

DENDROLASIN AND LATRUNCULIN A FROM THE FIJIAN SPONGE
SPONGIA MYCOFIJIENSIS AND AN ASSOCIATED
NUDIBRANCH *CHROMODORIS LOCHI*

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As a part of our search for new bioactive substances from sponges, we found that crude extracts of *Spongia mycofijiensis* Bakus were extremely cytotoxic to epithelial carcinoma of the larynx (HEP-2) and monkey kidney (MA-104) cells. During the course of collecting this sponge, we repeatedly observed that the nudibranch *Chromodoris lochi* Rudman was attached to it. We now report the two most abundant metabolites of both the sponge and nudibranch, which are latrunculin A, a 16-membered macrolide with an attached 2-thiazolidinone unit, and dendrolasin, a simple furano-sesquiterpene.

Collections were from two geographically distinct locations in the Fiji Islands. Both the sponge and nudibranch were obtained from Yanutha Island in the Benga lagoon. Alternatively, only the nudibranch was found at northern sites in the Astrolabe reef as no sponge could be located during more than 60 dives. The crude extracts from each collection were examined by ^{13}C nmr and alongside resonances from long-chain lipids were intense absorptions diagnostic for latrunculin A ($\delta_{\text{C}} = 61.8 \text{ d}, 62.2 \text{ d}, 68.1 \text{ d}, 96.9 \text{ s}, 126.1 \text{ d}, 136.4 \text{ d}, 158.4 \text{ s}, 165.7 \text{ s}, 175.4 \text{ s}$) and for dendrolasin ($\delta_{\text{C}} = 111.0 \text{ d}, 138.7 \text{ d}, 142.4 \text{ d}$). Intensities of the CH carbon signals provided the relative ratios of latrunculin A to dendrolasin for the crude extracts as follows: sponge, 0.95:1.0; Benga nudibranchs, 1.55:1.00; Astrolabe nudibranchs, 1.03:1.0. Latrunculin A is the most cytotoxic of these two compounds because it is completely

toxic to the HEP-2 and MA-104 cells at 0.072 $\mu\text{g}/\text{ml}$ and 0.23 $\mu\text{g}/\text{ml}$, respectively; whereas dendrolasin is completely toxic to HEP-2 at 24 $\mu\text{g}/\text{ml}$ but is inactive against MA-104 cells.¹

Latrunculin A has been previously described as being ichthyotoxic and capable of inducing changes in cell morphology (1). In 1980, Kashman isolated and characterized latrunculins A, B, and C from a red-colored sponge, *Latrunculia magnifica* Keller (Order Hadromerida; Family Latrunculiidae), occurring at a depth of 6 to 30 m, in the Gulf of Eilat, Red Sea (2,3). Recently, Smith reported the total synthesis of (+) latrunculin B (4). Dendrolasin has been obtained from diverse sources, including the ant, *Dendrolasius fuliginosus* (5), sweet potato fusel oil (6), the wood oil of *Torreya nucifera* (7), and the sponge *Oligoceras hemorrhages* collected in the lagoon at Bimini, Bahamas (8).

EXPERIMENTAL

ANIMAL IDENTIFICATION.—*S. mycofijiensis* n. sp. (described by GJB) [Order Dictyoceratida; Family Spongiidae]. Holotype: Smithsonian Institution, USNM 34659; collected south of Viti Levu, Fiji (18° 20' N.; 179° E). Depth 9-18 m; in crevices on sides of coral cliffs; Dr. Phil Crews No. 86-37. Paratypes: Smithsonian, USNM 34660 and British Museum (Natural History) BMNH 1986:9:18:1 & 2 collected as above. Description: The body is mushroom-like but more globose (Figure 1) and measures up to 7 cm (diameter) by 3 cm (thick). It has a firm but spongy consistency and is attached to the substratum by a stalk measuring up to 2 cm long. The surface is

¹We thank Dr. T. Matthews, Syntex Research, for this bioassay data.



FIGURE 1. Underwater photo of the sponge *Spongia mycofijiensis* and its associated Nudibranch *Chromodoris lochi*.

smooth and clean, with a thin dermal membrane. Numerous oscules measuring up to 3 mm in diameter open at the surface. Color in life is black above and tan below; in preservative these colors fade. The tan choanosome has a moderately dense mesenchyme. It contains a ladder-like reticulation of spongin fibers. Reduced primary fibers measuring 50 μm in diameter constitute the sides of the ladder and contain spicule debris. The cross fibers measure 20 μm in diameter and are clean.

The spaces within this reticulation are square or rectangular in shape. The skeleton becomes more irregular near the surface, forming oval, spherical, and polygonal spaces. Spaces in the skeletal reticulation measure from 50 to 300 μm in greatest diameter. The reticulated arrangement of the spongin fibers is considerably more organized than that of other species of *Spongia* that have been illustrated. The sponge has a ketone-like, pleasant odor.

C. locbi is a nudibranch extremely common in Fiji and was identified by Mrs. Gilianne Brodie of the University of The South Pacific and by comparisons to pictures and descriptions in the literature (9, 10).

ISOLATION PROCEDURES.—The freshly collected animals (−9 m, July 1986) including the sponge (1.2 kg, wet weight) and nudibranchs (Benga, 38.8 g; Astrolabe 3.61 g) were immediately extracted with CH₂Cl₂ and then MeOH. The organic fractions were combined, and the viscous crude oil concentrates (sponge 2.835 g, Benga nudibranch 0.201 g, Astrolabe nudibranch 0.128 g) were returned to UCSC for further examination by ¹³C nmr (CDCl₃, 75 MHz). The sponge crude oil (1.7 g) was successively partitioned between equal volumes of MeOH (wet, % of H₂O adjusted to give a biphasic solution of equal volume) and a solvent series of hexanes, CCl₄, and CH₂Cl₂. Dendrolasin was prominent in the hexane partition fraction (0.8 g) while latrunculin A was present in the CCl₄ fraction (0.3 g). Chromatography of these fractions (reverse phase hplc, ODS support, MeOH 4% to 15% aqueous afforded, respectively, pure dendrolasin (0.3 g) and latrunculin A (0.187 g). The ¹H, ¹³C, COSY (¹H-¹H), and hetero COSY (¹H-¹³C) nmr data were consistent with their structures. Our nmr assignments were in agreement with those in the literature for latrunculin A (2) and dendrolasin (7), but the ¹³C-nmr data for dendrolasin have not been reported [CDCl₃, 75 MHz numbering as in Vanderah and Schmitz (8)]: 142.4 (d) C-1, 110.0 (s), C-2, 124.8 (s) C-3, 138.7 (d) C-4, 25.0 (t) C-5, 28.5 (t) C-6, 123.8 (d) C-7, 135.5 (s) C-8, 39.7 (t) C-9, 26.6 (t) C-10, 124.4 (d) C-11, 131.0 (s) C-12, 16.0 (Q Me @ C-8), 25.7 & 17.7 (Q, Me's @ C-12).

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