Development of Novel Reagents for Understanding the Biological Functionalities from Natural Resources

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In the continuing search for biologically active substances from natural organisms, extreamely novel compounds were isolated. The structures of these compounds were elucidated mainly by detailed analysis of NMR data and MS spectral data.

Halichlorine was isolated from the marine sponge *Halichondria okadai*. This compound inhibits the induction of VCAM-1. Drugs that block the induced expression of VCAM-1 may be useful for treating atherosclerosis, coronary artery diseases, angina and noncardiovascular inflammatory diseases.

A $cPLA_2$ exhibits specificity for the release of arachidonic acid from membrane phospholipids. Therefore, compounds that inhibit $cPLA_2$ activity have been targeted as anti-inflammatory agents. Pinnaic acids were isolated from the Okinawan bivalve *Pinna muricata*. Interestingly, the structure of pinnaic acids are closely related to that of halichlorine.

Homocereulide, a potent cytotoxic lipopeptide was isolated from marine bacteria *Bacillus cereus*. Superoxide anion may be closely related to inflamentation, cancer and aging. Therefore, compounds that inhibit superoxide anion production may be useful for treating inflammatory diseases. Tanzawaic acids were isolated from *Penicillium citrinum*. Tanzawaic acids A, B and C inhibit the induction of superoxide anion.

Okadaic acid is a potent inhibitor of protein phosphatases 1 and 2A. Importance of the formation of a flexible cavity between carboxyl group and hydroxyl group was proposed by the NMR experiments. The optimum structure of okadaic acid, elucidated by Distance-Geometry method, suggested the flexible cavity hypothesis.

Absolute configuration and biogenetic pathway of norzoanthamines exhibiting inhibitory effect of IL-6 production were also described.