ISSN:2347-4742

Review Article

Journal of Pharmaceutical and Biomedical Analysis Letters

www.pharmaresearchlibrary.com/jpbmal

A Brief Description on Cancer and Natural Remedies with Potential Anti-cancer Activity: A Review

Amita Pandey* and ShaliniTripathi

Rameshwaram Institute of Technology and Management, Sitapur Road, Lucknow (U.P.), India

Abstract

At present times, Herbal remedies occupy an important position for being the paramount sources of drug discovery, irrespective of its categorized groups in which including herbs, Shrubs or trees. Plants have been indispensable in treating diverse form of diseases including cancer. Cancer is not just one disease but many diseases. There are more than 100 different types of cancer the plant based drug discovery resulted mainly in the development of anticancer agents including plants (vincristine, vinblastine, etoposide, paclitaxel, camptothecin, topotecan and irinotecan), marine organisms (citarabine, aplidine and dolastatin 10) and micro-organisms (dactinomycin, bleomycin and doxorubicin).

Key words: Cancer, Herbal remedies, Dietary remedies, Marine remedies, Micro-organism as a source of anti-cancer drugs.

Contents

Corresponding author
Amita Pandey
E-mail: pandey.amita2012@gmail.com
MS.ID: PRL2014-JPBMAL1955

PAPER-QR CODE

1. Introduction

Cancer is a dreadful disease characterized by the irregular proliferation of the cells. As a cell progresses from normal to cancerous, the biological imperative to survive and perpetuate drives fundamental changes in cells behaviour. So the actual cause of the disease in different sections is still to be explored clearly .Cancer is thus, a class of disease, classified by the type of cell that is initially affected. Today's global scenario indicates that breast cancer and colorectal cancer is the most prominent cancer in case of women and men. To combat cancer United States national cancer institute has undergone 2069 anticancer clinical trials, in which over 150 drug combination have been successfully recorded against cancer. There is no one definition that describes all cancers. They are a large family of diseases which form a subset of neoplasms, which show some features that suggest of malignancy. A neoplasm or tumour is a group of cells that have undergone unregulated growth, and will often form a mass or lump, but may be distributed diffusely. [3, 4]

Causesof cancer

Cancers are primarily an environmental disease with 90–95% of cases attributed to environmental factors and 5-10% due to genetics. *Environmental*, as used by cancer researchers, means any cause that is not inherited genetically, not merely pollution.Common environmental factors that contribute to cancer death include

tobacco(25–30%), diet and obesity (30–35%), infections (15–20%), radiation (both ionizing and non-ionizing, up to 10%), stress, lack of physical activity, and environmental pollutants.

It is nearly impossible to prove what caused a cancer in any individual, because most cancers have multiple possible causes. For example, if a person who uses tobacco heavily develops lung cancer, then it was probably caused by the tobacco use, but since everyone has a small chance of developing lung cancer as a result of air pollution or radiation, then there is a small chance that the cancer developed because of air pollution or radiation. [10'11]

Sign and Symptoms of cancer

Fever :Fever is very common with cancer, but it more often happens after cancer has spread from where it started, fast breathing, and abnormal lung sounds heard through a stethoscope,

Weight loss: Unexplained weight loss,this happens most often with cancers of the pancreas, stomach, oesophagus (swallowing tube), or lung.

Fatigue: Fatigue may happen early, though, in some cancers, like leukemia. Some colon or stomach cancers can cause blood loss that's not obvious. This is another way cancer can cause fatigue.

Pain: Pain may be an early symptom with some cancers like bone cancers or testicular cancer.Back pain can be a symptom of cancer of the colon, rectum, or ovary. Most often, pain due to cancer means it has already spread (metastasized) from where it started.

Skin changes: Along with cancers of the skin, some other cancers can cause skin changes that can be seen. These signs and symptoms include:

Darker looking skin (hyperpigmentation)

Yellowish skin and eyes (jaundice)

Reddened skin (erythema)

Itching (pruritis)

Excessive hair growth

Long-term constipation: Diarrhoea, or a change in the size of the stool may be a sign of colon cancer. Pain when passing urine, blood in the urine, or a change in bladder function (such as needing to pass urine more or less often than usual) could be related to bladder or prostate cancer.Skin cancers may bleed and look like sores that don't heal.

Sore: A long-lasting sore in the mouth could be an oral cancer. This should be dealt with right away, especially in people who smoke, chew tobacco, or often drink alcohol. Sores on the penis or vagina may either be signs of infection or an early cancer, and should be seen by a health professional.

