Natural Product Chemistry of Gorgonian Corals of Genus Junceella—Part II

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Received: 10 November 2011; in revised form: 6 December 2011 / Accepted: 15 December 2011 / Published: 19 December 2011

Abstract: The structures, names, bioactivities, and references of 81 new secondary metabolites obtained from gorgonian corals belonging to the genus Junceella are described
in this review. All compounds mentioned in this review were obtained from sea whip gorgonian corals *Junceella fragilis* and *Junceella juncea*, collected from the tropical and subtropical Indo-Pacific Ocean.

**Keywords:** *Junceella*; gorgonian; briarane; Indo-Pacific Ocean; South China Sea

1. **Introduction**

This review describes 81 new natural products from gorgonian corals belonging to the genus *Junceella* (phylum Cnidaria, class Anthozoa, order Gorgonacea, family Ellisellidae) [1–4]. Extending from a previous review in 2004 [5], this review describes compounds reported from November 2003 to September 2011 and provides structures, names, bioactivities and references for all compounds in tabular form.

2. **Natural Products from Gorgonian Corals Belonging to the Genus *Junceella***

2.1. *Junceella fragilis*

Two new chlorinated briarane-type diterpenoids (3,8-cyclized cembranoids), (−)-2-deacetyl-junceellin (1) and (−)-3-deacetyl-junceellin (2) (Table 1), along with five known briaranes, junceellin, praelolide, and junceellolides A, B and D, were isolated from the gorgonian *J. fragilis*, collected at the Pass Reef of Madang, Papua New Guinea [6]. The absolute stereochemistry of (−)-3-deacetyl-junceellin (2) was determined by the application of a new method using a combination of proton chemical shifts and molecular dynamic calculation.

**Table 1.** The new natural products from *Junceella fragilis*-I.

| Structure | No. | Name                                      | Biological Activity | Ref. |
|-----------|-----|-------------------------------------------|---------------------|------|
| ![Structure](image) | 1   | (−)-2-Deacetyl-junceellin (R₁ = OH, R₂ = OAc) | n.r. *a*          | [6]  |
| ![Structure](image) | 2   | (−)-3-Deacetyl-junceellin (R₁ = OAc, R₂ = OH) | n.r.               | [6]  |

*a n.r. = not reported.

During the past 30 years, a series of interesting and bioactive natural products has been isolated from various marine invertebrates collected off the South China Sea [7,8]. Five new briaranes, junceellonoids A–E (3–7) (Table 2) [9,10], eight known briaranes, junceellins A and B, junceellolides A–D, umbraculolide A and praelolide, along with three known steroids, 24α-methylcholest-7,22-dien-3β,5α,6β-triol, cholestan-3-ol and cholesterol, were isolated from
*J. fragilis* inhabiting the South China Sea [9–12]. Junceellonoids C (5) and D (6) exhibited cytotoxicity toward human breast carcinoma MDA-MB-231 and MCF-7 cells [10].

**Table 2.** The new natural products from *Junceella fragilis*-II.

| Structure | No. | Name | Biological Activity | Ref. |
|-----------|-----|------|---------------------|------|
| ![Structure 3](image1.png) | 3   | Junceellonoid A | n.r. | [9] |
| ![Structure 4](image2.png) | 4   | Junceellonoid B | n.r. | [9] |
| ![Structure 5](image3.png) | 5   | Junceellonoid C | exhibited cytotoxicity toward MDA-MB-231 and MCF-7 cells at a concentration of 100 µM | [10] |
| ![Structure 6](image4.png) | 6   | Junceellonoid D | (R₁ = R₂ = OH) exhibited cytotoxicity toward MDA-MB-231 and MCF-7 cells at a concentration of 100 µM | [10] |
| ![Structure 7](image5.png) | 7   | Junceellonoid E | (R₁ = R₂ = OAc) n.r. | [10] |

a n.r. = not reported.

