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# A Review: Biomedical Compounds and Anticancer drugs from Marine and Tropical Herbal medicine

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## Abstract

Cancer is one of the most common devastating disease affecting millions of people per year. Cancer has been estimated as the second leading cause of death in humans. So there has been an intense search on various biological sources to develop a novel anti-cancer drug to combat this disease. Plants have proved to be an important natural source of anti-cancer therapy for several years. The plant-derived compounds have been an important source of several clinically useful anti-cancer agents. Plants have played an important role as a source of effective anti-cancer agents, and it is significant that over 60% of currently used anti-cancer agents are derived in one way or another from natural sources, including plants, marine organisms and micro-organisms. The marine floras are rich in medicinally potent chemicals predominantly belonging to polyphenols and sulphated polysaccharides. The chemicals have displayed an array of pharmacological properties especially antioxidant, immune stimulatory, and anti-tumor activities. This paper deals with the Modern technologies have opened vast areas of research for the extraction of biomedical compounds from tropical herbals, marine and coastal associated medicinal plants for anticancer properties which could be further designed to produce novel cancer drugs.

**Keywords:** Anti-cancer, Plant derivatives, Herbal and Marine medicines, Clinical trials, Novel drugs.

## Contents



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## 1. Introduction

Plants have a long history of use in the treatment of cancer **[1].** According to him, lists of more than 3000 plant species that have reportedly been used in the treatment of cancer, but in many instances, the "cancer "is undefined, or reference is made to conditions such as "hard swellings", abscesses, calluses, corns, warts, polyps, or tumors, to name a few. Such symptoms would generally apply to skin, "tangible", or visible conditions, and may indeed sometimes correspond to a cancerous condition, but many of the claims for efficacy should be viewed with some skepticism because cancer, as a specific disease entity, is likely to be poorly defined in terms of folklore and

traditional medicine. This is in contrast to other plant-based therapies used in traditional medicine for the treatment of afflictions such as malaria and pain, which are more easily defined, and where the diseases are often prevalent in the regions where traditional medicine systems are extensively used. Nevertheless, despite these observations, plants have played an important role as a source of effective anti-cancer agents, and it is significant that over 60% of currently used anti-cancer agents are derived in one way or another from natural sources, including plants, marine organisms and micro-organisms **[2, 3].**

The search for anti-cancer agents from plant sources started in earnest in the 1950s with the discovery and development of the vinca alkaloids, vinblastine and vincrstine, and the isolation of the cytotoxic podophyllotoxins. As a result, the United States National Cancer Institute (NCI) initiated an extensive plant collection program in 1960, focused mainly in temperate regions. This led to the discovery of many novel chemotypes showing a range of cytotoxic activities **[4],** including the taxanes and camptothecins, but their development into clinically active agents spanned a period of some 30 years, from the early 1960s to the 1990s. This plant collection program was terminated in 1982, but the development of new screening technologies led to the revival of collections of plants and other organisms in 1986, with a focus on the tropical and sub-tropical regions of the world. It is interesting to note, however that no new plant derived clinical anti-cancer agents have, as yet, reached the stage of general use, but a number of agents are in preclinical development.

**Why herbal medicine**

Herbal medicines are being used by about 80% of the world population primarily in the developing countries for primary health care. They have stood the test of time for their safety, efficacy, cultural acceptability and lesser side effects. The chemical constituents present in them are a part of the physiological functions of living flora and hence they are believed to have better compatibility with the human body. Ancient literature also mentions herbal medicines for age-related diseases namely memory loss, osteoporosis, diabetic wounds, immune and liver disorders, etc. for which no modern medicine or only palliative therapy is available. These drugs are made from renewable resources of raw materials by eco-friendly processes and will bring economic prosperity to the masses growing these raw materials.

**Why Anti-cancer drugs**

Cancer is the second leading cause of death in the world **[5].** Throughout history and across the world, the plant kingdom has provided a variety of medicines for cancer treatment. In modern times, plants have been a source of analgesics, anti-inflammatory, anti-asthmatics, anti-arrhythmic agents, anti-hyper tansies, and anti-microbial agents known to be numerous. Currently over 60% of the drugs are derived in one or other way from natural source including plant, marine organism and micro-organism **[6].**There are worldwide efforts to discover anticancer drugs from plants.

