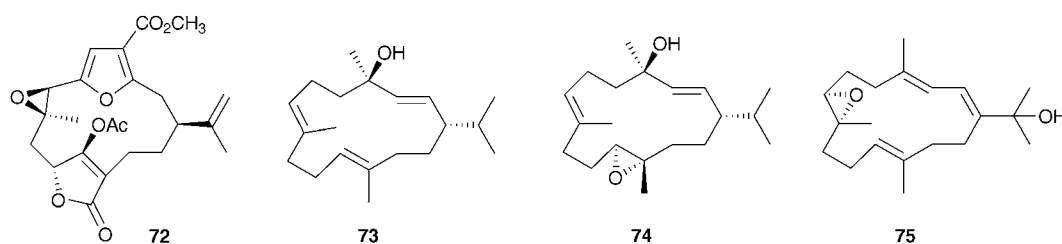


levels in the mantle and viscera, respectively.<sup>92</sup> Trace concentrations of this metabolite were also noted in the mucus and egg masses of this cladobranch species. 11 $\beta$ -Acetoxypukalide **72** deters feeding by the pufferfish *Canthigaster solandri*. *P. guamensis* was found actively grazing on the soft coral *Simularia maxima* containing the same diterpene but in smaller quantities.<sup>92</sup> *Phyllodesmium longicirrum* from the Great Barrier Reef accumulates the cembranoid diterpenes (+)-thunbergol **73**, (+)-trocheliophorol **74**, and diterpene alcohol **75**, which it sequesters from its food source, the soft coral *Sarcophytum trochelioforum*.<sup>93</sup> Analysis of *Phyllodesmium lizardensis*, a species endemic to Lizard Island (Great Barrier Reef, Fig. 3A, B), led to the isolation of the known metabolite (+)- $\alpha$ -muurolene **76**, and the previously unknown sesquiterpenes (+)-3 $\beta$ -hydroxy- $\alpha$ -muurolene **77** and (+)-3 $\beta$ -acetoxy- $\alpha$ -muurolene **78**.<sup>94</sup> By employing GC-MS the two latter compounds were detected in the host coral *Heteroxenia* sp. This was not the case for sympatric *Xenia* sp. where these sesquiterpenes could not be detected, potentially explaining the slugs' preference for *Heteroxenia* sp. over *Xenia* sp. as a food source.<sup>94</sup> A metabolite related to **76–79**, (+)-6-hydroxy- $\alpha$ -muurolene **79**, possesses antifungal properties and is active in the brine shrimp lethality test,<sup>95</sup> thereby suggesting a defensive role for the muurolenes.

*Aeolidia papillosa* (Aeolidiidae, Fig. 3D) incorporates a pheromone, the betaine anthopleurine **80**, while feeding on its anthozoan prey, the anemone *Anthopleura elegantissima*.<sup>96</sup> However, accumulation of anthopleurine **80** in *Aeolidia* does not seem to play a role in the chemical defence of the predator, but in contrast appears to benefit the prey *Anthopleura*: the alarm pheromone causes the anemone to enclose the delicate tentacles and the oral disk inside the body wall, thereby ensuring that the preferred sites of attack are less available for predation. Interestingly, those regions that remain exposed after an alarm response contain highest concentrations of the alarm pheromone.<sup>96</sup>

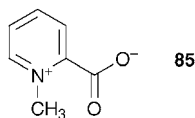


*Phestilla melanobrachia* (Tergipedidae) displayed carotenoids<sup>97</sup> and alkaloids such as 3-indolecarboxaldehyde **81** and the respective 6-bromo analogue **82** as well as further indole derivatives **83–84**<sup>37</sup> from its hexacoral food *Tubastraea coccinea*. In *P. lugubris*, sterols were detected.<sup>98</sup> The origin of these compounds in the latter species was not investigated.