In continuing research on the new substances obtained from gorgonian corals distributed in the waters of Taiwan at the intersection of the Kuroshio current and the South China Sea surface current, the gorgonian *J. fragilis* was studied to examine the properties of its organic extract. Thirty-one new briaranes, 9-O-deacetylumbraculolide A (8) [13], juncellolides H–L (9–13) [14–16], fragilides A–J (14–23) [17–24] and frajunolides A–O (24–38) [25–27] (Table 3); 16 known briaranes, prarelolide [14,26,28], juncellin A [12,14,26,28], (1R,2R,SZ,7R,8S,9R,10R,12R,14R,17S)-2,14-diacetoxy-8,17-epoxide-9,12-dihydroxybriara-5,11(20)-dien-19-one [15], (−)-11β,20β-epoxy-4-deacetoxyjuncellolide D [16,25,26,29], juncellonoid D [22], juncins Y, Z and ZI [22,26], (+)-11β,
20β-epoxyjunceellolide D [23,29], juncellolides A–E and K [25,26], and umbraculolide A [25,26]; and three known steroids, ergosterol peroxide [26], deoxycholic acid 3,12-diacetate, and deoxycholic acid 3,12-diacetate methyl ester [30], were isolated from J. fragilis collected off the waters of Taiwan. The structure, including the absolute configuration, of juncellolide J (11) was confirmed by single-crystal X-ray diffraction analysis and chemical conversion [16]. Fragilide A (14) was the first briarane derivative found to possess a 6-hydroxy group [17]. The geometry of the Δ\(^{3,5(16)}\)-butadiene system in fragilide B (15) was found to be of an \(s\)-cis form [18]. The \(^{13}\)C NMR data for the known briaranes praelolide and juncellin were reassigned by 2D NMR experiments [14].

**Table 3.** The new natural products from *Junceella fragilis*-III.

| Structure | No. | Name                  | Biological Activity                                      | Ref. |
|-----------|-----|-----------------------|----------------------------------------------------------|------|
| ![Structure](image) | 8   | 9-O-Deacetylumbraculolide A | n.r. \(^a\)                                               | [13] |
| ![Structure](image) | 9   | Juncellolide H          | not active in cytotoxicity testing with P-388D1, DLD-1, IMR-32, RPMI 7951 and CCRF-CEM tumor cells \(^b\) | [14] |
| ![Structure](image) | 10  | Juncellolide I          | n.r.                                                     | [15] |
| ![Structure](image) | 11  | Juncellolide J          | not active in anti-inflammatory bioassay                 | [16] |
| No. | Compound                  | Activity Description                                     | References |
|-----|---------------------------|----------------------------------------------------------|------------|
| 12  | Junceellolide K           | weakly anti-inflammatory                                   | [16]       |
| 13  | Junceellolide L           | not active in anti-inflammatory bioassay                 | [16]       |
| 14  | Fragilide A               | n.r.                                                      | [17]       |
| 15  | Fragilide B               | weakly anti-inflammatory                                   | [18]       |
|     | (R<sub>1</sub> = OC(O)CH<sub>2</sub>CH<sub>3</sub>, R<sub>2</sub> = H) |                                                          |            |
| 20  | Fragilide G               | not active in cytotoxicity testing with DLD-1 and CCRF-CEM cells | [22]       |
|     | (R<sub>1</sub> = R<sub>2</sub> = OAc) |                                                          |            |
| 16  | Fragilide C               | weakly anti-inflammatory                                   | [19]       |
|     | (R<sub>1</sub> = OCOCH<sub>2</sub>CH<sub>3</sub>, R<sub>2</sub> = H, R<sub>3</sub> = OH) | | |
| 23  | Fragilide J               | weakly anti-inflammatory                                   | [24]       |
|     | (R<sub>1</sub> = OH, R<sub>2</sub> = OAc, R<sub>3</sub> = H) |                                                          |            |
| 17  | Fragilide D (= Frajunolide G) | n.r.                                                  | [20,26]  |
Table 3. Cont.

