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A new polyacetylene derivative with protein tyrosine phosphatase 1B inhibitory activity from the marine sponge *Halichondria* cf. *panicea* collected at Iriomote Island

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Protein tyrosine phosphatase 1B (PTP1B) is a negative regulator of the insulin and leptin signaling pathways. Therefore, PTP1B inhibitors may be candidate drugs for the treatment of type-2 diabetes mellitus and obesity.

During our screening program for PTP1B inhibitors from marine invertebrates and microorganisms, we have reported the discovery of several new inhibitors. With continuous efforts on the extracts of marine organisms, we found that the EtOH extract of the marine sponge *Halichondria* cf. *panicea* collected at Iriomote Island exhibited the inhibitory activity against PTP1B. Bioassay-guided separation led to the isolation of a new polyacetylene, named isopetrosynol (**1**), together with four known compounds (**2**–**5**). In this presentation, the isolation, structures, and biological activities of compounds **1**–**5** will be presented.

The EtOH extract of the marine sponge displayed the inhibitory activity against PTP1B (approximately 75% at 50 μg/mL) and was separated into seven fractions using an ODS column. The bioactive fractions were then purified by repeated HPLC to give compounds **1** (3.3 mg), **2** (16.4 mg), **3** (7.6 mg), **4** (2.2 mg), and **5** (6.5 mg).

Compounds **2**–**5** were identified as petrosynol (**2**), adociacetylene D (**3**), (5*R*)-3,15,27-triacontatriene-1,29-diyn-5-ol (**4**), and petrosterol (**5**), respectively, by comparing their spectroscopic data with those of the literature values.

The structure of **1** including the absolute configuration was revealed as a diastereomer of **2** on the basis of spectroscopic data for **1** and **2**. Compound **1** inhibited the PTP1B activity with an IC_{50} value of 8.2 μM, while **2** showed only 29% inhibition at 21.6 μM. The IC_{50} values of compounds **3**–**5** were 7.8, 12.2, and >24.8 μM, respectively. This is the first study to show the inhibitory effects of polyacetylene derivatives on PTP1B.