#### 4.4 Homarine

Homarine **85** was first isolated in 1933<sup>99</sup> and is widely distributed in the marine environment, mainly in invertebrates such as crustaceans and molluscs, but also in fish.<sup>100,101</sup> Its biological function is, however, controversial. Due to its apparently exclusive occurrence in the marine environment, a role in osmoregulation was suggested.<sup>102</sup> However, although other studies failed to confirm a contribution of homarine **85** in osmotic processes in crustaceans,<sup>103</sup> it is widely accepted that it serves as an osmolyte in marine algae (for example, see ref. 104). Homarine **85** was also found in anthozoans<sup>105–107</sup> and hydrozoans,<sup>108,109</sup> where it was assigned antimicrobial properties<sup>105</sup> and a role in the regulation of colony morphology and prevention of metamorphosis in larvae.<sup>108,109</sup> For the Antarctic gastropod *Marseniopsis mollis*, McClintock *et al.*<sup>110</sup> have shown that homarine **85** serves as a feeding deterrent against the seastar *Odontaster validus*. It seems that this compound is also frequently encountered within the Cladobranchia and their food sources (see refs. 32 and 111, summarized in Table 1). However, its function within cladobranche species still remains to be shown.



## 5 Conclusion

For shell-less Cladobranchia, the sequestration or synthesis of biochemicals and the uptake of cleptocnides from cnidarian prey organisms represent successful defence strategies which are employed differently in the three cladobranche groups.

Dendronotoidea (Table 1) do not store cleptocnides (with the exception of the genus *Hancockia*), but possess gland structures of unknown function that could serve the storage of defensive chemicals. The occurrence of defensive metabolites has been reported for several species of the family Tritoniidae where compounds are sequestered from the octocoral prey, and the Tethyidae where compounds are produced *de novo*.

The Arminoidea (Table 2) likewise do not store cleptocnides and possess potentially defensive glandular structures. Defensive compounds were traced back to the octocoral food in the families Charcotiidae and Arminidae. Defensive chemistry was also found within Zephyrinidae, which commonly feed on bryozoans; however, in the corresponding study<sup>75</sup> the cladobranche's diet was not investigated.

In contrast, Aeolidioidea (Table 3) appear to rely on the defence provided by cleptocnides, an amazing strategy evolved at the base of this taxon.<sup>22</sup> No defensive glands worthy of consideration have been described for this taxon. Pigments and some sterols are the only metabolites reported from within the family Flabellinidae, suggesting that members of this group do not possess any chemical defence. *Pteraeolidia ianthina*, a member of another family, the Facelinidae, possesses functional cnidocysts sequestered from its hydrozoan food, but no defensive metabolites. The same seems to be true for Aeolidiidae, which switched to hexacorals as major food source. Only one member of the genus *Aeolidia* was investigated, and shows the accumulation of an alarm pheromone

derived from the food anemone. This, however, is a defensive strategy of the prey directed against the cladobranche. So far, these reports suggest that Aeolidioidea exclusively rely on cleptocnides which supersede defensive chemicals in this taxon. It is all the more striking that in contrast to the former examples, one genus within the family Facelinidae that has undergone a broad radiation,<sup>112</sup> *Phylloidesmium*, exhibits a potent chemical defence by storing octocoral-derived terpenes. Secondary metabolites have also been found in *Phestilla* species (Tergipedidae). Interestingly, these two latter genera have cnidosacs, but according to the literature do not store functional cnidocysts.<sup>36,113,114</sup> It is probably the switch to food organisms that do not have defensive cnidocysts, but provide defensive metabolites instead, that allows specialization on this alternative prey.

In general, the studies reported in this review indicate that Dendronotoidea and Arminoidea are protected chemically by sequestration or *de novo* biosynthesis of defensive metabolites, whereas Aeolidioidea mainly employ food-derived cleptocnides for defence. Due to the fact that Aeolidioidea species by far outnumber the Dendronotoidea and Arminoidea, it seems justified to discuss the incorporation of functional cnidocysts as a key feature for the radiation within this group. Exceptions are provided by aeolidioideans lacking functional cnidocysts which sequester toxic or deterrent compounds from their octocoral food sources. The high species number within the aeolidioidean genus *Phylloidesmium* (20 species described so far, plus at least ten undescribed species<sup>34,112</sup>) shows that a switch back from a defence relying on cleptocnides towards the sequestration of toxic compounds is a successful strategy in habitats providing appropriate food sources. Since the cnidosac is still present in those species, it seems possible that the ability to store functional cnidocysts can be restored with comparably little effort, yielding a "backup" strategy when accessing habitats deprived of toxic food sources. Such an intermediate stage appears to exist in *Phylloidesmium jakobsenae*, where cnidocysts can still be found within cnidosacs of the smaller back appendages.<sup>114</sup> Therefore this species potentially provides an example for a plastic defence depending on the slug's habitat and/or ontogenetic state. Unfortunately, the chemistry of neither the slug nor its specific host coral (belonging to the octocoral family Xenidae) has been described, and thus it is currently not known whether *P. jakobsenae* sequesters toxic compounds. If it does, this species would represent the only example where both defensive strategies occur – uptake of cleptocnides as well as sequestration of secondary metabolites. A similar situation may hold true for *Phestilla lugubris*, where functional cleptocnides appear to be only present in juveniles,<sup>32</sup> but not in adult individuals.<sup>36</sup>