**Significance of plant secondary metabolites:**

Plant secondary metabolites have proved to be an excellent reservoir of new medical compounds. Many anti-cancer agents have been isolated from various plant sources like *Catharanthus roseus*, *Podophyllum* species, *Taxus brevifolia*, *Camptotheca acuminate*, *Betula alba*, *Cephalotaxus* species, *Erythroxylum pervillei*, *Curcuma longa*, *Ipomoeca batatas*, *Centaurea schischkinii* and many others. Scientists are still attempting to explore the bioavailability of anti-cancerous compounds in unexplored plant species. Vinca alkaloids belong to an important class of anti-cancer drugs. The mechanism of action of Vinca alkaloids is that they inhibit the cell proliferation by affecting the micro tubular dynamics during mitosis, and this causes a characteristic block during mitosis leading to apoptosis. Certain semi-synthetic analogues have been developed to increase the therapeutic index. Vinblastine (VLB) and Vincristine (VCR) are the two major naturally occurring active compounds obtained from the *Madagascar periwinkle*, *Catharanthus roseus* G. Don. (Apocynaceae). These compounds reported potential activity against lymphocytic leukemia in mice. Vinorelbine (VRLB) and Vindesine (VDS) are the two semi synthetic analogs obtained from the active compounds. They showed potential activity against leukemia's, lymphomas, advanced testicular cancer, breast cancer, lung cancer and Kaposi's sarcoma when treated in combination with other chemotherapeutic drugs **[7].** Vinflunine, bifluorinated derivatives of vinorelbine exhibits a superior anti-tumor activity compared to other vinca alkaloids. This novel Vinca alkaloid is currently under Phase II clinical trials. Both Vinflunine and Vinorelbine exhibits reduced toxicity in animal models **[8, 9].**

A more recent addition to the armamentarium of plant derived chemotherapeutic agents are the taxanes **[10].** Paclitaxel (taxol®) initially was isolated from the bark the Pacific Yew, *Taxus brevifolia* Nutt. (Taxaceae), as part of a random collection program for the NCI by the U.S. Department of Agriculture (USDA). The use of various parts of *Taxus brevifolia* and other *Taxus* species (e.g., *Taxus Canadensis* Marshall, *Taxus baccata* L.) by several Native American tribes for the treatment of some non-cancerous conditions has been reported, while the leaves of *Taxus baccata* are used in the traditional Asiatic Indian (Ayurvedic) medicine system, with one reported use in the treatment of "cancer" **[11].** Paclitaxel, along with several key precursors (the baccatins), occurs in the leaves of various *Taxus* species, and the ready semi-synthetic conversion of the relatively abundant baccatins to paclitaxel, as well as active paclitaxel analogs, such as docetaxel (Taxotere®), has provided a major, renewable natural source of

this important class of drugs. Paclitaxel is used in the treatment of breast, ovarian and non-small cell lung cancer (NSCLC), and has also shown efficacy against Kaposi sarcoma, while docetaxel is primarily used in the treatment of breast cancer and NSCLC. Paclitaxel has also attracted attention in the potential treatment of multiple sclerosis, psoriasis and rheumatoid arthritis. In addition, 23 taxanes are in preclinical development as potential anti-cancer agents.

The two clinically active agents, etoposide (VM 26) and teniposide (VP 16-213), which are semi-synthetic derivatives of the natural product, epipodophyllotoxin (an isomer of podophyllotoxin), may be considered as being more closely linked to a plant originally used for the treatment of "cancer" **[12].** The *Podophyllum* species (Podophyllaceae), *Podophyllum peltatum* Linnaeus (commonly known as the American mandrake or Mayapple), and *Podophyllum emodii* Wallich from the Indian subcontinent, have a long history of medicinal use, including the treatment of skin cancers and warts. The major active constituent, podophyllotoxin, was first isolated in 1880, but its correct structure was only reported in the 1950s. Many closely related podophyllotoxin like lignans were also isolated, and several of them were introduced into clinical trials, only to be dropped due to lack of efficacy and unacceptable toxicity. Extensive research led to the development of etoposide and teniposide as clinically effective agents which is used in the treatment of lymphomas and bronchial and testicular cancers.

