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# SPONGIONELLIN AND DEHYDROSPONGIONELLIN, NEW FURANOSESTERTERPENES WHICH INHIBIT CELL DIVISION OF FERTILIZED STARFISH EGGS, FROM THE MARINE SPONGE *SPONGIONELLA* SP.[1)]

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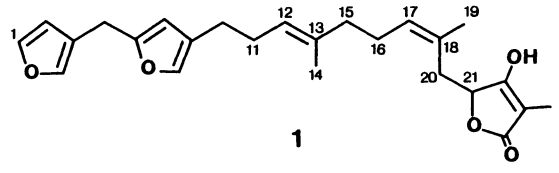
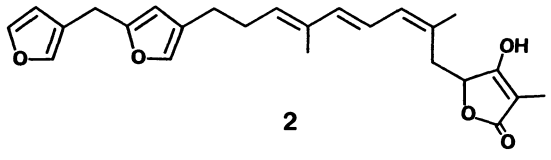
Two new furanosesterterpenes, spongionellin and dehydrospongionellin, have been isolated from the marine sponge *Spongionella* sp. Both compounds inhibit cell division of starfish eggs.

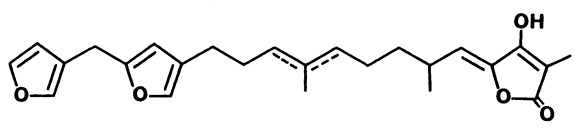
Marine sponges of the family Thorectidae are reported to contain two types of secondary metabolites, sesterterpenoids and indolic compounds.[2)] The former include several linear furanosesterterpenes which may be represented by ircinins 1 and 2(**3**) and variabilin(**4**).[3-5)] In the course of search for bioactive metabolites from Japanese marine organisms, we found that the lipophilic extract of a marine sponge *Spongionella* sp. inhibited the cell division of starfish embryos. The active compounds have been elucidated to be two new furanosesterterpenes **1** and **2**, which we designated spongionellin and dehydrospongionellin, respectively.



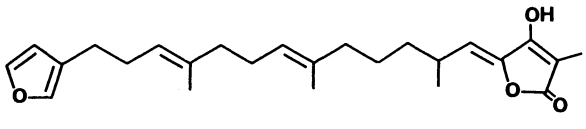

**1**




**2**




**3**




**4**

The sponge (400 g, wet weight) was collected in the Gulf of Suruga by using SCUBA (-20 m) and extracted with ethanol, whose extract was partitioned between water and ether. The organic layer was subjected to low pressure column chromatography on silica gel with dichloromethane/methanol (97:3). The active fractions thus obtained were purified by reversed-phase HPLC (ODS, 85 % MeOH) to yield spongionellin (**1**) and dehydrospongionellin (**2**) both as labile colorless oils (18 mg each); each compound inhibited cell division of fertilized starfish (*Asterina pectinifera*) eggs at 2.0 μg/mL.

Spongionellin (**1**), $[\alpha]_D$ +16°(*c* 0.1, $CH_2Cl_2$), was positive to Ehrlich reagent and showed IR absorption at 3500, 1720, and 1650 $cm^{-1}$. The molecular formula of $C_{25}H_{30}O_5$ was established by $^{13}C$ NMR and FAB mass spectrum [*m/z* 411$(M+H)^+$, 433$(M+Na)^+$]. EIMS fragment ions at *m/z* 81 and 161 were reminiscent of a difurano methylene constellation,[4] which was supported by $^1H$ NMR [δ 7.36, 7.28, 7.08, 6.31, 5.90 (1H, brs, each), 3.72 (2H, brs)] and by $^{13}C$ NMR (δ 154.0 s, 143.0 d, 139.8 d, 137.5 d, 135.3 s, 125.8 s, 111.3 d, 107.5 d, 24.2t). The molecule contains, in addition to a difurano methylene moiety, a nonconjugated tetronic acid functionality[6] (δ 175.9 s, 177.4 s, 97.1 s, 77.3 d, 77.3 d, 6.0 q), two trisubstituted double bonds (δ 125.9 d, 124.3 d, 129.2 s, 121.4 s), five methylenes (δ 39.6 t, 34.5 t, 28.5 t, 26.6 t, 25.3 t) and two methyls (δ 24.1 q, 16.1 q) (Table 1).