Amongst others, these cases show that more comprehensive studies that add to the scarce reports on the chemistry of these organisms and their functional cnidosacs and gland structures, in relation to ontogeny and habitat, are clearly needed in order to understand the evolution of defensive strategies in the Cladobranchia and their impact as key features for radiation within this group.

## 6 Tables

Please see following pages.

**Table 1** Secondary metabolites and uptake of endocysts in Dendronotoidea (predator) and chemistry of respective food sources (prey). N. k.: Not known. Data on food organisms taken from ref. 47 if not indicated otherwise

| Predator   | Prey   |                     |  |  |  |   |  |
|--|--|---------------------|--|--|--|---|--|
|  | Secondary metabolites  | Uptake of endocysts | Subepithelial defensive glands                         | Epithelial defensive glands            | Higher ranking                                   | Species   | Secondary metabolites  |
| Family: Tritonidae<br><i>Tritoniella belli</i>                   | Glycerol ethers  | No                  | No <sup>32</sup>                                       | Homogenous violet glands <sup>49</sup> | Anthozoa: Octocorallia                           | <i>Clavularia frankliniana</i>  | Glycerol ethers 1–3 <sup>66</sup>  |
| <i>Tritonia hamnerorum</i>                                       | Furanoterpene<br>Punaglandins 5–23 <sup>58</sup>   | No                  | N. k.  | N. k.                                  | Anthozoa: Octocorallia                           | <i>Gorgonia ventalina</i>   | Julieannafuran 4 <sup>57</sup>   |
| <i>Tritonia</i> sp.  |  | No                  | N. k.  | N. k.                                  | Anthozoa: Octocorallia                           | <i>Telesto riisei</i>   | Punaglandins 5–23 <sup>58</sup>  |
| (probably <i>T. wellsi</i> )                                     |  | No                  | No <sup>32</sup>                                       | Homogenous violet glands <sup>49</sup> | Anthozoa: Octocorallia                           | <i>Alcyonium</i> sp.<br><i>Eunicella</i> sp.  | Millercrone A 37 <sup>74</sup><br>Homarine 85, 32 eunicellane and cladiellane diterpenes, 115, 116 pregnane derivatives, 117 cytotoxic steroids <sup>118</sup>       |
| <i>Tritonia plebeia</i><br>(formerly <i>Divaucella plebeia</i> ) | Porphyrin  | No                  | No <sup>32</sup>                                       | Homogenous violet glands <sup>49</sup> | Anthozoa: Octocorallia                           | <i>Lophogorgia sarmentosa</i>   | Homarine 85, 106 cembrane diterpenes, 66, 119 diketone cembrenolides, 120 lophotoxin, 121 sesquiterpenes <sup>122</sup>  |
| <i>Tritonia striata</i>  | N. k.  | No                  | No <sup>32</sup>                                       | Homogenous violet glands <sup>49</sup> | Hydrozoa: Leptothecata<br>Anthozoa: Octocorallia | <i>Obelia geniculata</i><br><i>Paralcyonium elegans</i>   | Cytotoxic linderazulenes, 123, 124 indoles, 25 caffeine <sup>126</sup> Sterols, 127 obelin <sup>128</sup> N. k.  |
| <i>Tritonia manicata</i>   | N. k.  | No                  | N. k.  | N. k.                                  | Anthozoa: Octocorallia                           | <i>Clavularia</i> sp.   | No homarine, 32 glycerol ethers <sup>86</sup>  |
| <i>Tochuina tetraquetra</i>                                      | Sesquiterpenoids   | No                  | N. k.  | Homogenous violet glands <sup>49</sup> | Anthozoa: Octocorallia                           | <i>Gersonia rubiformis</i>  | Tochuinyl acetate 28, dihydrotochuinyl acetate 29, rubifolide 24 <sup>62</sup><br>Pulosarcenone 26 <sup>65</sup>   |
| <i>Marionia blainvillea</i>                                      | Alkaloid   | No                  | No <sup>32</sup>                                       | Homogenous violet glands <sup>49</sup> | Anthozoa: Octocorallia                           | <i>Ptilosarcus gurneyi</i><br><i>Eunicella singularis</i><br><i>E. graminea</i> + <i>E. verrucosa</i><br>Other gorgonians | Homarine 85, 32 eunicellane diterpenes <sup>115</sup><br>Eunicellane and cladiellane diterpenes, 116 pregnane derivatives, 117 tryptamine derivatives <sup>129</sup> |
| Family: Tethyidae<br><i>Melibe iconina</i>                       | Aldehyde   | No                  | Structures like mantle dermal formations <sup>49</sup> | No <sup>32</sup>                       | Crustacea  | Planktonic crustaceans  | Probably none <sup>65</sup>  |
| <i>Tethys fimbria</i>  | Degraded monoterpenes <sup>64</sup><br>Prostaglandin derivatives <sup>66,70,130,69</sup> | No                  | N. k.  | N. k.                                  | Crustacea  | Planktonic crustaceans  | N. k.  |