Another important addition to the anti-cancer drug armamentarium is the class of clinically active agents derived from camptothecin, which is isolated from the Chinese ornamental tree, *Camptotheca acuminata* Decne (Nyssaceae) Camptothecin (as its sodium salt) was advanced to clinical trials by the NCI in the 1970s, but was dropped because of severe bladder toxicity, but extensive research led to the development of more effective derivatives, Topotecan and Irinotecan (CPT-11; Camptosar). Topotecan is used for the treatment of ovarian and small cell lung cancers, while Irinotecan is used for the treatment of colorectal cancers.

Betulinic acid, another plant-derived compound with a long history, is a lupane-type triterpene which has been isolated from many taxonomically diverse plant genera. A major source is the birch tree, *Betula* spp. (Betulaceae), which is also a primary source of its C28 alcohol precursor, betulin, whose isolation was first reported in 1788. A variety of biological activities have been reported for betulinic acid, including anti-bacterial, anti-inflammatory and antimalarial, but the most important activities have been associated with inhibition of the replication of strains of the human immunodeficiency virus (HIV), and cytotoxicity against a range of cancer cell lines. Significant in vivo activity has been observed in animal models bearing human melanoma xenografts, and the NCI is assisting in the development of systemic and topical formulations of the agent for potential clinical trials.

Colchicine is a plant secondary metabolite extracted from *Colchicum autumnale* and *Gloriosa superba* L. It causes mitotic arrest during cell cycle and thus they are considered as potent anti-mitotic drug both in-vitro and in-vivo. Due to severe toxic effects, certain derivatives of colchicine were synthesized namely, 3-demethyl colchicine, colchicoside, thiocolchicocide which showed improved activity against certain leukemic cells and solid tumors. Research is still undergone in the area of anti-cancer therapy **[15].**

Daphnoretin, a bis-coumarin derivative, extracted in good amounts from the root bark of *Wikstroemia indica* (Thymelaeaceae) was found to have good anti-cancer activity (Lu et al., 2011). Daphnoretin causes suppression of protein and DNA synthesis in Ehrlich ascites carcinomas. It is also seen to suppress the hepatitis B surface antigen expression on human hepatoma Hep3B cells **[16].** Emodin (1, 3, 8-trihydroxy-6-methylanthraquinone) is one of the active component isolated from the rhizome of rhubarb. Rhubarb is used as a traditional Chinese medicine for treating various diseases. This anthraquinone compound causes apoptosis in many types of cancers including lung cancer, liver cancer, ovarian cancer and blood cancer by several pathways **[17].**

## 2. Marine Sources for Biomedical and Anti-Cancer drugs

Numerous types of bioactive compounds have been isolated from plant sources. Several of them are currently in clinical trials or preclinical trials or undergoing further investigation. Although marine compounds are underrepresented in pharmacopoeia, it is anticipated that the marine environment will become an invaluable source of novel compounds in the future, as it represents 95% of the biosphere **[18].** However, development of marine floral compounds as therapeutic agents is still in its embryonic stage due to lack of an analogous ethno-medical history as compared to terrestrial habitats, together with the relative technical difficulties in collecting the marine floral samples. Over the last few decades, significant efforts have been made, by both pharmaceutical companies and academic institutions, to isolate and identify new marine-derived, natural products especially from faunal species. However, the marine floras are only little unexplored and these works are reviewed here as a base line data for promoting further research in this field. Marine floras include micro flora (bacteria, actinobacteria, cyanobacteria and fungi), micro algae, macro algae (seaweeds) and flowering plants (mangroves and other halophytes). Occupying almost 71% of globe, the ocean is rich in biodiversity and the micro flora and micro algae alone constitute more than

90% of oceanic biomass **[19].** The vast marine floral resource will offer a great scope for discovery of new drugs. It is increasingly recognized that ocean contains a huge number of natural products and novel chemical entities with unique biological activities that may be useful in finding the potential drugs with greater efficacy and specificity for the treatment of human diseases **[20].** It cannot be denied that with 3.5 billion years of existence on earth and experience in biosynthesis, the marine micro floras remain nature's best source of chemicals. The marine organisms produce novel chemicals to withstand extreme variations in pressure, salinity, temperature, and so forth, prevailing in their environment, and the chemicals produced are unique in diversity, structural and functional features **[21].**