| Entry | Structure | Description | References |
|-------|-----------|-------------|------------|
| 18    | ![](image1.png) | Fragilide E (R₁ = β-OH, R₂ = α-CH₂OAc) weakly anti-inflammatory | [21] |
| 19    | ![](image2.png) | Fragilide F (R₁ = α-OH, R₂ = β-CH₂Cl) not active in cytotoxicity testing with DLD-1 and CCRF-CEM cells | [22] |
| 20    | ![](image3.png) | Fragilide E (R₁ = β-OH, R₂ = α-CH₂OAc) weakly anti-inflammatory | [21] |
| 21    | ![](image4.png) | Fragilide H not active in cytotoxicity testing with P-388D1, DLD-1, HL-60 and CCRF-CEM cells | [23] |
| 22    | ![](image5.png) | Fragilide I (R = OC(O)CH₂CH(CH₃)₂) not active in cytotoxicity testing with P-388D1, DLD-1, HL-60 and CCRF-CEM cells | [23] |
| 24    | ![](image6.png) | Frajunolide A (R₁ = α-OAc, R₂ = H) weakly anti-inflammatory | [25] |
| 25    | ![](image7.png) | Frajunolide B (R₁ = α-OAc, R₂ = OAc) weakly anti-inflammatory | [25] |
| 28    | ![](image8.png) | Frajunolide E (R₁ = H, R₂ = OAc) frajunolides E, J and L were weakly anti-inflammatory | [26] |
| 33    | ![](image9.png) | Frajunolide J (R₁ = α-OC(O)Et, R₂ = H) frajunolides E and J were not active in cytotoxicity testing with Hep2, Doay, WiDr and Hela cells | [26] |
| 35    | ![](image10.png) | Frajunolide L (R₁ = β-OAc, R₂ = H) frajunolides E and J were not active in cytotoxicity testing with Hep2, Doay, WiDr and Hela cells | [26] |
| 26    | ![](image11.png) | Frajunolide C (R = Cl) weakly anti-inflammatory | [25] |
| 27    | ![](image12.png) | Frajunolide D (R = OAc) not active in anti-inflammatory bioassay | [25] |
Table 3. Cont.

|   | Compound | Activity                        | Notes                                      |
|---|----------|---------------------------------|--------------------------------------------|
| 29 | Frajunolide F | weakly anti-inflammatory not active in cytotoxicity testing with Hep2, Doay, WiDr and Hela cells | [26]                                      |
| 30 | Frajunolide G (= Fragilide D) \( (R = \text{OC(O)CH}_2\text{OC(O)} \text{CH}_2\text{CH(CH}_3)_2) \) | not active in anti-inflammatory bioassay not active in cytotoxicity testing with Hep2, Doay, WiDr and Hela cells | [20,26]                                  |
| 31 | Frajunolide H | not active in anti-inflammatory bioassay not active in cytotoxicity testing with Hep2, Doay, WiDr and Hela cells | [26]                                      |
| 32 | Frajunolide I | weakly anti-inflammatory not active in cytotoxicity testing with Hep2, Doay, WiDr and Hela cells | [26]                                      |
| 34 | Frajunolide K \( (R = \text{OC(O)CH}_2\text{OC(O)} \text{CH}_2\text{CH(CH}_3)_2) \) | not active in anti-inflammatory bioassay | [26]                                      |
| 36 | Frajunolide M | weakly anti-inflammatory | [27]                                      |
Table 3. Cont.

![Chemical Structures](image)

| Compound          | Description                                      | Reference |
|-------------------|--------------------------------------------------|-----------|
| 37 Frajunolide N  | modestly anti-inflammatory not active in cytotoxicity testing with Hep2, Doay, WiDr and Hela cells | [27]      |
| 38 Frajunolide O  | weakly anti-inflammatory                         | [27]      |

*a n.r. = not reported; b P388D1 (mouse lymphoid neoplasm), DLD-1 (human colon adenocarcinoma), IMR-32 (human neuroblastoma), RPMI 7951 (human malignant melanoma), CCRF-CEM (human T-cell acute lymphoblastic leukemia), HL-60 (human promyelocytic leukemia), Hep2 (human liver carcinoma), Doay (medulloblastoma), WiDr (human colon adenocarcinoma), Hela (human cervical epitheloid carcinoma).

In order to determine the stereochemistry of briaranes possessing an exocyclic 11,20-epoxy group, the $^{13}$C NMR data of the exocyclic 11,20-epoxy groups have been summarized; these appeared at $\delta_C$ 62–63 and 58–60 ppm, respectively, when the epoxy group existed in the 11$S^*$ form and led the cyclohexane rings to exhibit a twist boat conformation. If the epoxy group was in an 11$R^*$ configuration, the $^{13}$C NMR data for C-11 and C-20 appeared at $\delta_C$ 55–61 and 47–52 ppm, respectively, and the cyclohexane rings were in a chair conformation [16]. The 11,20-epoxybriaranes were only obtained from gorgonian corals belonging to the Ellisellidae family, and, thus compounds of this type could be a chemical marker for gorgonian corals belonging to the Ellisellidae family [31].