Table 1 (Contd.)

| Predator  |                       | Prey   |                             |  |  |  |   |
|---|-----------------------|--|-----------------------------|--|--|--|---|
| Species   | Secondary metabolites |  | Epithelial defensive glands | Higher ranking   | Species                                | Secondary metabolites  |   |
|   | Class                 | Compound   |                             |  |  |  | Uptake of encysted glands   |
| Family: Bornellidae<br><i>Bornella anguilla</i> | N. k.                 | Homarine <b>85</b> <sup>32</sup>                           | No                          | Large subepithelial glandular follicles staining violet <sup>32</sup>  | Homogenous violet glands <sup>49</sup> | Hydrozoa: Anthoathecata<br><i>Plumularia</i> sp.<br><i>Thyrosocyphus</i> sp.             | N. k.<br>N. k., homarine <b>85</b> <sup>32</sup>  |
| Family: Dotidae<br><i>Doto paulinae</i>         | N. k.                 | Homarine <b>85</b> <sup>32</sup>                           | No                          | Many subepithelial glands staining bluish <sup>27,32</sup><br>Tips of cerata and tubercles: special glandular cells staining weakly <sup>27,32</sup> | Homogenous violet glands <sup>49</sup> | Hydrozoa: Leptothecata<br><i>Aglaophenia</i> sp.   | Homarine <b>85</b> <sup>32</sup><br>carbolines, <sup>131</sup> sterols, <sup>132</sup><br>polyhalogenated monoterpenes <sup>133</sup><br>Sterols, <sup>127</sup> obelin <sup>128</sup><br>Homarine <b>85</b> <sup>32</sup> sterols, <sup>132</sup><br>polyhydroxylated steroids, <sup>94,96,134</sup><br>polyhalogenated monoterpenes <sup>133</sup><br>N. k. |
| <i>Doto pinnatifida</i>                         | N. k.                 | Homarine <b>85</b> , trigonelline, terpenoid <sup>32</sup> | No                          | N. k.  | N. k.                                  | Hydrozoa: Leptothecata<br><i>Nemertesia antemina</i>                                     | N. k.   |
| <i>Doto coronata</i>                            | N. k.                 | —  | No                          | Many subepithelial glands staining bluish <sup>27,32</sup><br>Tips of cerata and tubercles: special glandular cells staining weakly <sup>27,32</sup> | Homogenous violet glands <sup>49</sup> | Hydrozoa: Leptothecata<br><i>Aglaophenia</i> sp.   | Homarine <b>85</b> <sup>32</sup><br>carbolines, <sup>131</sup> sterols, <sup>132</sup><br>polyhalogenated monoterpenes <sup>133</sup><br>N. k.  |
|   |                       |  |                             |  |  | Hydrozoa: Leptothecata<br><i>Abietinaria</i><br><i>Campanularia</i> and other hydrozoans | N. k.   |