**Availability of Marine Natural Products:**

Natural products have long been used as foods, fragrances, pigments, insecticides, medicines etc. due to their easy accessibility, terrestrial plants have served as the major source of medicinally useful products, especially for traditional or folk medicine. According to **[22],** about 25% of all pharmaceutical sales are drugs derived from plant natural products and additional 12% are based on microbially produced natural products. The marine environment covers a wide thermal range ( from the below freezing temperatures in Antarctic waters to about 350 C in deep hydrothermal vents), pressure range (1-1000 atm), nutrient range (oloigotropic to eutrophic) and its extensive photic and non- photic zones.

## 3. Chemical Constituents from Marine Flora

Marine floras are rich in biologically active and medicinally potent chemicals. Polyphenols and polysaccharides are the most predominant group of compounds which are applicable for antioxidant and anticancer activities. There are more than 40,000 different species of phytoplankton, 680 species of marine algae belonging to Rhodophyta, phaeophyta, Chlorophyta commonly known as red, brown, and green seaweeds respectively and 71 mangrove plant species have been documented in the global marine biotope. They provide essential fatty acids, ionic trace minerals, vitamins, enzymes, bio flavonoids, amino acids and other nutrients.

This review deals with the selective herbal medicinal plants including marine sources and their anticancer properties to utilize the discovery of new anticancer drug developments.

**Table 1. List of Tropical herbal plant derivatives used in cancer therapy**

| S.NO | Anticancer Plants | Active Compounds | Biological Activity | References |
|---|---|---|---|---|
| 1 | *Aglaia foveolata* Panell | Silvestrol | Apoptosome/mitochondrial pathway was involved in triggering extrinsic pathway of programmed cell death of tumor cells | Kim et al.,2007 Kinghom et al., 2009 |
| 2 | *Amoora rohituka* | Flavopiridol | Inhibits cell cycle progression at GI or GII phase | Mans et al., 2000 |
| 3 | *Berberis amarensis* | Berbamine | Caspase -3-dependent Apoptosis | Xie et al., 2009 |
| | *Betula alba* | Betulinc acid | Triggers mitochondrial pathway of apoptosis | Fulda, 2008 |
| 4 | *Berberineeris sp* | Berberine | Not known | Patil et al., 2010 Wang et al., 2011 |
| 5 | *Catharanthus roseus* | Vinflunine | Mitotic block | Okouneva et al., 2003, Simeons et al., 2008. |
| 6 | *Catharanthus roseus* | Vindesine and Vinorelbine | Mitotic block | Cragg and New man, 2005 |
| 7 | *Camptotheca acuminate* | Topotecan, Exatecan , LE-SN-38, Irinotecan | DNA topoisomerase I Inhibition | Creemers et al., 1996, Mineko et al., 2000, Zhang et al., 2004, Fuchs et al., 2006 |
| 8 | *Cephalotaxus harrintonia*, | Harringtonine | Inhibition of protein synthesis and chain elongation during translation | Cragg and Newman, 2005; |
| 9 | *Cephalotaxus hainanensis* | Homoharringtonine | Inhibition of protein synthesis and chain elongation during translation | Efferth et al., 2007 |

