MARINE NATURAL PRODUCTS - AS A SOURCE OF CYTOTOXIC DRUGS

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Summary

Approximately one third of today´s best selling drugs are natural. Among that nearly 3 lakh described species of plants and animals are from marine sources. Marine natural products have their stronghold in many phytopharmacotherapy including the area of anti-cancer chemotherapy. This article summarizes cytotoxic marine compounds from various marine plants like *Cephalotaxus fortunei, Scilla sibirica, Aconitum hemsleyanum* var *leueanthus, Murraya koenigii,* Marine sponge Halichondria sp, Singaporean ascidian etc.

Introduction

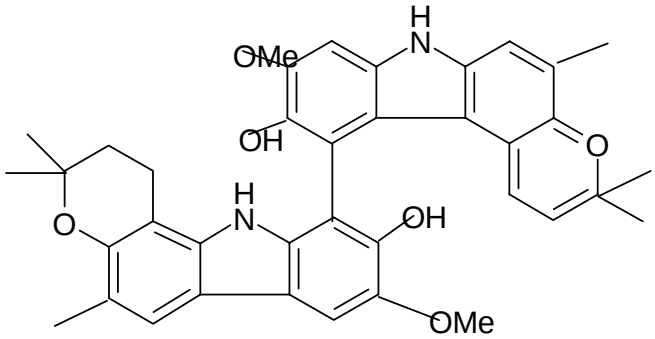
Approximately one third of today´s best selling drugs are natural products. Among that most are from terrestrial origin. Oceans cover 70% of the earth's surface and possess nearly 3 lakh described species of plants and animals from marine sources. It is reported that the living organisms were appeared in the sea more than 3500 million years ago [1,2] and evolutionary development has equipped many marine organisms with the appropriate mechanism to survive in a hostile milieu in terms of extreme temperature, changes in salinity and pressure as well as overcoming the effect of mutation, bacteria and viral pathogens[3]. Marine organisms have developed exquisitely complex biological mechanisms showing cross phylum activity with terrestrial organisms[4]. It is no surprise therefore that marine natural products have their stronghold in the area of anti-cancer chemotherapy as indicated by the list of compounds currently under clinical investigation[5]. Marine organisms comprise approximately a half of the total biodiversity, thus offering a vast source to discover useful therapeutics.

Table 1. Cytotoxic active principles from marine sources.

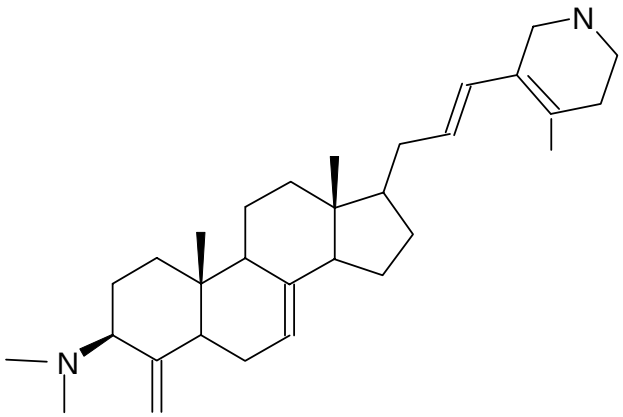
Name of the plant	**Extract/part**	**Active principles**	**Reference number**
Cephalotaxus fortunei	Methanol extract of fruit portioned between ethyl acetate and 5% HCl	• Cephalocyclidine • Cephalotaxine • Wilsonine,Drupacine • 11-hydroxy cephalotaxine • Esters of harringtanine • deoxy harringtanine, iso harringtanine	6
Scilla sibirica	Bulbs extracted with 60% aq ethanol	22 alkaloids isolated. • homoDMDP • 6-deoxy homoDMDP • 2,5,imino-2,5,6-trideoxyD-gulo-heptitol	7
Aconitum hemsleyanum var *leueanthus*	Roots percolated with 0.15% HCl	• Leueantine A • Leueantine B • Leueantine C • Leueantine D • ezochasmanine	8
Murraya koenigii	Plant extracted with 95% ethanol. Extract partitioned between water and chloroform	Compound (1)- brown powder Compound (2)- brown gum i.e. two carbazole alkaloids. (1) Murrayanine (2) 8,8”-biskoenigine	9
Marine sponge Halichondria sp.	Extract with ethyl acetate-mathanol-water(5:5:1)	• halichondramine	10
Unidentified Newzealand ascidian Anchorina colonis	Methanol/ DCM	• coproverdine	11
Marine sponge corticum	Extracted with methanol	• plakinamine G • plakinamine H • 4-α-hydroxydemethyl-plakinamine B • tetrahydro plakinamine A	12
Singaporean ascidian. May belong to one of three familiar	Methylene chloride: methanol(1:1)	• kuanoniamine A,C,D,E,F • Subarine	13