**Table 2** Secondary metabolites and uptake of cnidocysts in Arminoidea (predator) and chemistry of respective food sources (prey). N. k.: Not known. Data on food organisms taken from ref. 47 if not indicated otherwise

| Predator   |                                   | Prey   |                         |  |  |   |  |
|--|-----------------------------------|--|-------------------------|--|--|---|--|
| Species  | Secondary metabolites             |  | Uptake of<br>cnidocysts | Epithelial<br>defensive glands               | Higher ranking                                   | Species   | Secondary metabolites  |
|  | Class                             | Name   |                         |  |  |   |  |
| Family: Charcotiidae<br><i>Leminda millecra</i>  | Sesquiterpenes                    | Millecrones <b>A 37</b> + <b>B 38</b><br>millecrols <b>A</b> + <b>B 39</b> + <b>40</b> <sup>73,74</sup><br>isofuranodiene <b>41</b> , (+)-8-<br>hydroxycalamene <b>42</b> ,<br>algaofuran <b>43</b> , cubebenone <b>44</b> ,<br>pretylquinones and<br>hydroquinones <b>45–50</b> <sup>74</sup> | No                      | N. k.  | Anthozoa: Octocorallia<br>Anthozoa: Octocorallia | <i>Alcyonium fauri</i><br><i>Leptogorgia palma</i>  | Millecrone <b>A 37</b> <sup>74</sup><br>Millecrone <b>B 38</b> , cubebenone <b>44</b> <sup>74</sup>  |
| <i>Pseudotrionia</i> sp.                         | N. k.                             | —  | No                      | Single subepithelial<br>glands <sup>52</sup> | Bryozoa  | <i>Arachnopusia inchoata</i>  | N. k.  |
| <i>Charcotia</i> sp.                             | N. k.                             | —  | No                      | Single subepithelial<br>glands <sup>52</sup> | Bryozoa  | <i>Benia erecta</i>   | N. k.  |
| Family: Zephyrinidae<br><i>Janolus cristatus</i> | Toxic tripeptide                  | Janolusimide <b>51</b> <sup>75</sup>   | No                      | No <sup>52</sup>                             | Bryozoa  | <i>Alcyonidium gelatinosum</i><br><i>Bicellaria</i> sp.<br><i>Bugula</i> sp.<br><i>Cellaria</i> sp. | (2-Hydroxyethyl)-<br>dimethylsulfoxonium ion <sup>135</sup><br>N. k.<br>Macrolides (bryostatins), <sup>66, 77</sup><br>ceramides, cerebrosides <sup>76</sup><br>Homarine <b>85</b> , betaine, free<br>nucleosides, tetramethylammonium<br>ion <sup>136</sup>                   |
| Family: Arminidae<br><i>Armina maculata</i>      | Briarane diterpenes,<br>cembranes | Verecynarmins A–G <b>52–58</b> ,<br>preverecynarmin <b>59</b> , cembrene<br>C <b>60</b> <sup>78–80</sup>   | No                      | Marginal sacs <sup>69</sup>                  | Anthozoa: Octocorallia                           | <i>Veretillum cynomorium</i>  | Homarine <b>85</b> , <sup>32</sup> verecynarmins A–G<br><b>52–58</b> , preverecynarmin <b>59</b> ,<br>cembrene C <b>60</b> , briarane<br>diterpenoids, cembranoids <sup>78–80</sup><br>Ophirin <b>61</b> , <sup>85</sup> calciphirin derivatives<br><b>62–64</b> <sup>81</sup> |
| <i>Dermatobranchius ornatus</i>                  | Diterpenes<br>(eunicelline class) | Ophirin <b>61</b> , calciphirin<br>derivatives <b>62–64</b> <sup>81</sup>  | No                      | Marginal sacs <sup>69</sup>                  | Anthozoa: Octocorallia                           | <i>Muriceella sinensis</i>  |  |