White patches/white spot: White patches inside the mouth and white spots on the tongue may be leukoplakia. Leukoplakia is a pre-cancerous area that's caused by frequent irritation. It's often caused by smoking or other tobacco use. People who smoke pipes or use oral or spit tobacco are at high risk for leukoplakia. If it's not treated, leukoplakia can become mouth cancer. Any long-lasting mouth changes should be checked by a doctor or dentist right away.

Coughing and unusual bleeding: Unusual bleeding can happen in early or advanced cancer. Coughing up blood in the sputum (phlegm) may be a sign of lung cancer. Blood in the stool (which can look like very dark or black stool) could be a sign of colon or rectal cancer. Cancer of the cervix or the endometrium (lining of the uterus) can cause abnormal vaginal bleeding. Blood in the urine may be a sign of bladder or kidney cancer. A bloody discharge from the nipple may be a sign of breast cancer.

Lumps and nodes: A lump or thickening in breast, lymph nodes and testis may be an early or late sign of cancer, especially if it has grown in size. Some breast cancers show up as red or thickened skin rather than the expected lump.

Indigestion or swallowing:

Indigestion or swallowing problems that don't go away may be signs of cancer of the oesophagus (the swallowing tube that goes to the stomach), stomach, or pharynx (throat). But like most symptoms on this list, they are most often caused by something other than cancer.A cough that does not go away may be a sign of lung cancer. Hoarseness can be a sign of cancer of the voice box (larynx) or thyroid gland. [2]

Types of cancer

Cancer is not just one disease but many diseases. There are more than 100 different types of cancer. Most cancers are named for the organ or type of cell in which they start - for example, cancer that begins in the colon is called colon cancer; cancer that begins in melanocytesof the skin is called melanoma.

Cancer types can be grouped into broader categories. The main categories of cancer include:

Carcinoma - cancer that begins in the skin or in tissues that line or cover internal organs. There are a number of subtypes of carcinoma, including adenocarcinoma, basal cell carcinoma,

Sarcoma - cancer that besquamous cell carcinoma, and transitional cellcarcinoma.gins in bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.

Leukemia - cancer that starts in blood-forming tissue such as the bone marrow and causes large numbers of abnormal blood cells to be produced and enter the blood.

Lymphoma and myeloma - cancers that begin in the cells of the immune system.

Central nervous system cancers - cancers that begin in the tissues of the brain and spinal cord.

Germ cell tumor: Cancers derived from pluripotent cells, most often presenting in the testicle or the ovary (seminoma and dysgerminoma, respectively).

Blastoma: Cancers derived from immature "precursor" cells or embryonic tissue. Blastomas are more common in children than in older adults.[9]

Stages of cancer

Overall Stage Grouping is also referred to as Roman Numeral Staging. This system uses numerals I, II, III, and IV (plus the 0) to describe the progression of cancer.

Stage 0: carcinoma in situ.

Stage I: cancers are localized to one part of the body. Stage I cancer can be surgically removed if small enough.

Stage II: cancers are locally advanced. Stage II cancer can be treated by chemo, radiation, or surgery.

Stage III: cancers are also locally advanced. Whether a cancer is designated as Stage II or Stage III can depend on the specific type of cancer; for example, in Hodgkin's disease, Stage II indicates affected lymph nodes on only one side of the diaphragm, whereas Stage III indicates affected lymph nodes above and below the diaphragm. The specific criteria for Stages II and III therefore differ according to diagnosis. Stage III can be treated by chemo, radiation, or surgery

Stage IV: cancers have often metastasized, or spread to other organs or throughout the body. Stage IV cancer can be treated by chemo, radiation, or surgery.[5,6]