The gross structure of **1** was evidenced by the 500 MHz $^1H$ NMR spectroscopy (Table 1) including decoupling experiments. Irradiation of H-21 proton (δ 4.74 m) collapsed H-20 geminal methylene protons at δ 2.64(dd, 14.0, 4.5) and 2.33(dd, 14.0, 8.5). H-19 methyl protons at δ 1.75(3H, brs) was sharpened when a proton at either δ 2.64($H_a$-20) or δ 5.31(t, 7.0; H-17) was irradiated. The latter proton (H-17) was found to be coupled to H-16 methylene protons at δ 2.07(2H, m), which were in turn coupled to another methylene at δ 1.98(2H, t, 7.5; H-15). The remaining olefinic proton at δ 5.14(t, 7.0; H-12) was sharpened upon irradiation of either methyl protons at δ 1.55(3H, brs; H-14) or methylene protons at δ 2.19(2H, q, 7.0; H-11), the latter of which were observed to be also coupled to the H-10 methylene protons at δ 2.36(2H, t, 7.0). The geometry of $\Delta^{12,13}$ double bond was determined to be *E* on the basis of the $^1H$ and $^{13}C$ NMR signals at δ 1.55(H-14) and 16.1(C-14), respectively.[7] The C-19 methyl signals ($\delta_H$ 1.75 and $\delta_C$ 24.1) indicated *Z* geometry of $\Delta^{17,18}$ double bond,

Table 1. $^{1}H$ and $^{13}$ NMR Shifts for **1** and **2**

| | **1** | | **2** | |
|---|---|---|---|---|
| C | $^{1}H$ $\delta(CDCl_3)$[a] | $^{13}C$ $\delta(CDCl_3)$[b] | $^{1}H$ $\delta(CDCl_3)$[c] | $^{13}C$ $\delta(CDCl_3)$[b] |
| 1 | 7.36(1H, brs) | 143.0 d | 7.36(1H, brs) | 143.1 d |
| 2 | 6.31(1H, brs) | 111.3 d | 6.32(1H, brs) | 111.4 d |
| 3 | | 135.3 s | | 134.8 s |
| 4 | 7.28(1H, brs) | 139.8 d | 7.28(1H, brs) | 139.9 d |
| 5 | 3.72(2H, brs) | 24.2 t | 3.72(2H, brs) | 24.4 t |
| 6 | | 154.0 s | | 154.2 s |
| 7 | 5.90(1H, brs) | 107.5 d | 5.90(1H, brs) | 107.5 d |
| 8 | | 125.8 s | | 125.5 s |
| 9 | 7.08(1H, brs) | 137.5 d | 7.08(1H, brs) | 137.7 d |
| 10 | 2.36(2H, t, 7.0) | 28.5 t | 2.42(2H, t, 7.0) | 29.0 t |
| 11 | 2.19(2H, q, 7.0) | 25.3 t[d] | 2.36(2H, q, 7.0) | 25.1 t |
| 12 | 5.14(1H, t, 7.0) | 124.3 d | 5.48(1H, t, 6.5) | 122.4 d |
| 13 | | 121.4 s[e] | | 121.5 s |
| 14 | 1.55(3H, s) | 16.1 q | 1.70(3H, s) | 12.7 q |
| 15 | 1.98(2H, t, 7.5) | 39.6 t | 6.15(1H, d, 15.0) | 137.1 d[g] |
| 16 | 2.07(2H, m) | 26.6 t[d] | 6.27(1H, dd, 15.0, 11.0) | 130.0 d[g] |
| 17 | 5.31(1H, t, 7.0) | 129.5 d | 6.03(1H, d, 11.0) | 132.3 d[g] |
| 18 | | 129.2 s[e] | | 131.5 s |
| 19 | 1.75(3H, s) | 24.1 q | 1.88(3H, s) | 24.9 q |
| 20 | 2.33(1H, dd, 14.0, 8.5) | 34.5 t | 2.53(1H, dd, 14.0, 7.5) | 34.9 t |
| | 2.64(1H, dd, 14.0, 4.5) | | 2.80(1H, dd, 14.0, 4.5) | |
| 21 | 4.74(1H, m) | 77.3 d | 4.76(1H, m) | 78.5 d |
| 22 | | 177.4 s[f] | | 176.9 s[h] |
| 23 | | 97.1 s | | 97.3 s |
| 24 | 1.71(3H, s) | 6.0 q | 1.72(3H, s) | 6.1 q |
| 25 | | 175.9 s[f] | | 175.3 s[h] |