Pseudodistomidae; polycylinidae or polycitoridae			
Myriastra clavosa	Methanol extract	• 4,6,8,10,12,16-heptamethoxy-17-methyltricosa-1,17-diene • 4,6,8,10,12,16,18-octamethoxy-19-methyl pentacosa-1,19-diene • 4,6,8,10,12,16,18,20-nanomethoxy-21-methyl heptacosa-1,22-diene • 4,6,8,10,12,16,18,20,22-decamethoxy-23-methylnanocosa-1,2,3-diene • 4,6,8,10,12,16,18,20,22,24-undecamethoxy-25-methyluntriacont-1,25-diene • Clavosolides A,B	14
Consolida orientalis	Methanol extract	• 18-demethylpubescenine • 14-demethyltuguaconitine • Takaosamine • Gigactonine • Delcisine	15
Leucetta chagosensis	Methylene chloride extract	-	16
Alkaloid from *Tuniate cystodytes* species	Methanol extract	Rigidin B,C,D	17

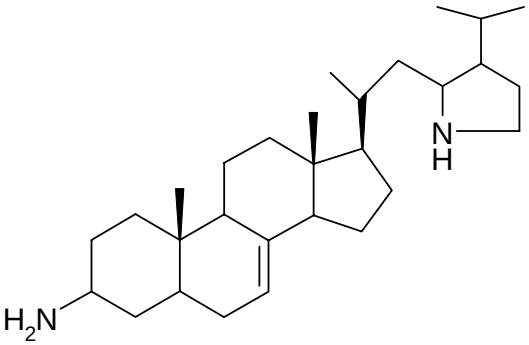
Figure 1. Cytotoxic active marine compounds.