Herbal Remedies with Potential Anti-Cancer Activity

The history of plant as source of anti-cancer agents started in earnest in the 1950s with the discovery and development of the vinca alkaloids (vinblastine and vincristine) and the isolation of the cytotoxic podophyllotoxins. Vinca alkaloid was responsible for an increase in the cure rates for Hodgkin's disease and some forms of leukemia[12]. Vincristine inhibits microtubule assembly, inducing tubulin self-association into coiled spiral aggregates [13].Etoposide is anepipodophyllotoxin, derived from the mandrake plant Podophyllumpeltatumandthe wild chervil Podophyllumemodi[14]. It has also significant activity against small-cell lung carcinoma [15].Etoposide is a topoisomerase II inhibitor, stabilizing enzyme–DNA cleavable complexes leading to DNA breaks [16]. The taxanes paclitaxel and docetaxel has been show antitumor activity against breast, ovarian and other tumor types in the clinic trial. Paclitaxel stabilizes microtubules and leading to mitotic arrest [17]. In addition, the camptothecin derivatives irinotecan and topotecan, have shown significant antitumor activity against colorectal and ovarian cancer respectively [18, 19]. These compounds were initially obtained from the bark and wood of NyssaceaCamptothecaaccuminata and act by inhibiting topoisomerase I [20]. The taxanes and the camptothecins are presently approved for human use in various countriesRohitukine the plant alkaloid , isolated from the leaves and stems of Dysoxylumbinectariferum (Maliaceae) [21, 22]. Synthetic flavone derived from rohitukine, Flavopiridol representing the first cyclin-dependent kinase inhibitor to enter the clinical trial [23]. The mechanism of action involves interfering with the phosphorylation of cyclin-dependent kinases and arrest cell-cycle progression at growth phase G1 or G2 [24, 25].Homoharringtonine an alkaloid isolated from the Chinese tree Cephalotaxusharringtonia (Cephalotaxacea) [26]. The mechanism of action is the inhibition of protein synthesis and blocking cell-cycle progression [27]. It has shown efficacy against various leukemias[28]. A lung-cancer-specific antineoplastic agent 4-Ipomeanol is isolated from the sweet potato Ipomoea batata (Convolvulaceae) [29]. The mechanism of action is converted into DNA-binding metabolites upon metabolic activation by cytochrome P450 enzymes that are present incells of the lung [30]. DNA topoisomerase I inhibitor β-lapachone, that induces cell-cycle delay at G1 or S (synthesis) phase before inducing either apoptotic or necrotic cell death in a variety of human carcinoma cells, including ovary, colon, lung, prostate and breast [31]Beside this there are so many plants which are used in cancer; following enlist the plant which prevent and target for future studies as potential anticancer agent (Table.1)

Table 1: Herbal remedies used as anti-cancer[32]

S.No	Plant Species	Family	Plant Part
1.	Salvia officinalis	Labiatae	Leaves
2.	Viscum album	Loranthaceae	Leaves
3.	Combretumcaffrum	Combretaceae	Bark
4.	Melaleucaalternifolia	Myrtaceae	Leaves
5.	Lavandulaangustifolia	Labiatae	Leaves
6.	Aglaia foveolata	Meliaceae	Fruit
7.	Maytenusserrata	Celastraceae	Seed
8.	Tabebuiaimpetiginosa	Bignoniaceae	Stem bark and trunk wood
9.	Tabebuiarosea	Bignoniaceae	Stem bark and trunk wood
10.	Tabebuiaserratifolia	Bignoniaceae	Stem bark and trunk wood
11.	Dipteryxodorata	Fabaceae	Seed
12.	Thapsiagarganica	Apiaceae	Fruit
13.	Indigoferatinctoria	Leguminosae	Aerial part
14.	Matricariachamomilla	Asteraceae	Flower
15.	Erythroxylumpervillei	Erythroxylaceae	Root