From the characteristics of the chemical shifts, it was shown that the briarane derivatives contained an exocyclic double bond between C-11/12. The proton chemical shifts were summed up for the olefin protons H$_2$-20; these appear at $\delta_H$ 4.95–5.30 and 4.85–5.15 ppm, respectively, when the cyclohexane rings are in a twist boat conformation. Likewise, the $^1$H NMR data for H$_2$-20 appear at $\delta_H$ 4.95–5.10 and 4.40–4.75, if the cyclohexane rings were found to exist in a chair conformation [22].

Symbiotic algae (zooxanthella) exist throughout the life cycle of *J. fragilis*, while *J. juncea* is a gorgonian coral free of zooxanthellae [32]. Two known chlorine-containing briaranes, junceellin and praelolide, were isolated in the same proportions from both *J. fragilis* and *J. juncea*, and this observation suggests that junceellin and praelolide could be chemical markers that enable one to infer that the briarane-type compounds are originally synthesized by the host corals [28] and are not produced by their zooxanthella.
In biological activity experiments, the new briaranes, junceellolide K (12) [16], fragilides B, C, E and J (15, 16, 18, 23) [18,19,21,24], frajunolides A–C (24–26), E (28), F (29), I (32), J (33), L–O (35–38) (Table 3), and the known compounds (−)-11β,20β-epoxy-4-deacetoxyjuncellolide D [16,25], junceellolide E [25] and umbraculolide A [25], displayed anti-inflammatory activity [33]. Juncin Z was found to exhibit cytotoxicity toward CCRF-CEM cells [22].

2.2. Junceella juncea

Five new steroidal glycosides, 4′-O-acetyl-3-O-[β-D-arabino-pyranosyl-oxy]-cholest-5-ene-3β,19-diol (39) [34] and junceellosides A–D (40–43) [35], and a new glycerol, 1,2-O-[2′-hydroxyoctadecyl]-glycerol (44) [34] (Table 4) along with various known metabolites, including four sterols, 24α-methylcholest-7,22-dien-3β,5α,6β-triol, 24α-methylcholest-3β,5α,6β-triol-25-monoacetate, 24α-methylcholest-3β,5α,6β-triol, and 24α-methylcholest-5,23-dien-3β-ol; six amines, 1-O-β-D-glucopyranosyl-(2S,3S,4R,8Z)-2-N-(2′-hydroxypalmitoyl)-octadecasphinga-8-ene, (2S,3R)-2-N-palmitoyloctadecasphinga, (2S,3R,4E)-2-N-palmitoyloctadecasphinga-4-ene, thymine, uracil, and adenosine; and batyl alcohol, were isolated from the gorgonian coral J. juncea, collected off the South China Sea in 2004–2005 [34,35].

| Structure | No. | Name | Ref. |
|-----------|-----|------|-----|
| ![Structure](image) | 39 | 4′-O-Acetyl-3-O-[β-D-arabino-pyranosyl-oxy]-cholest-5-ene-3β,19-diol (R1 = H, R2 = OH, R3 = OAc) | [34] |
| ![Structure](image) | 40 | Junceelloside A (R1 = R2 = OH, R3 = OAc) | [35] |
| ![Structure](image) | 41 | Junceelloside B (R1 = R3 = OH, R2 = OAc) | [35] |
| ![Structure](image) | 42 | Junceelloside C (R1 = OAc, R2 = R3 = OH) | [35] |
| ![Structure](image) | 43 | Junceelloside D (R1 = R2 = R3 = OH) | [35] |
| ![Structure](image) | 44 | 1,2-O-[2′-Hydroxyoctadecyl]-glycerol | [34] |

In addition, 14 new briarane derivatives, juncins O–Q (45–47) [36], R–ZI (48–57) [37], and ZII (58) [38] (Table 5), along with eight known briaranes, praelolide, junceellin, gemmacolides A–C and F, junceellolide D [34,38], and (+)-11β,20β-epoxyjuncellolide D [30,38], were also isolated from J. juncea.
Table 5. The new natural products from *Junceella juncea*-V.

