PUUPEHENONE, A CYTOTOXIC METABOLITE FROM A DEEP WATER MARINE SPONGE, *STRONGLYOPHORA HARTMANI*

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From our efforts to identify antineoplastic compounds from marine organisms we have isolated and identified puupehenone (1), a cytotoxic sesquiterpene-methylene quinone, from a deep water sponge, *Strongylophora hartmani* van Soest, (family Petrosiidae)[1](2). Puupehenone was isolated previously from an Hawaiian and Eniwetok Atoll species of the genus *Heteronema* (1), and a Tahitian sponge, *Hyrtios eubnamma* (3). Neither the halopuupehenones (1), bispuupehenone (3), nor the stronglyophorines, which are meroditerpenoids isolated from *Stronglyophora durissima* (4), were detected in *S. hartmani*. From in-vitro assays puupehenone yielded IC_{50} values of 1 μg/ml against P388 mouse leukemia, 0.1-1 μg/ml against A-549 (human lung cancer cell line), 1-10 μg/ml against HCT-8 (human colon cancer cell line), and 0.1-1 μg/ml against MCF-7 (human mammary cancer cell line).[2] From P388 in-vivo assay of puupehenone at the National Cancer Institute, a T/C value of 119 at 25 mg/kg (administered daily for 9 days) was obtained.[3] Puupehenone also yielded a minimum inhibitory concentration of 3 μg/ml against the fungus, *Candida albicans* [see (1) for similar results].

EXPERIMENTAL

ANIMAL COLLECTION AND EXTRACTION.—*S. hartmani* was collected in December 1984, at -225 m adjacent to Goulding Cay, Bahamas, using the Harbor Branch Oceanographic Institution's submersible, the Johnson-Sea-Link II. The fresh frozen sponge was subsequently homogenized and extracted with EtOAc. A voucher specimen is preserved in 70% aqueous EtOH and is located at the Harbor Branch Oceanographic Institution/SeaPharm research laboratory in Ft. Pierce, Florida.

ISOLATION OF PUUPEHENONE.—The residue from EtOAc extraction (1.7% of frozen wt.) was subjected directly to multilayer coil planet centrifuge countercurrent chromatography (ccc) (5,6). The ccc solvent system consisted of heptane-CH_2Cl_2-acetonitrile (10:3:7); the upper phase was used as the mobile phase. Pure puupehenone was delivered directly from one countercurrent chromatography and comprised 35% of the EtOAc residue (0.6% of frozen wt.). Puupehenone was identified by comparison of the $[\alpha]^{25}D$, uv, ir, ms, ^{1}H-nmr and ^{13}C-nmr values with the literature values (1). Full details of the isolation and identification are available on request.

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[1]The sponge was identified by Dr. S. Pomponi.

[2]The human cancer cell lines were obtained from ATCC.

[3]The P-388 in-vivo assay data were supplied by Dr. M. Suffness (NCI) and Prof. P.J. Scheuer.