16.	Broussonetiapapyrifera	Urticaceae	Entire
17.	Cyclopiaintermedia	Fabaceae	Leaves
18.	Scutellariae radix, Scutellariaeindica	Labiatae	Root
19.	Physalisphiladelphica	Solanaceae	Seed
20.	Dysoxylumbinectariferum	Meliaceae	Stem bark
21.	Aristoteliachilensis	Elaeocarpaceae	Leaf and Stem
22.	Cyathostemmaargentium	Annonaceae	Root
23.	Epimediumhunanense	Berberidaceae	Aerial parts
24.	Croton urucurama	Euphorbiacaeae	Bark
25.	Epilobiumhirsutum	Onagraceae	Entire
26.	Pleionebulbocodioides	Orchidaceae	Tuber
27.	Cassia quinquangulata	Caesalpiniaceae	Root
28.	Begonia glabra	Begoniaceae	Entire
29.	Celastrusorbiculatus	Celastraceae	Entire
30.	Croton draco	Euphorbiacaeae	Aerial parts
31.	Smilax sieboldii	Liliaceae	Entire
32.	Ximenia Americana	Olacaceae	Root
33.	Maytenusemarginata	Celastraceae	Entire
34.	Sarcandraglabra	Choranthaceae	Entire
35.	Salvia plebeian	Labiatae	Aerial
36.	Scutellariabarbata	Labiatae	Entire
37.	Ocoteacaparrapi	Lauraceae	Essential oil
38.	Caraganacuneata	Leguminosae	Leaf
39.	Croton flavens	Euphorbiacaeae	Leaf
40.	Euphorbia heterophylla	Euphorbiacaeae	Stem
41.	Echitesvucatanensis	Apocynaceae	Latex
42.	Thevetiaahouia	Apocynaceae	Leaf and Stem
43	Thevetiagaumeri	Apocynaceae	Leaf and Stem
44.	Thevetiaperuciana	Apocynaceae	Leaf and Stem
45.	Euphorbia ebracteolata	Euphorbiacaeae	Aerial parts
46.	Dioscoreacollettii	Dioscoreaceae	Rhizome
47.	Juglansmandshurica	Juglandaceae	Root
48.	Maackiatenuifolia	Leguminosae	Root
49	Juncusacutus	Juncaceae	Leaf
50.	Hedyotischrysotricha	Rubiaceae	Entire
51.	Arisaemaerubescens	Araceae	Root
52.	Leptadenia hastate	Asclepiadaceae	Bark
53.	Viscumcalcaratum	Loranthaceae	Entire
54	Aphanamixispolystachya	Meliaceae	Stembark
55.	Pratianummularia	Campanulaceae	Entire
56.	Aeonium arboretum	Crassulaceae	Leaf
57.	Ocoteafoetens	Lauraceae	Branchlets
58.	Maytenuscanariensis	Celastraceae	Fruit juice
59.	Sedum alboroseum	Crassulaceae	Entire
60.	Euphorbia micractina	Euphorbiacaeae	Entire
61.	Euphorbia prolifera	Euphorbiacaeae	Latex
62.	Scirpusholoschoenus	Cyperaceae	Inflorescence
63.	Dilleniasuffruticosa	Dilleniaceae	Fruit
64	Hypoxisrooperii	Hypoxiaceae	Tuber
65.	Inulalinariaefolia	Compositae	Flowers
66.	Ziziphusmauritiana	Rhamnaceae	Stem bark and Fruit
67.	Adiantummacrophyllum	Pteridaceae	Entire
68.	Thalictrumfabri	Ranunculaceae	Root
69.	Scutellariaindica	Labiatae	Root
70.	Hypericumjaponicum	Guttiferae	Entire
71.	Cyatheafauriei	Cyatheaceae	Shoot

72.	Fissistigmaoldhamii	Annonaceae	Stem
73.	Monninaobtusifolia	Polygalaceae	Aerial parts
74.	Coriolusversicolor	Polyporaceae	Fruitbody
75.	Melastomamalabathricum	Melatomataceae	Flower
76.	Carapaguianensis	Meliaceae	Seed oil
77.	Swieteniahumilis	Meliaceae	Seed
78.	Ficuspretoiae	Moraceae	Sap
79.	Croton lechleri	Euphorbiacaeae	Latex
80.	Aster amellus	Compositae	Entire
81.	Crassocephalumbojeri	Compositae	Entire
82.	Echinopsgrijisii	Compositae	Root
83.	Adeniumobesum	Apocynaceae	Leaf
84.	Ipomeabatata	Convolvulaceae	Rhizome
85.	Uncariatomentosa	Rubiaceae	Bark
86.	Plantagoasiatica	Plantaginaceae	Leaf
87.	Phymatosorusdiversifolium	Polydiaceae	Root
88.	Rabdosiarubescens	Labiatae	Leaf
89.	Salvia chinensis	Labiatae	Entire
90.	Ganodermalucidum	Ganodermataceae	Fruitbody
91.	Euphorbia kansui	Euphorbiacaeae	Root
92.	Echinopslatifolius	Compositae	Root
93.	Euphorbia marginata	Euphorbiacaeae	Entire
94.	Ligustrumlucidum	Oleaceae	Seed
95.	Phytolaccaesculenta	Phytolaccaceae	Root
96.	Pinusparviflora	Pinaceae	Strobilus
97.	Dysosmapleiantha	Berberidaceae	Root
98.	Alnus japonica	Betulaceae	Wood
99.	Ruellia tuberose	Acanthaceae	Bark
100.	Acacia xanthophloea	Leguminosae	Fruit
101.	Lanneastuhlmannii	Anacardiaceae	Root
102.	Maytenusobscura	Celastraceae	Leaf
103.	Plicosepalussagittifolius	Loranthaceae	Branches
104.	Piper latifolium	Piperaceae	Leaf
105.	Morindacitrifolia	Rubiaceae	Root
106.	Knematenuinervia	Myristicaceae	Stembark
107.	Deeringiaamaranthoides	Amaranthaceae	Fruit
108.	Cynanchumhancoekianum	Asclepiadaceae	Entire
109.	Azadirachtaindica	Meliaceae	Leaf
110.	Virolabicuhyba	Myristicaceae	Seed
111.	Sempervivumarmenum	Crassulaceae	Leaf
112.	Sempervivumarvense	Crassulaceae	Leaf
113.	Hippophaesalicifolia	Elaeagnaceae	Fruit
114.	Hypoxisnyasica	Hypoxiaceae	Rhizome
115.	Astragalusmembranaceus	Leguminosae	Root
116.	Maytenusmacrocarpa	Celastraceae	Stembark
117.	Cephalotaxus Harrington	Cephlotaxaceae	Entire