| No. | Name | Biological Activity | Ref. |
|-----|------|---------------------|------|
| 45  | Juncin O (R = OC(O)CH₂CH(CH₃)₂) | juncins O–Q showed medium antifeedant activity (90.7, 69.0, 46.5%) toward the second-instar larvae of *Spodoptera litura* at a concentration of 500 µg/mL | [36,38] |
| 46  | Juncin P | medium cytotoxicity (cell mortality: 8.7% in 24 h and 11.9% in 48 h) toward the second-instar larvae of *S. litura* at a concentration of 100 µg/mL | [36,38] |
| 47  | Juncin Q | medium cytotoxicity (cell mortality: 31.3% in 24 h and 44.0% in 48 h) toward the second-instar larvae of *S. litura* at a concentration of 100 µg/mL | [36,38] |
| 54  | Juncin X | | [37] |
| 55  | Juncin Y (R = CH₂OAc) | | [37] |
| 56  | Juncin Z (R = CO(O)CH₃) | | [37] |
Table 5. Cont.

| No. | Compound          | Structure | Description                                                                 |
|-----|-------------------|-----------|-----------------------------------------------------------------------------|
| 48  | Juncin R          | ![Structure](image1) | (R₁ = R₂ = R₃ = OAc, R₄ = OC(O)CH₂CH(CH₃)₂, R₅ = Cl) antifouling activity toward the barnacle *Balanus amphitrite* larvae (EC₅₀ = 0.004, 0.3, 2.7, 1.6, 3.8, 21.1, 0.004, 0.1, 1.5, 0.5 and 0.004 µg/mL) |
| 49  | Juncin S          | ![Structure](image2) | (R₁ = R₃ = R₄ = OAc, R₂ = OC(O)CH₂CH(CH₃)₂, R₅ = Cl)                          |
| 50  | Juncin T          | ![Structure](image3) | (R₁ = OC(O)CH₂OC(O)CH₂CH(CH₃)₂, R₂ = R₃ = R₄ = OAc, R₅ = OH)                 |
| 51  | Juncin U          | ![Structure](image4) | (R₁ = R₂ = R₄ = OAc, R₃ = OC(O)CH₂CH(CH₃)₂, R₅ = OCH₃)                       |
| 52  | Juncin V          | ![Structure](image5) | (R₁ = R₃ = OAc, R₂ = R₄ = OH, R₅ = OCH₃)                                     |
| 53  | Juncin W          | ![Structure](image6) | (R₁ = R₃ = R₄ = OAc, R₂ = R₄ = OH)                                          |
| 57  | Juncin ZI         | ![Structure](image7) |                                                                                         |
| 58  | Juncin ZII        | ![Structure](image8) | (R = OC(O)(CH₂)₂CH(CH₃)₂) medium antifeedant activity (84.5%) toward the second-instar larvae of *Spodoptera litura* at a concentration of 500 µg/mL. medium cytotoxicity (cell mortality: 20.5% in 24 h and 43.2% in 48 h) toward the second-instar larvae of *S. litura* at a concentration of 100 µg/mL. |

* K562 (human erythromyeloblastoid leukemia), A549 (human lung adenocarcinoma), Hela (human cervical epitheloid carcinoma), Hep2 (human liver carcinoma).
In biological activity testing, juncins R–ZII (48–58) showed potent antifouling activities against the larval settlement of barnacle *Balanus amphitrite* at a nontoxic concentration (Table 5), and the structure–activity relationships have been discussed [37,38]. The potency of these compounds to inhibit larval settlement was increased when the C-16 exocyclic oxymethylene was substituted by a methylene-bearing chlorine atom and decreased when the exocyclic oxymethylene C-16 was esterified or the acetoxy methylene C-16 was oxygenated to become an esterified group. The chain lengths of the ester moieties at C-1, C-12, C-13 and C-14 and the 11,20-epoxy group could also affect the antifouling activities [37,38].

The known briaranes, gemmacolides A, B, and junceellolide D, were also found to exhibit an antifouling activity as potent as that of juncins R–ZII [38], and these three compounds were not cytotoxic towards the K562, A549, Hela and Hep2 cells. In addition, all the known briaranes showed medium antifeedant activity toward the second-instar larvae of *Spodoptera litura* at a concentration of 500 µg/mL [38].