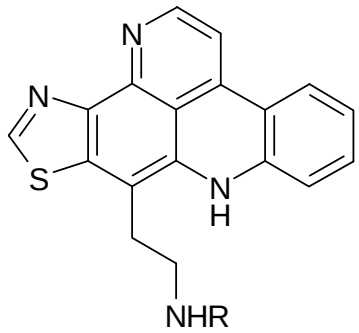
8,8''-Biskoenigine



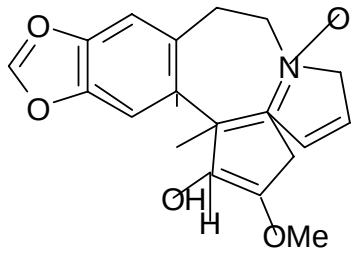
Plakinamine



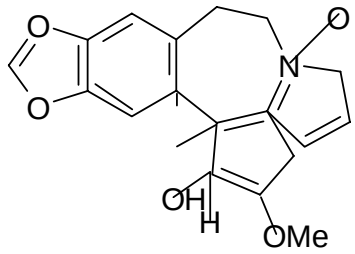
4 α-hydroxydemethyl plakinamine B



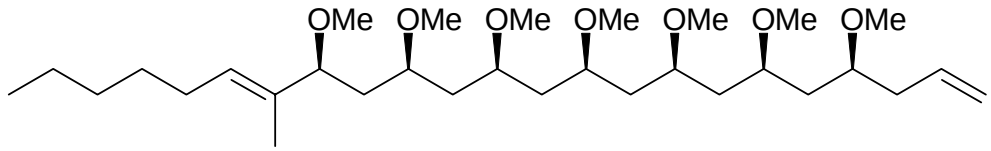
Kuanoniamine C



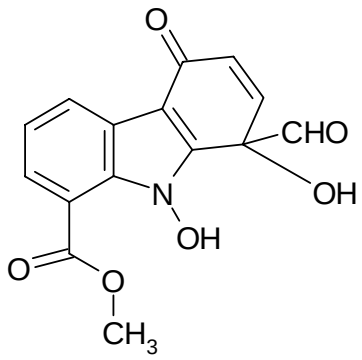
Cephalotoxine –N- Oxide



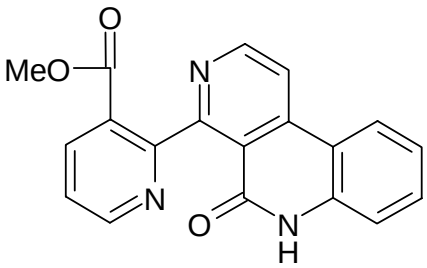
Leueantine B



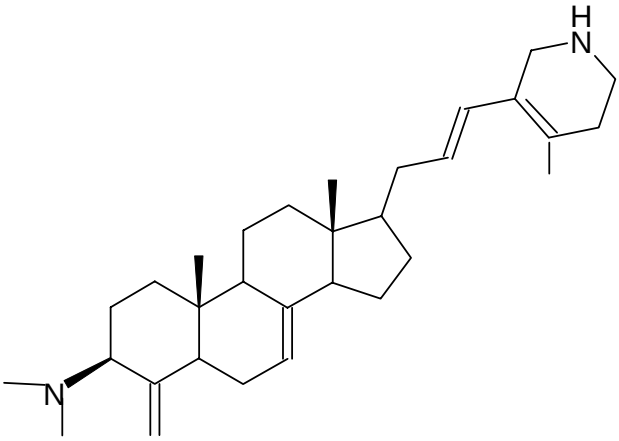
4,6,8,10,12,14,16,18-Octamethoxy-19-methyl pentacosa-1,19-diene