| | | | | |
|---|---|---|---|---|
| 10 | *Cephalotaxus qinensis* | Homoharringtonine | Inhibition of protein synthesis and chain elongation during translation | Efferth et al., 2007 |
| 11 | *Centaurea schischkinii* | Schischkinnin | Not known | Shoeb et al., 2005 |
| 12 | *Centaurea Montana* | Montamine | Not known | Shoeb et al., 2005 |
| 13 | Chinese herb, *Danggui longhui* Wan | Indirubin | Inhibits cyclindependent Kinases | Nam et al., 2005 |
| 14 | *Colchicum autumnale* | Colchicine | Anti-mitotic | Dubey et al., 2008 |
| 15 | *Combretum caffrum* Kuntze | Combretastatin A- | Tubulin structure disruption | Thomson et al., 2006; Ley et al., 2007 |
| 16 | *Cucurbitaceae sp* | Cucurbitacin | Inhibits signal transducer/JAK 2 activity and activates STAT3 pathway | Molavi et al.,2008 Bernard & Olayinka et al., 2010 |
| 17 | *Curcuma longa* | Curcumin | Exact mechanism of action is still unknown | Goel et al., 2008, Sa et al., 2010 |
| 18 | *Dysoxylum binectariferum* | Flavopiridol | Inhibits cell cycle progression at GI or GII Phase | Mans et al., 2000 |
| 19 | *Erythroxylum pervillei* | Pervilleines | Inhibitors of Pglycoprotein | Mi et al., 2001 Mi et al., 2002; Mi et al., 2003 |
| 20 | *Euphorbia peplus L.* | Ingenol 3-oangelate | Causes necrosis of tumor by the activation of PKC | Hampson et al., 2005 |
| 21 | *Excavatia coccinea*, | Ellipticine | DNA intercalation and inhibition of topoisomerase II | Kao et al., 2006 |
| 22 | *Gloriosa superba L.* | Colchicine | Anti-mitotic | Dubey et al., 2008 |
| 23 | *Glycine max* | Diadzein and Genistein | Inhibits 3A 4-mediated metabolism and oxidative metabolism | Dixon and Ferreira et al/., 2002 |
| 24 | *Hydrastis Canadensis L.*, | Berberine | Not known | Wang et al., 2011 |
| 25 | *Iridaceaelatea pallasii* | Irisquinone | Act as a chemosensitizer | Hazra et al., 2004 |
| 26 | *Iris kumaoensis* | Irisquinone | Act as a chemosensitizer | Hazra et al., 2004 |
| 27 | *Ipomoeca batatas* | 4-Ipomenol | Cytochrome P-450-mediated conversion into DNA-binding metabolites | Ancuceanu and Istudor, 2004 |
| 28 | *Lupinus species* | Diadzein and Genistein | Inhibits 3A 4- mediated metabolism and oxidative Metabolism | Kaufman et al., 1997; Dixon and Ferreira et al., 2002 Moon et al., 2006; |
| 29 | *Many species like mints, cherries, lavenders and many others* | Perillyl alcohol | Exact mechanism is yet to be identified | Bardona et al., 2002, Yeruva et al., 2007, Pan et al., 2010. |
| 30 | *Ochrosia borbonica* | Ellipticine | DNA Intercalation and inhibition of topoisomerase II | Kao et al., 2006 |
| 31 | *Ochrosia elliptica* | Ellipticine | DNA Intercalation and inhibition of topoisomerase II | Kao et al., 2006 |
| 32 | *Podophyllum emodi* | Etoposide, Teniposide | Mitotic block | Shoeb, 2006 |
| 33 | *Podophyllum peltatum* | Etoposide, Teniposide | Mitotic block | Shoeb, 2006 |
| 34 | *Psoralea corylifolia* | Diadzein and Genistein | Inhibits 3A 4- mediated metabolism and oxidative | Kaufman et al., 1997; |

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|---|---|---|---|---|
| | | | Metabolism | Dixon and Ferreira et al., 2002<br>Moon et al., 2006; |
| 35 | *Rhizome of rhubarb* | Emodin | Apoptosis of cancer cells by several pathways | Huang et al., 2009 |
| 36 | *Salvia prionitis Hance* | Salvicine | Inhibition of topoisomerase II | Deng et al., 2011 |
| 37 | *Saponins of ginseng* | Pandimex TM | Cell cycle arrest and act as P-glycoprotein blocker | Pan et al., 2010 |
| 38 | *Taxus baccata* | Taxotere | Anti-mitotic | Hai et al., 2007 |
| 39 | *Taxus baccata* | Taxol | Anti-mitotic | Kingston, 2007 |
| 40 | *Taxus brevifolia Nutt,* | Taxotere | Anti-mitotic | Hai et al., 2007 |
| 41 | *Taxus brevifolia Nutt,* | Taxol | Anti-mitotic | Kinston, 2007 |
| 42 | *Tabebuia avellanedae* | Beta-lapachone | Inhibition of topoisomerase I and II | Lie et al., 2000<br>De Almeida, 2009 |
| 43 | *Tripterygium wilfordii Hook.F* | PG 490-88 | Enhances the anti-tumor effects of cytotoxic and chemotherapeutic agents, therby induces apoptosis. | Liu, 2011 |
| 44 | *Vicia faba* | Diadzein, Genistein | Inhibits 3A 4- mediated metabolism and oxidative Metabolism | Kaufman et al., 1997;<br>Dixon and Ferreira et al., 2002<br>Moon et al., 2006; |
| 45 | *Wikstroemia indica* | Daphnoretin | a) suppression of protein and DNA synthesis<br>b) suppresses Hepatitis B surface antigen expression | Diogo et al., 2009<br>Lu et al. 2011; |