Natural Dietary Remedies of Anti Cancer Agents

Natural dietary agents including fruits, vegetables, and spices have drawn a great deal of attention from both the scientific community and the general public owing to their demonstrated ability to suppress cancers. Recentstudies suggest that the consumption of food rich in fruits, vegetables and spices have a lower incidence of cancers (stomach, esophagus, lung, oral cavity and pharynx, endometrium, pancreas and colon).Dietary agents consist of a wide variety of biologically active components that are responsible for the anti-cancer effects like curcumin, genistein, resveratrol, diallylsulfide, S-allyl cysteine, allicin, lycopene, capsaicin, diosgenin, gingerol, ellagic acid, ursolic acid, silymarin, anethol, catechins, eugenol, isoeugenol, dithiolthiones, isothiocyanates, indole-3-carbinol, isoflavones, saponins, phytosterols, inositol hexaphosphate, Vitamin C, D-limonene, lutein, folic acid, beta carotene,selenium, Vitamin E and flavonoids. Many of which have been used

in traditional medicines for thousands of years. These dietary agents are believed to suppress the inflammatory processes that lead to transformation, hyperproliferation, and initiation of carcinogenesis. Their inhibitory influences may ultimately suppress the final steps of carcinogenesis i.e angiogenesis and metastasis (Table 2).

Table 2: Dietary sources as anticancer agent[32]

S. No.	Botanical Name	Family	Source	Compound
1	Carica papaya,	Caricaceae	Berries	β-Cryptoxanthin
2	Glycyrrhizaglabra; Glycyrrhiza radix; Glycyrrhizauralensis,	Leguminosae	Licorice root	Glycyrrhizin
3	Cannabis sativa	Cannabiaceae	Hemp	Cannabinol
4	Rosmarinusofficinalis	Lamiaceae	Rosemary	Carnosol
5	Puerarialobata radix	Fabaceae		Genistein
6	Glycine max	Fabaceae	Soybeans	Genistein
7	Prunusarmeniaca	Rosaceae	Apricots	Carotenoids
8	Zingiberofficinale	Zingiberaceae	Tuber	Gingerol
9	Lycopersiconesculentum	Solanaceae	Tomato	Lycopene, Lutein, Kaempferol
10	Piper nigrum; Piper longum	Piperaceae	Black pepper	Purpurogallin; Piperine
11	Ocimum sanctum	Lamiaceae	Basil	Ursolic acid
12	Betula alba	Betulaceae	Birch tree	Betulinic acid
13	Crocus sativus	Iridaceae	Saffron	Carotenoids
14	Silymarinmarianum	Asteraceae	Milk thistle	Silymarin
15	Capsaicum annum; Capsaicumfrutens	Solanaceae	Red chilli	Capsaicinoids, Capsaicin
16	Camellia sinensis	Theaceae	Green and black teas	Catechin and theaflavins
17	Vitisvinifera	Vitaceae	Grapes	Resveratrol
18	Daucuscarotasativus	Apiaceae/umbel liferae	Carrot	β-Carotene
19	Tabebuiaavellanedae	Bignoniaceae	Lapacha tree	Lapachone
20	Citrus aurantium	Rutaceae	Orange	Hesperidin
21	Prunusdulcis	Rosaceae	Almond	Morin
22	Aloe arborescens	Asphodelaceae	Aloe vera	Emodin
23	Opium poppy	Paparveraceae	Poppy	Morphine and its analogues
24	Curcurbitamoschata	Cucurbitaceae	Pumpkin	β-Carotene
25	Azadirachataindica	Meliaceae	Neem	Polyphenolics

Marine Remedies as Source of Anti-Cancer Agents

Marine organisms are a rich source for natural products [40]. In recent time, advancement in deep-sea collection and aqua culture technology gives significant number of compounds derived from marine organisms entering preclinical and early clinical evaluation as potential anticancer agent [41, 42]. Overall, more than 3000 new substances have been identified from marine organisms that demonstrate the great potential as a source of novel chemical classes [43]. Marine belongs to very diverse structural classes including polyketides, terpenes, steroids and peptides. The organisms yielding these bioactive marine compounds include invertebrate animals, algae, fungi and bacteria [44].