**Table 3** Secondary metabolites and uptake of cnidocysts in Acolidoidea (predator) and chemistry of respective food sources (prey). N. k.: Not known. Data on food organisms taken from ref. 47 if not indicated otherwise

| Predator   | Prey                         |  |  |                                   |                                |                         |  |  |
|--|------------------------------|--|--|-----------------------------------|--------------------------------|-------------------------|--|--|
|  | Class                        | Name   | Uptake of<br>cnidocysts                        | Subepithelial<br>defensive glands | Epithelial<br>defensive glands | Higher ranking          | Species  | Secondary metabolites  |
| Family: Flabellinidae<br><i>Flabellina affinis</i>         | Polyhydroxylated<br>steroids | Compounds <b>68–69</b> <sup>84</sup>   | Yes <sup>26</sup>                              | No <sup>32</sup>                  | No <sup>32</sup>               | Hydrozoa: Anthoathecata | <i>Eudendrium racemosum</i><br><i>Eudendrium</i> sp. | Polyhydroxylated steroids <b>68–69</b> <sup>84</sup><br>Sterols <sup>132</sup>   |
|  | Alkaloid                     | Homarine <b>85</b> <sup>111</sup>  |  |                                   |                                |                         | <i>Eudendrium glomeratum</i>                         | Polyhydroxylated steroids, <sup>86,134</sup><br>polyhalogenated mono terpenes <sup>133</sup>   |
| <i>Flabellina</i> (formerly<br><i>Coryphella lineata</i> ) | Polyhydroxylated<br>steroids | Compounds <b>68–69</b> <sup>84</sup>   | Yes  | N. k.                             | N. k.                          | Hydrozoa: Anthoathecata | <i>Eudendrium racemosum</i><br><i>rametum</i>        | Homarine <b>85</b> , <sup>32</sup> steroids, <sup>132</sup><br>polyhydroxylated steroids, <sup>84,86,134</sup><br>polyhalogenated mono terpenes <sup>133</sup> |
| <i>Flabellina iodinea</i>                                  | Carotenoids                  | Astaxanthin <b>70</b> <sup>87</sup>  | Yes  | N. k.                             | N. k.                          | Hydrozoa: Anthoathecata | <i>Eudendrium racemosum</i>                          | Homarine <b>85</b> , <sup>32</sup> steroids, <sup>132</sup>  |
| <i>Flabellina bicolor</i>                                  | N. k.                        | —  | Yes <sup>32</sup>                              | N. k.                             | N. k.                          | N. k.                   | N. k.  | polyhydroxylated steroids, <sup>84,86,134</sup>  |
| <i>Flabellina pedata</i>                                   | N. k.                        | Homarine <b>85</b> <sup>32</sup>   | N. k.  | No <sup>32</sup>                  | No <sup>32</sup>               | Hydrozoa: Anthoathecata | <i>Eudendrium</i> sp.                                | polyhalogenated mono terpenes <sup>133</sup><br>norzoanemonin <sup>138</sup>   |
| <i>Flabellina verrucosa</i>                                | N. k.                        | —  | Yes <sup>30,139</sup>                          | N. k.                             | N. k.                          | Hydrozoa: Anthoathecata | <i>Tubularia</i> sp.                                 | Homarine <b>85</b> , <sup>32</sup> carbolines, <sup>131</sup><br>sterols, <sup>132</sup> polyhalogenated<br>mono terpenes <sup>133</sup>                       |
| <i>Flabellina pellicida</i>                                | N. k.                        | —  | Yes <sup>139</sup>                             | N. k.                             | N. k.                          | Hydrozoa: Anthoathecata | <i>Aglaophenia</i> sp.                               | Sterols, <sup>127</sup> obelin <sup>128</sup>  |