The gorgonian *J. juncea* collected off the Indian Ocean was proven to be a rich source of interesting natural products. The ethyl acetate extract of *J. juncea* exhibited anti-inflammatory activity at concentrations of 30–100 mg/kg body weight, while the oral median lethal dose (LD$_{50}$) for the extract in albino mice was above 1000 mg/kg. The ethyl acetate extract of *J. juncea* also showed antibacterial activities toward *Bacillus subtilis*, *B. pumilis* and *Escherichia coli* [39]. Six new briaranes, juncins I–M (59–63) [40] and juncenolide B (64) [41], a new sphingolipid, (2R,3R,4E)-1,3-dihydroxy-2-[[nonadecanoyl] amino]-octadec-4-ene (65) [42] (Table 6), along with four known briaranes, gemmacolides A–C and juncin H [40], were obtained from the gorgonian coral *J. juncea*, collected from Tuticorin Coast of the Indian Ocean.

### Table 6. The new natural products from *Junceella juncea*-VI.

| Structure   | No. | Name                          | Biological Activity | Ref.  |
|-------------|-----|-------------------------------|---------------------|-------|
| ![Structure](image) | 59  | Juncin I (R$_1$ = R$_3$ = OAc, R$_2$ = OCOCH$_2$CH(CH$_3$)$_2$) | n.r. *a*            | [40]  |
| ![Structure](image) | 60  | Juncin J (R$_1$ = R$_2$ = OCOCH$_2$CH(CH$_3$)$_2$, R$_3$ = OAc) | n.r.                | [40]  |
| ![Structure](image) | 61  | Juncin K (R$_1$ = R$_3$ = OCOCH$_2$CH(CH$_3$)$_2$, R$_2$ = H) | n.r.                | [40]  |
| ![Structure](image) | 62  | Juncin L (R$_1$ = R$_2$ = OCOCH$_2$CH(CH$_3$)$_2$, R$_3$ = OAc) | n.r.                | [40]  |
| ![Structure](image) | 63  | Juncin M (R$_1$ = R$_3$ = OCOCH$_2$CH(CH$_3$)$_2$, R$_2$ = H) | n.r.                | [40]  |
The molecular formula of juncenolide B was reported as \( C_{30}H_{42}O_{11} \) (M.W. = 578), but the structure presented in the article was found to possess the molecular formula \( C_{30}H_{42}O_{12} \) (M.W. = 594). The spectral data (such as from NOESY experiments) was not sufficient to support the structure presented in the article. We therefore suggested that the structure of this compound (juncenolide B) should be reexamined [41].

Sixteen new briaranes, juncenolides E–K (66–72) [43–45], juncin N (73) [46], and junceols A–H (74–81) [20,47] (Table 7), and two known briaranes, junceellolides B and C, were isolated from the gorgonian \( J. \) juncea, collected off the waters of Taiwan. Juncenolide G (68) is the first naturally-occurring briarane found to have an ether linkage between C-5/C-8 [44], and juncin N (73) is the first briarane derivative found to contain a carboxylic group [46].

### Table 7. The new natural products from \( Junceella \) juncea-VII.

| Structure | No. | Name | Biological Activity | Ref. |
|-----------|-----|------|---------------------|------|
| ![Structure](image1.png) | 66  | Juncenolide E | n.r. \(^a\) | [43] |
| ![Structure](image2.png) | 67  | Juncenolide F | n.r. | [44] |
| ![Structure](image3.png) | 69  | Juncenolide H | modestly anti-inflammatory | [45] |
| ![Structure](image4.png) | 70  | Juncenolide I | weakly anti-inflammatory | [45] |
| ![Structure](image5.png) | 71  | Juncenolide J | not active in | [45] |

\(^a\) n.r. = not reported.
Table 7. Cont.