**Table 2. Some of the Marine Biomedical derivatives and Anti-Cancer agents isolated from Marine sources**

| S.No | Marine organisms | Biomedical Compounds | Biological activity | References |
|---|---|---|---|---|
| **Marine bacteria** | | | | |
| 1. | *Elysia rubefescens* (Hawaii) | Kahalalide F (KF) depsipeptide | Induce the cytotoxicity | P.R.Jensen et al, 1996. |
| 2 | *Noctiluca scintillans* | Macrolactin-A | It inhibits B16-F10 murine melanoma cancer cells | B.K.Carte, 1996. |
| **Marine cyanobacteria** | | | | |
| 3 | *Gambierdiscus toxicus* | Novel antibiotic agents | Anti-fungal agents | Nagai.H et al, 1992. |
| 4 | *Goniodoma psedogoniaulax* | Goniodomin-A | Anti-fungal activity | Murakami et al, 1988. |
| 5 | *Lyngbya boulloni* | Apratoxin-A | Cytotoxicity to adenocarcinoma | H.Luesch, 2001. |
| 6 | *Lyngbya majusculata* | Immunosuppressive linear peptide Microcolin-A | Suppress the two way murine mixed lymphocytic reaction | Abe,M et al, 2002. |
| 7 | *Lyngbya majusculata* | Thiozoline-containing compound, Curacin-A | Anti-proliferative agent | Gerwick et al, 1994. |
| 8 | *Prorocentrum spp* | Okadaic acid (a polyether fatty acid) | It is signal transduction pathways in eukaryotic cells and it is a selective protein phosphatase inhibitor. | Cohen.P, 1990. |
| 9 | *Ptychodiscus brevis* | Brevitoxins | Depolarize the excitable membranes and their | Carte, B.K, 1996 & Shimizu.Y, 1993. |

