

Anti-Angiogenic Substances from Marine Sponge

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In search of new pharmaceutically valuable substances from marine organisms, we have been engaged in chemical studies [1) structural elucidation; 2) asymmetric total synthesis; 3) elucidation of pharmacophore by analysis of structure-activity relationship; 4) action mechanism and search for target protein] on the bioactive substances, which was isolated from marine invertebrates and marine microorganisms on the guidance of new practical bioassay. We have collected marine invertebrates at Japanese coasts and Indonesian coral reefs.

Angiogenesis, a formation of new blood capillaries from preexisting blood vessels, is critical for tumor growth and metastasis. A growing tumor needs an extensive network of capillaries to provide nutrients and oxygen etc. In addition, the new blood vessels provide a way for tumor cells to enter in the circulation and to metastasize to another organ. Therefore, substances that inhibit angiogenesis have a considerable potential to be therapeutic agents.

On the guidance of selective growth inhibition against human umbilical vein endothelial cells (HUVECs), we searched for anti-angiogenic substances from extracts of marine invertebrates.

1) Bastadins Bastadins, cyclic tetramers of brominated-tyrosine derivatives, were isolated from the marine sponge *Ianthella basta*.

2) Globostellatic acid Four novel triterpene isomers named globostellatic acid X were isolated as methyl esters from the marine sponge *Rhabdastorella globostellata*. Globostellatic acid X methyl esters are olefinic isomers of isomalabarican-type triterpene having long conjugated enone system.

3) Cortistatins A-D Four novel steroidal alkaloids named cortistatins A, B, C, and D have been isolated from the marine sponge *Corticium simplex*. Cortistatins are unique 9(10-19)-abeo-androstane-type steroidal alkaloid having isoquinoline unit.