The first anticancer product didemnin B, a cyclic depsipeptide isolated from the tunicate Tridemnumsolidum from marine source enter in clinical trials. Preliminary results showed a partial activity against non-Hodgkin's lymphoma [45]. It can inhibit protein synthesis and arrest G1 phase of cell-cycle. Another depsipeptideAplidine appear to be more active as comparison with didemninB in preclinical trial and does not produce life-threatening neuromuscular toxicity. Preclinical data indicate that aplidine is active against several tumors through blockade of cell-cycle progression at G1 phase [46]. There are number of ecteinascidins have been isolated from the marine source tunicate Ecteinascidiaturbinata. One of these ecteinascidins (ET-743) was selected for clinical trials and antitumor effects have been observed in phase I studies [47]. ET-743 is a tetrahydroisoquinilone alkaloid and they acts by selective alkylation of guanine residues in the DNA minor groove [48] and also interacts with nuclear

proteins [49]. In Europe and the United States ET-743 is currently in phase II clinical trials [47]. The dolastatins are a class of peptides obtained from the Indian Ocean, Dolabellaauricularia. These peptides have cytotoxic activity and now a day, dolastatin10 and dolastatin15 of this class have received the greatest clinical interest. Dolastatin10 has entered in Phase I and Phase II clinical trials, after showing significant antitumor activity in preclinical models [50]. Its mechanism of action involves inhibition of microtubule assembly ultimately result in cell-cycle arrest in metaphase [51, 52]. The bryostatins, 20 macrocyclic lactones isolated from Bugulaneritina and other marine bryozoa. These macrocyclic compounds have shown significant activity against lymphocytic leukemia cell line [53]. Bryostatin1 has recently entered phase II clinical trials for the treatment of melanoma, non-Hodgkin's lymphoma, renal cancer and colorectal cancer [54-56] and continues to be evaluated in phase I clinical trials. Bryostatin1 has been found to promote the normal growth of bone marrow progenitor cells, to provide in vivo protection against normally lethal doses of ionizing radiation and to serve as an immune stimulant, enhancing the normal production of interleukin2 and interferons[57].

Beside this there are the number of compounds isolated from marine as potential anti-cancer agents included in Table 3[59, 58]

Table 3: Marine derived potential anticancer agent. [32]

S.No.	Compound	Organism	Chemistry	Mechanism of action
1.	Aaptamine	Sponge	Alkaloid	Induction of p21 and G2/M cell cycle arrest
2.	Cortistatin A	Sponge	Alkaloid	Selective inhibiton of angiogensis
3.	Aplidine	Ascidian	Depsipeptide	Oxidation and inactivation of low molecular weight-protein tyrosine phosphatase activity
4.	Bastadine 6	Sponge	Alkaloid	Inhibition of angiogenesis in vitro and in vivo involves apoptosis
5.	Fucoxanthinol	Ascidian	Carotenoid	Induction of apoptosis
6.	Lamellarin D	Mollusk	Alkaloid	ErbB3 protein and PI3K- Akt pathway involved in necrosis induction
7.	Clavulone II	Soft coral	Prostanoid	G1 cell cycle arrest and apoptosis
8.	Geodiamolides	Sponge	Peptide	Disorganization of actin filaments
9.	Ircinin-1	Sponge	Sesterterpene	G1 phase inhibition and apoptosis induction
10.	Laxaphycins A and B	Bacterium	Cyclic peptides	Increased polyploidy by putative topoisomerase II alterations
11.	Leptosins C and F	Fungus	Alkaloid	DNA topoisomerase I and II inhibition and apoptosis induction
12.	Onnamide A	Sponge	Polyketide	Protein synthesis inhibition
13.	Philinopside A	Sea cucumber	Saponin	Inhibition of angiogenesis and receptor tyrosine kinases
14.	Variolin B	Sponge	Alkaloid	Inhibition of cyclin-dependent kinases and apoptosis induction
15.	Aplidine	Ascidian	Depsipeptide	Induction of apoptosis with concomitant G1 arrest and G2 blockage
16.	Ascididemin	Ascidian	Alkaloid	Direct iminoquinone reduction and reactive oxygen species generation
17.	Cammbrescidin 800	Sponge	Alkaloid	Induction of eythroid differentiation and cell cycle arrest
18.	Dideoxypetrosynol A	Sponge	Fatty acid	Induction of apoptosis via mitochondrial signaling pathway
19.	Dolastatin 10	Mollusc	Peptide	Binds to amino-terminal peptide of β-tubulin containing cysteine
20.	Girolline	Sponge	Alkaloid	Induction of G2/M cell cycle arrest and p53 proteasome recruitment
21.	Halichondrin B analogues	Sponge	Macrolide derivative	Induction of mitotic blockage and apoptosis
22.	Lissoclinolide	Ascidian	Fatty acid	G2/M cell cycle arrest
23.	Neoamphimedine	Sponge	Alkaloid	Induction of topoisomerase II α-mediated catenation of DNA
24.	Psammaplin A	Sponge	Alkaloid	Inhibition of aminopeptidase N and