|  | N. k.                        | —  |  |                                   |                                | Hydrozoa: Anthoathecata | <i>Obelia</i> sp.                                    | N. k.  |
|  | N. k.                        | —  |  |                                   |                                | Hydrozoa                | Other hydrozoans                                     | Homarine <b>85</b> , trigonelline, <sup>111,137</sup><br>norzoanemonin <sup>138</sup>  |
| <i>Flabellina gracilis</i>                                 | N. k.                        | —  | Yes <sup>139</sup>                             | No <sup>32</sup>                  | No <sup>32</sup>               | Hydrozoa: Anthoathecata | <i>Eudendrium</i> sp.                                | N. k.  |
| <i>Flabellina exoptata</i>                                 | N. k.                        | Homarine <b>85</b> <sup>32</sup>   | N. k.  | N. k.                             | N. k.                          | Hydrozoa: Anthoathecata | <i>Pennaria disticha</i>                             | Homarine <b>85</b> , trigonelline, <sup>111,137</sup><br>norzoanemonin <sup>138</sup>  |
| <i>Flabellina ischitana</i>                                | N. k.                        | Homarine <b>85</b> <sup>32</sup>   | Yes <sup>32</sup>                              | N. k.                             | N. k.                          | Hydrozoa                | “Orange hydroid”<br><i>Eudendrium</i> sp.            | Homarine <b>85</b> , <sup>32</sup> steroids, <sup>132</sup><br>polyhydroxylated steroids, <sup>84,86,134</sup><br>polyhalogenated mono terpenes <sup>133</sup> |
| <i>Cuthona caerula</i>                                     | Alkaloid                     | Homarine <b>85</b> <sup>111</sup>  | Yes  | No <sup>32</sup>                  | No <sup>32</sup>               | Hydrozoa                | Diverse species                                      | N. k.  |
| <i>Cuthona gymnota</i>                                     | Alkaloid                     | Homarine <b>85</b> <sup>111</sup>  | Yes  | N. k.                             | N. k.                          | Hydrozoa: Anthoathecata | <i>Tubularia</i> and other<br>hydrozoans             | Homarine <b>85</b> , trigonelline, <sup>111,137</sup><br>norzoanemonin <sup>138</sup>  |
| <i>Hermisenda crassicornis</i>                             | Alkaloid                     | Homarine <b>85</b> <sup>111</sup>  | Yes  | N. k.                             | N. k.                          | Hydrozoa: Anthoathecata | <i>Tubularia crocea</i>                              | <i>Tubularia</i> : Homarine <b>85</b> ,<br>trigonelline, <sup>111,137</sup> norzoanemonin <sup>138</sup>   |
| Family: Fionidae<br><i>Fiona marina</i>                    | Protein (?)                  | Blue pigment <sup>88</sup> (not<br>characterized), pink pigment <sup>89</sup><br>(not characterized) | No, but<br>cnidocyst<br>present <sup>140</sup> | N. k.                             | N. k.                          | Hydrozoa                | Other hydrozoans                                     | N. k.  |
|  |                              |  |  |                                   |                                | Siphonophora            | <i>Velella spirans</i>                               | Blue pigment <sup>88</sup>   |
|  |                              |  |  |                                   |                                | Crustacea               | <i>Lepas anatifera</i>                               | Pink pigment, <sup>89</sup> homarine <b>85</b> <sup>32</sup>   |