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|---|---|---|---|---|
| | | | binding sites | |
| 10 | *Stigonema spp* | Scytonemin | Anti-inflammatory & Anti-proliferative properties. | A.K.Rshak et al, 2002. |
| **Marine Actinomycetes** | | | | |
| | *Microcystis aeruginosa* | Micro viridian Toxin BE-4, Siatoxin | Anti cancer and antibiotic | A.R.Arment and W.W. Carmichael, 1996. L.Shi, W.W.Carmichael and P.J.Kennelly, 1999. |
| 11 | *Micromonosperma marina* (Mozambique Strait) | Thiocoraline (Novel bioactive depsipeptide) | It inhibits RNA synthesis. It also selectively cytotoxic against lungand colon cancer cell-lines as well as melanoma. | S.Ronzoni et al, 1999. |
| 12 | *Streptomyces peucetius* | Daunorubicin | Anticancer activities on acute myeloid leukemia and acute lymphocytic leukemia | G.Minotti et al, 2004. |
| 13 | *Streptomycetes sp* (Gulf of Mexico) | Gutingimycin | Anti-cancer agents | R.P.Maskeyet al, 2002 |
| **Marine fungi** | | | | |
| 14 | *Leptosphaeria oraemaris* | Leptosphaerin | Production of secondary metabolites | G.A. Schiehser et al, 1986 A.J.Pallenberg & J.D. White,1986. |
| **Marine Bryozoans** | | | | |
| 15 | *Amathia convoluta* | Convolutamide-A | It exhibits *in vitro* cytotoxicity against L1210 murine leukemia cells and KB human epidermoid carcinoma cells. | H.Zhang et al, 1994 |
| 16 | *Amathia convolutea* (East Coast of Tasmania) | Tribrominated alkaloids i.e. Convolvutamine-H Convolvutindole-A | It against a parasitic nematode of rumnants. | Narkowicz,C.K. et al, 2002. |
| 17 | *Begula neritina* | Bryostatin | Anticancer activity. It against the human leukemia, renal cancer, melanoma non-smallcell, lung cancer cell-lines. | Lilies.G, 002 |
| 18 | *Cribricellina cribreria* | B-Carboline alkaloid | Exhibited cytotoxic, anti bacterial, antifungal & anti viral activites. | M.R. Princep et al, 1991. |
| 19 | *Flustra foliacea* | Indole alkaloides | Antimicrobial activity | P.B.Holst et al, 1994. |
| 20 | *Flustra foliacea* (Southern North Sea) | Deformyl flustra bromine | It against the HCT-116 cell-line. | Lysek.N et al, 2002 |
| 21 | *Watersipora subtorquata* (Tsutsumi Island, Japan) | Bryoanthrathiophene | Anti-angiogenic activity on bovine aorta endothelial cell (BAEC) proliferation. | Jeong S.J. et al, 2002. |
| **Marine sponges** | | | | |
| 22 | *Axinyssa* (Okinawan sponge) | Peroxy steroid | Inhibit the growth of several human cancer cell-lines. | Iwashima. M et al, 2002 |

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| 23 | *Batzella* sp (Carribean sponge) | Batzelladine A & B, Novel polycyclic guanidine alkaloides | It exhibt potent inhibition to the binding of HIV glycoprotein | Carte,B.K, 1996. |
| 24 | *Caminus sphaeroconia* (Domnican specimen) | Caminoside-A | Inhibitor of the bacterial type-3 secretion system. | Lenington.R.G. et al, 2002 |
| 25 | *Cribrochalina* sp (Indian Ocean Sponge) | Isoquinoline quinine, metabolite cribostatin | Aganst all human melanoma cells. | Pettit.G.R. et al, 1992. |
| 26 | *Cryptotethia crypta* (Caribbean sponge) | Spongouridine | A potent tumor-inhibiting arabinosyl nucleoside | C.Ireland et al, 1993. |
| 27 | *Dercitus spp* (Deep-water sponge) | Aminoacridine alkaloid, derctin | Cytotoxic activity | Burres.N.S et al, 1989. |
| 28 | *Discodermia calyx* | Calyculin | Phosphate inhibitors | De Silva et al, 1992 & Kato.Y et al, 1986 |
| 29 | *Haliclona* (Indonesian sp) | Lembehynes B &C | Neuritogenic activity against neuroblastama cells. | Aoki.K et al, 2002. |
| 30 | *Halichondria okadai* | Okadaic acid | Phosphate inhibitors | De Silva et al, 1992 & Kato.Y et al, 1986 |
| 31 | *Hyrtios erecta* (Egyptian Red Sea) | Salmahyrtisol A and B, Sesterstatins | Cytotoxicity in human cancer cell-lines. | Yousaf.M, et al, 2002. |
| 32 | *Mycale sp* (New Zealand sp) | Mycalamide –A | Invitro cytotoxicity & in vivo antitumor activity in many leukemia and solid tumor model systems. | Perry N.G, Blunt.J.W. & Munro.H.H.G. 1988. |
| 33 | *Polymastia tenax* | Oxygenated sterols | Significant cytotoxicity to a range of human and murine cancer cell-lines. | Santafe.G et al, 2002 |
| 34 | *Spongia sp* (Indian Ocean Sponge) | Spongstatin | Highly chemoresistant tumor | Pettit.G.R. et al,1993. |
| 35 | *Theonella* sp (Japanese sponge) | Halichondrin-B | A potential anticancer agent | Fuestani.N, Sugawara.T & Matsunago, 1992. |
| 36 | Theonella sp (Okinawa) | Onnamide-A | Invitro cytotoxicity & in vivo antitumor activity in many leukemia and solid tumor model systems. | Burres.N.S. & Clement. J.J, 1989. |
| 37 | *Theonella swinhoei* | Metuporin | Phosphate inhibitors | De Silva et al, 1992 & Kato.Y et al, 1986 |
| 38 | *Xestosporangia berguista* | Xestoberg sterol | It inhibits immunoglobulin E-mediated histamine | Shoji et al, 1992 |
| **Seaweeds** | | | | |
| 39 | *Acanthophora spicifera* | Crude | Anti-oxidants and inhibiting cancer cell proliferation | H.R.Vasanthi, 2002. H.R. Vasanthi, G.V. Rajamanickam & A.Saraswathy, 2004 |
| 40 | *Acanthophora spicifera* | Crude | Tumoricidal activity on Ehrlich's ascites carcinoma cells developed in mice | H.R.Vasanthi, 2002. H.R. Vasanthi, G.V. Rajamanickam & A.Saraswathy, 2004 |
| 41 | *Ascophyllum nodosum* | Fucoidan | Anti-proliferative, antitumor, anti cancer, | P. Vischer and E.Buddecke, 1991. |