a) 500 MHz. b) 25 MHz. c) 400 MHz.
d-h) Assignments may be interchanged.

which was also supported by an upfield shift of C-20 methylene signal ($\delta_C$ 34.5) comparing with that of palinulin ($\delta_C$ 41.6).[6] However, absolute configuration at C-21 remains to be determined.

The other active compound, dehydrospongionellin, $[\alpha]_D$ +21° (*c* 0.1, $CH_2Cl_2$), had chemical and spectral features similar to those of spongionellin. FAB mass and $^{13}C$ NMR led to the molecular formula of $C_{25}H_{28}O_5$. UV absorption [UV(EtOH) 290(ε 8200), 279(11000), 270(9100), and 221(5200) nm] implied the presence of a triene functionality, which was supported by $^{1}H$ NMR signals at δ 6.15(d, 15.0Hz; H-15), 6.27(dd, 15.0, 11.0; H-16), 6.03(d, 11.0; H-17). The $^{1}H$ and $^{13}C$ NMR signals (Table 1) of the remaining portion were superimposable to those of

spongionellin, indicating the gross structure of dehydrospongionellin (**2**). A large coupling constant (15.0 Hz) between H-15 and H-16 showed *E* geometry of the $\Delta^{15,16}$ double bond. *Z* geometry of the $\Delta^{17,18}$ double bond was deduced by NOE enhancements observed at H-17 and H-21 proton signals upon irradiation of methyl protons at $\delta$ 1.88 and by the $^{13}C$ NMR shift of the C-19 methyl signal ($\delta$ 24.9), while the *E* geometry of $\Delta^{12,13}$ double bond determined as mentioned above.

Linear furanosesterterpenes possessing conjugated tetronic acid moiety are common to marine sponges of the family Thorectidae. However, furanoterpenes with nonconjugated tetronic acid were rare, and this is the first report for isolation of furanosesterterpenes from marine sponges of the genus *Spongionella*. Our compounds are also inhibitory against *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis*, indicating defensive roles of the compounds.

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References

1) Bioactive Marine Metabolites XI; Part X: N. Fusetani, Y. Yasukawa, S. Matsunaga, and K. Hashimoto, Comp. Biochem. Physiol., submitted.

2) P. R. Bergquist and R. J. Wells, "Marine Natural Products: Chemical and Biological Perspectives," ed by P. J. Scheuer, Academic Press, New York (1983), Vol. V, p.1 ff.

3) G. Cimino, S. De Stefano, L Minale, and E. Fattorusso, Tetrahedron, 28, 333 (1972).

4) I. Rothberg and P. Shubiak, Tetrahedron Lett., 1975, 769.

5) N. Fusetani, Y. Kato, S. Matsunaga, and K. Hashimoto, Tetrahedron Lett., 25, 4941 (1984).

6) G. Alfano, G. Cimino, and S. De Stefano, Experientia, 35, 1136 (1979)

7) L. Carey, J. M. Clough, and G. Pattenden, J. Chem. Soc., Perkin Trans. 1, 1983, 3005.

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