Table 3 (Contd.)

| Predator  |  | Prey   |   |                  |                  |  |   |
|---|--|--|---|------------------|------------------|--|---|
| Secondary metabolites                                   |  | Uptake of  | Subepithelial   | Epithelial       | Higher ranking   | Species  | Secondary metabolites   |
| Species   | Class  | Name   | defensive glands                                      | defensive glands | defensive glands |  |   |
| Family: Faceliidae<br><i>Cratena peregrina</i>          | Alkaloid<br>Polyhydroxylated<br>steroids<br>Prenylphenols<br>Prenyl- <i>p</i> -hydroxy<br>acid   | Homarine <b>85</b> <sup>32</sup><br>Compounds <b>68–69</b> <sup>84</sup><br>Compounds <b>65–66</b><br>Compound <b>67</b> <sup>85</sup>   | Yes <sup>86</sup>                                     | No <sup>32</sup> | No <sup>32</sup> | Hydrozoa: Anthoathecata  | <i>Eudendrium</i> sp.<br><br>Homarine <b>85</b> , <sup>32</sup> steroids, <sup>132</sup><br>polyhydroxylated steroids, <sup>84,86,134</sup><br>polyhalogenated monoterpene <sup>133</sup> ,<br><b>65–67</b> not detected  |
| <i>Cratena pilata</i>                                   | Alkaloid   | Homarine <b>85</b> <sup>111</sup>  | Yes   | N. k.            | N. k.            | Hydrozoa: Anthoathecata  | Homarine <b>85</b> , trigonelline, <sup>111,137</sup><br>norzoanemonin <sup>136</sup>   |
| <i>Pteraeolida ianithina</i>                            | Carotenoids derived<br>from zooxanthellae  | No homarine, <sup>32</sup> peridinin <b>71</b><br>and further carotenoids <sup>89,132</sup>  | Yes <sup>32</sup>                                     | No <sup>32</sup> | No <sup>32</sup> | Hydrozoa<br>Hydrozoa: Anthoathecata  | N. k.<br>No homarine, <sup>32</sup> polyhalogenated<br>monoterpenes <sup>133</sup>  |
| <i>Phyllodesmium guamensis</i>                          | Diterpene  | 11- $\beta$ -Acetoxypukalide <b>72</b> <sup>92</sup>   | No, but<br>cnidosac<br>present <sup>113</sup>         | N. k.            | N. k.            | Hydrozoa: Anthoathecata<br>Hydrozoa: Anthoathecata<br>Anthozoa: Octocorallia<br>Anthozoa: Octocorallia | N. k.<br>N. k.<br>N. k.<br>11- $\beta$ -Acetoxypukalide, <b>72</b> no<br>homarine, <sup>142</sup> diterpenes <sup>8,8,92,141</sup><br>sesquiterpenes, <sup>8,8,142</sup> steroids, <sup>8,8,143</sup><br>glycosides <sup>8,8,144</sup>                                      |
| <i>Phyllodesmium longicirrum</i>                        | Diterpene  | (+)-Thunbergol <b>73</b> , <sup>93</sup><br>(+)-trocheliophorol <b>74</b> <sup>93</sup><br>Compound <b>75</b> <sup>93</sup>  | No, but<br>cnidosac<br>present <sup>32</sup>          | No <sup>32</sup> | No <sup>32</sup> | Anthozoa: Octocorallia   | (+)-Thunbergol <b>73</b> , <sup>93</sup><br>(+)-trocheliophorol <b>74</b> , <sup>93</sup> diterpene<br>alcohol <b>75</b> <sup>93</sup>  |
| <i>Phyllodesmium lizardensis</i>                        | Sesquiterpene  | No homarine, <sup>111</sup> (+)- $\alpha$ -<br>murrrolene <b>76</b> , (+)-3 $\beta$ -hydroxy-<br>$\alpha$ -murrrolene <b>77</b> , (+)-3 $\beta$ -<br>acetoxy- $\alpha$ -murrrolene <b>78</b> <sup>94</sup> | No, but<br>cnidosac<br>present <sup>114</sup>         | No <sup>32</sup> | No <sup>32</sup> | Anthozoa: Octocorallia   | No homarine, <sup>111</sup> (+)- $\alpha$ -murrrolene <b>76</b> ,<br>(+)-3 $\beta$ -hydroxy- $\alpha$ -murrrolene <b>77</b> ,<br>(+)-3 $\beta$ -acetoxy- $\alpha$ -murrrolene <b>78</b> , <sup>94</sup><br>terpenes ( <i>e.g.</i> , sarcoalosterol <b>A</b> ) <sup>95</sup> |
| <i>Caloria indica</i>                                   | N. k.  | —  | Yes <sup>32</sup>                                     | N. k.            | N. k.            | Hydrozoa: Anthoathecata  | No homarine, <sup>32</sup> polyhalogenated<br>monoterpenes <sup>133</sup>   |
| Family: Aecolididae<br><i>Aecolida papillosa</i>        | Betaine  | Anthopleurine <b>80</b> <sup>86</sup>  | Yes <sup>32</sup>                                     | No <sup>32</sup> | No <sup>32</sup> | Anthozoa: Hexacorallia   | Anthopleurine <b>80</b> (alarm<br>pheromone) <sup>86</sup>  |
| Family: Tergipedidae<br><i>Phestilla melanobranchia</i> | Carotenoids <sup>97</sup><br>Indole alkaloids <b>83–</b><br><b>84</b> <sup>37</sup><br>Aromatic<br>compound <sup>87</sup><br>Sterols <sup>98</sup> | —<br><i>e.g.</i> 3-Indol-carboxaldehyde <b>81</b><br>and its 6-bromo analogue <b>82</b> <sup>37</sup><br>—   | N. k.   | N. k.            | N. k.            | Anthozoa: Hexacorallia   | Carotenoids, <sup>97</sup> indole alkaloids <b>81–</b><br><b>84</b> , <sup>37</sup> not detectable <sup>37</sup>  |
| <i>Phestilla lugubris</i>                               | —  | —  | No <sup>86</sup><br>(Juvenile:<br>Yes <sup>32</sup> ) | N. k.            | N. k.            | Anthozoa: Hexacorallia   | UV-absorbing compounds <sup>145</sup>   |

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