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| | | | anti metastatic and fibrinolytic | P.Religa et al, 2000. |
| 42 | *Caulerpa* sp | Caulerpenyne | Cytotoxicity, anticancer, antitumor and antiproliferative activity. | Formento et al, 1995. P.Amade et al, 1996. P.Huitorel et al, 2001. |
| 43 | *Chondria* sp | Condriamide –A | Cytotoxici activity. | J.A. Palermo, P.B. Flower & A.M. Seldes, 1992. |
| 44 | *Codium iyengarii* | Steroid, Iyengadione | Antibacterial activity | Ali,M.S. et al, 2002. |
| 45 | *Hypnea valitiae* | Iodinated novel nucleoside | Specific inhibitor of adenosine kinase | Ireland.C et al, 1993 |
| 46 | *Portieria hornemannii* | Halomon | Pre clinical drug development | Carte,B.K, 1996. |
| 47 | *Sargassum carpophyllum* | Bioactive sterols | Induced morphologically abnormality in plant pathogenic fungus Pyricularia oryzae and against several cultured cancer cell lines. | Tang, H.F et al, 2002 |
| 48 | *Sargassum thunbergii* | Crude | Anti-tumor activity, inhibition of tumour metastasis in rat mammary adeno carcinoma cell (13762 MAT) | C. Zhuang et al, 1995. D.R. Coombe et al, 1987. |
| 49 | *Sphaerococus coronofolius* | Anti infective agent | Antibacterial activity | Mc Carthy.P.J & Pomponi.S.A. 2004. |
| 50 | *Stypodium zonale* | Cytotoxic metabolite, stypoldione | Inhibits microtubule polymerization, prevents mitotoxic spindle formation | Gerwick, W.H & Fenical.W, 1981. Jacobs.R.S et al, 1985. |
| 51 | *Ulva fasciata* | Novel sphingosine derivative | In vivo antiviral activity | Garg H.S. et al, 1992 |
| **Mangroves and other salt tolerant plants** | | | | |
| 52 | *Acanthus ilicifolius* | Ribose derivatives of benzoxazoline | Anticancer | A.S. Kabil, S.Sharma and Wahidulla, 1994. P.K.Minocha and K.P.Tiwari, 1981. |
| 53 | *Calophyllum inophyllum* | Xanthone, biflavonoids, benzophenones, neoflavanoids and coumarin derivatives | Anticancer, antitumor and lipid peroxidation | S.H. Goh and I.Jantan, 1991. M.Linuma et al, 1994. |
| 54 | *Ceriops decandra* | Lignins | Anti oxidant | M.Toguchi et al, 1998. |
| 55 | *Ceriops decandra* | Mangrove tea | Anticancer | N.S.Boopathy et al. |
| 56 | *Excoecaria agallocha* | Diterpenes exhibited remarkable antitumor promoting activity in vivo on two stage carcinogenesis test of tumor | Antitumor activity of methanol extract based on three assays: 1.DPPH radical scavenging 2.linoleic acid oxidation assay 3. Oxidative cell death assay. | Oyama et al, 1999. |

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