				suppression of angiogenesis in vitro
25.	Alkylpyridiniu m	Sponge	Alkaloid	Induction of apoptosis and reduced cell adhesion
26.	Aeroplysinin	Sponge	Alkaloid	Induction of apoptosis on proliferating endothelial cells
27.	Bryostatin-1	Bryozoan	Macrolide	Potentiation of ara-C induced apoptosis by PKC-dependent release of TNF-α
28.	Cephaiostatin	Worm	Steroid	Apoptosis and increased mitochondrial matrix density
29.	Chondropsin A	Sponge	Macrolide	In Vitro inhibition of V-ATPase enzyme
30.	Dehydrothrysife rol	Alga	Triterpene	Enhanced apoptosis induction in estrogen receptor negative breast cancer cells
31.	Diazonamide-A	Ascidian	Peptide	Disruption of mitosis and cellular microtubules with inhibition of GTP hydrolysis
32.	Dictyostatin	Sponge	Polyketide	Induction of tubulin polymerization
33.	Dolastatin 11	Mollusc	Peptide	F-actin stabilization by connection between two long-pitch strands
34.	Ecteinascidin-743	Ascidian	Isoquinoline alkaloid	Telomere dysfunction increases susceptibility to ET-743
35.	GA3 polysaccharide	Alga	Polysaccharide	Inhibition of topoisomerase I and II
36.	Hemiasterlin analogue	Sponge	Tripeptide	Induction of microtubule depolymerisation
37.	Kahalalide F	Mollusc	Depsipeptide	Potent cytotoxicity and induction of necrosis
38.	Lamellarin D	Mollusc	Alkaloid	Potent inhibition of topoisomerase I
39.	omega-3 fatty acids	Fish	Fatty acid	--

Microorganisms as Source of Anti-Cancer Agents

Antitumor antibiotics are among the most important cancer chemotherapeutic agents, and include members of the anthracycline, bleomycin, actinomycin, mitomycin and aureolic acid families [6]. Clinically useful agents from these above families are the daunomycin and related agents like doxorubicin, idarubicin and epirubicin; the peptolides (exemplified by dactinomycin), the mitosanes (such as mitomycin C) and the glycosylated anthracenonemithramycin. The anthracyclines are among the most used antitumor antibiotics in the clinic and exert antitumor activity mainly by inhibiting topoisomerase II [60,61].Wortmannin is a product of the fungus Talaromyceswortmanni and inhibits signal transduction pathways by forming a covalent complex with an active-site residue of phosphoinositide 3 kinase (PI3K), inhibiting PI3K activity [62]. Thus, toxins that originally evolved to kill competing micoorganisms can have a variety of physiological effects in animals. In many cases, the targets of these compounds are components of signal transduction cascades that are conserved in many species, and that have been considered novel targets for anticancer drug discovery (Table 4) [63]

Table 4: Microorganism derived anti-cancer agents. [32]

S.No.	Compound	Microorganism	Used in Cancer
1.	Actinomycin	Streptomyces spp.	Sarcoma and germ-cell tumors
2.	Bleomycin	Streptomyces verticillus	Germ-cell, cervix and head and neck cancer
3.	Daunomycin	Streptomyces coeruleorubidus	Leukemia
4.	Doxorubicin	Streptomyces Pneuceticus	Lymphoma, breast, ovary, lung and sarcomas
5.	Epirubicin	Streptomyces pneuceticus	Breast cancer
6.	Idarubicin	Streptomyces Pneuceticus	Breast cancer and leukemia
7.	Mitomycin C	Streptomyces caespitosus	Gastric , colorectal, anal and lung

			cancer
8.	Geldanamycin	Streptomyces Hygroscopicus	Experimental
9.	Rapamicin	Streptomyces hygroscopicus	Experimental
10.	Wortamannin	Talaromyceswortmanni	Experimental