68 Juncenolide G  
\[\text{n.r.} \]  
\[\text{[44]}\]

72 Juncenolide K  
\[\text{weakly anti-inflammatory} \]  
\[\text{[45]}\]

73 Juncin N  
\[\text{not active in cytotoxicity testing with P-388D1, DLD-1, IMR-32, RPMI 7951 and CCRF-CEM cells}^b \]  
\[\text{[46]}\]

74 Junceol A  
\[\text{(R = OC(O)CH}_2\text{CH(CH}_3\text{)}_2\text{)} \]  
\[\text{significantly anti-inflammatory} \]  
\[\text{[20]}\]

75 Junceol B  
\[\text{(R}_1\text{ = OAc, R}_2\text{ = OC(O)CH}_2\text{CH(CH}_3\text{)}_2\text{)} \]  
\[\text{significantly anti-inflammatory} \]  
\[\text{[20]}\]

76 Junceol C  
\[\text{(R}_1\text{ = R}_2\text{ = OC(O)CH}_2\text{CH(CH}_3\text{)}_2\text{)} \]  
\[\text{anti-inflammatory} \]  
\[\text{[20]}\]
Table 7. Cont.

| Compound | Structure | Description |
|----------|-----------|-------------|
| Junceol D | ![Structure](image1) | (R₁ = OC(O)CH(CH₃)₂, R₂ = OC(O)CH₂CH(CH₃)₂, R₃ = OAc) not active in anti-inflammatory bioassay [47] |
| Junceol E | ![Structure](image2) | (R₁ = OC(O)CH(CH₃)₂, R₂ = OAc, R₃ = H) exhibited cytotoxicity toward CCRF-CEM and DLD-1 (IC₅₀ = 1.3, 10.0 µg/mL) cells weakly anti-inflammatory [47] |
| Junceol F | ![Structure](image3) | (R₁ = OC(O)CH(CH₃)CH₂CH₃, R₂ = OAc, R₃ = H) exhibited cytotoxicity toward CCRF-CEM (IC₅₀ = 4.9 µg/mL) cells |
| Junceol G | ![Structure](image4) | (R₁ = OC(O)CH(CH₃)CH₂CH₃, R₂ = H, R₃ = OAc) weakly anti-inflammatory [47] |
| Junceol H | ![Structure](image5) | (R₁ = OAc, R₂ = H, R₃ = OC(O)CH(CH₃)₂) weakly anti-inflammatory [47] |

* n.r. = not reported. *P388D1 (mouse lymphoid neoplasm), DLD-1 (human colon adenocarcinoma), IMR-32 (human neuroblastoma), RPMI 7951 (human malignant melanoma), CCRF-CEM (human T-cell acute lymphoblastic leukemia).

3. Conclusions

The chemical class distribution of the natural products obtained from the organisms Junceella fragilis and Junceella juncea compiled in this review indicates that terpenoid derivatives, particularly briarane-type diterpenoids, are the major components of the natural products isolated. Of the 81 new metabolites, 74 compounds are briarane-type diterpenoids (91.4%). Of these briaranes, over 50% are chlorinated briaranes (38/74 = 51.4%), which are rarely found. Briarane-type compounds continue to attract attention owing to their structural novelty, complexity and interesting bioactivities, such as anti-inflammatory activity [48–51]. Terpenoid compounds are often present in large amounts in marine invertebrates, and as a major class represent the largest percentage of natural products isolated from marine organisms [52]. Over 500 naturally-occurring briarane derivatives have been isolated from various marine organisms [48–51]. However, owing to their structural complexity, it is difficult to obtain sufficient amounts of the bioactive metabolites, such as junceols B (75) and C (76), for further study of their potential medicinal usage. We have therefore begun to culture the potential useful gorgonian corals J. fragilis and J. juncea (Figure 1) in tanks using our highly developed aquaculture technology for extraction of natural products to establish a stable supply of bioactive materials, which also protects the natural population and habitats from over-exploitation.
Figure 1. The cultured-type gorgonian corals *Juncella fragilis* (white) and *Juncella juncea* (red).

Acknowledgments

This work was supported by grants from the National Dong Hwa University; the National Museum of Marine Biology and Aquarium (Grant No. 100100101 and 100200311); the Division of Marine Biotechnology, Asia-Pacific Ocean Research Center, National Sun Yat-sen University (Grant No. 00C-0302-05); and the National Science Council, Taiwan, awarded to P.-J.S. (Grant No. NSC 100-2325-B-291-001, 99-2323-B-291-001, and 98-2320-B-291-001-MY3) and J.-H.S. (Grant No. NSC 98-2113-M-110-002-MY3).

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