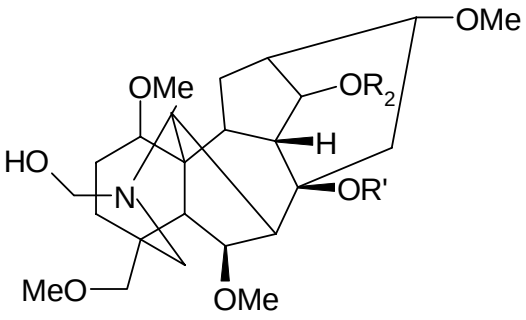
Coproverdine



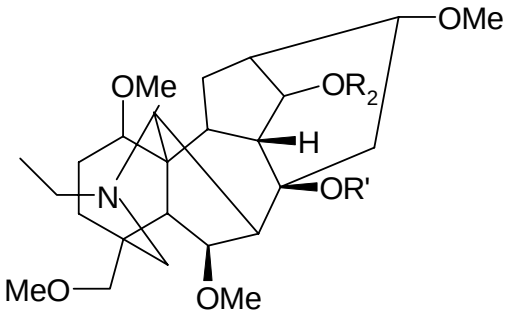
Subarine



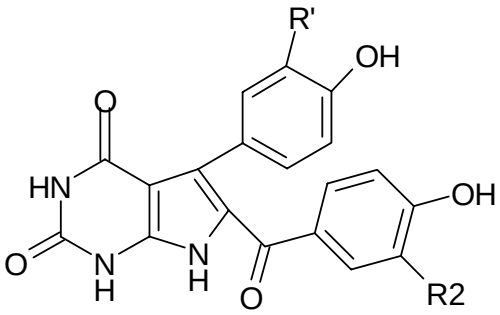
Plakinamine H



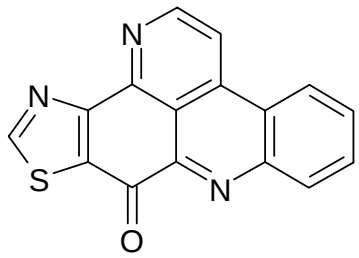
Leuceantine A



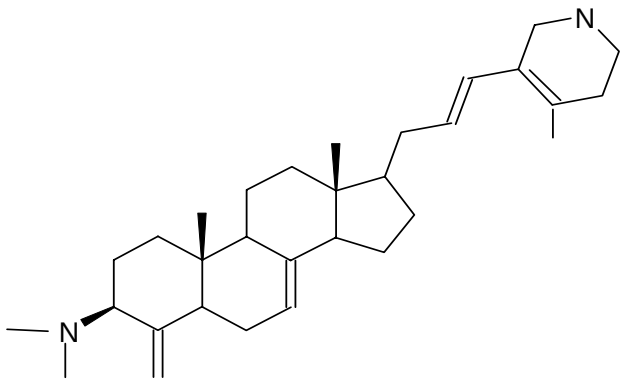
Leueantine B



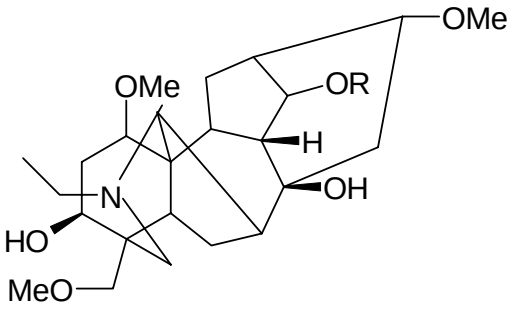
Rigidine B



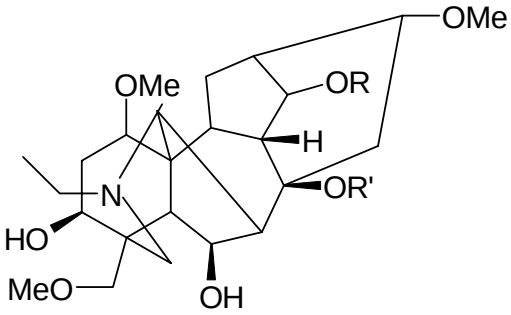
Kuanoniaminc A



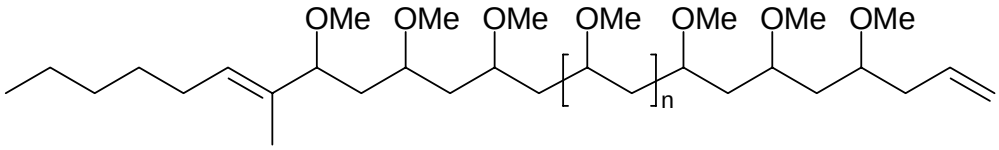
4 α- hydroxydemethylplakinamine B



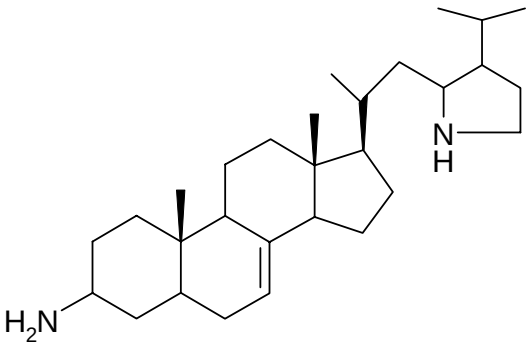
Leueantine C



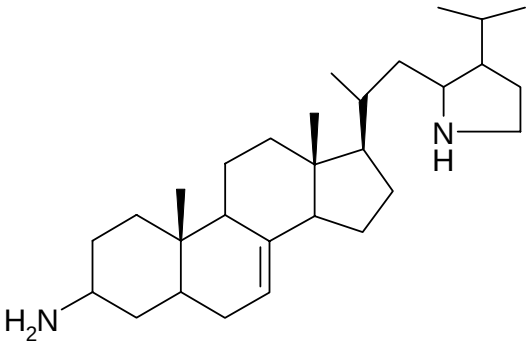
Leueantine D



(4,6,8,10,12,14,16) heptamethoxy-17-methyltricosa-1,17,diene



pllakinamine G



Tetrahydroplakinamine A.

Conclusion

The marine ecosystem offers a huge potential in the naturally based drug discovery. This article shows that the marine ecosystem is not only productive to discover anticancer entities but it is also a tool to identify new cellular targets for therapeutic intervention. The steady increase in the number of scientific publications and patents on marine genetic resources observed that this area is of growing importance for both the scientific community and bioprospecting. So it appears that a better and more pragmatic approach is urgently needed in order to translate innovative discoveries into active clinical therapeutics. The greater part of earth surface is covered by seas and ocean which contains about 5 lack species of marine organisms, since the natural products chemist diverted their attention to exploit the vast researches of marine flora and animal world, numerous novel compounds have been isolated from these marine organisms during the second half of 20th century. Many of these compounds have shown pronounced biological activities. However the compounds which have failed to show the activities for which those were assayed cannot be recorded as not having other biological activities. Many of these compounds might show some other activities if studied extensively during the course of time. Although the impact of marine natural products is presently lesser on the pharmaceutical industry, it may come forward in a big way to provide a new lead compound for the development of potential therapeutically active compounds.[18]

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