2.Conclusion

According to World Health Organisation, 80% of people living in the rural areas depend on medicinal plants as primary health care system. These practices are solely based on the knowledge of traditional use of herbal remedies, natural dietary remedies, marine remedies and micro-organism as a source of medicine. These products are formulated to generate different types of effective drugs to enhance anti-cancer activities.This review revealed that many of medicinal plants used by traditional healer are reported to have scientific evidence. All the natural products discussed in this review exhibit anticancer activities. Natural products offer a great opportunity to evaluate not only totally new chemical classes of anticancer agents, but also novel and potentially relevant mechanisms of action.

3. Acknoledgement

I am cordially grateful to my Parents and my esteemed respected guide Dr. (Prof.) ShaliniTripathi, Department of Pharmacy, Rameshwaram Institute of Technology and Management for her supervision, advice and guidance from the very early stage of this research as well as giving me extraordinary experiences throughout the work.

4. References

1. Department of Health and Human Services. Agency for Toxic Substances and Disease Registry. Cancer Fact Sheet. Accessed at www.atsdr.cdc.gov/COM/cancer-fs.html on August 10, 2012.
2. National Cancer Institute. Cancer: Questions and Answers. Accessed at www.cancer.gov/cancertopics/factsheet/Sites-Types/general on December 18, 2009.
3. NarahMerina, kalicajogen Chandra and kotokyjibon medicinal and plants with potential anti-cancer activity: Areview. International research journal of pharmacy.2012, 26-30
4. Ashworth A, Christopher Lj, Reis-Filho S. Genetic Interactions in cancer progression and Treatment. Cell 2011; 145(1):30-38.
5. "Cancer Glossary". *Cancer.org*. American Cancer Society. Retrieved September 11, 2013.
6. "What is cancer?".*Cancer.gov*. National Cancer Institute. Retrieved September 11, 2013.
7. Hanahan, Douglas; Weinberg, Robert A. (January 7, 2000). "The hallmarks of cancer". *Cell***100** (1): 57–70.
8. Hanahan, Douglas; Weinberg, Robert A. (2011). "Hallmarks of Cancer: The Next Generation". *Cell***144** (5): 646–74.
9. Varricchio, Claudette G. (2004). A cancer source book for nurses. Boston: Jones and Bartlett Publishers. p. 229
10. Anand P, Kunnumakkara AB, Kunnumakara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, Sung B, Aggarwal BB (September 2008). "Cancer is a preventable disease that requires major lifestyle changes". Pharm. Res. 25 (9): 2097–116.
11. Kravchenko J, Akushevich I, Manton, KG (2009). Cancer mortality and morbidity patterns in the U. S. population: an interdisciplinary approach. Berlin: Springer. ISBN 0-387-78192-7.
12. DeVita VT Jr, Serpick AA, and Carbone PO. Combination chemotherapy in the treatment of advanced Hodgkin's disease. Ann Intern Med. 1970; 73:881-895.
13. Noble RL. The discovery of the vinca alkaloids – chemotherapeutic agents against cancer. Biochem Cell Biol. 1990; 68:1344-1351.
14. Stähelin H. Actvity of a new glycosidiclignan derivative (VP-16-213) related to podophyllotoxin in experimental tumors. Eur J Cancer. 1973; 9:215-221.
15. Harvey AL. Medicines from nature: are natural products still relevant to drug discovery. Trends Pharmacol Sci. 1999; 20:196-198.
16. Liu LF. DNA topoisomerase poisons as antitumor drugs. Annu Rev Biochem. 1989; 58:351-375.
17. Wani MC, Taylor HL, Wall ME, et al. Plant antitumor agents. VI. The isolation and structure of taxol, a novel antileukemic and antitumor agent from Taxusbrevifolia. J Am Chem Soc. 1971; 93:2325-2327.
18. Creemers GJ, Bolis G, Gore M, et al. Topotecan, an active drug in the second-line treatment of epithelial ovarian cancer. J ClinOncol. 1996; 14:3056-3061.
19. Bertino JR. Irinotecan for colorectal cancer. SeminOncol. 1997; 24:S18-S23.
20. Liu LF, Desai SD, Li TK, et al. Mechanism of action of camptothecin. Ann New York Acad Sci. 2000; 922:1-10.
21. Harmon AD, Weiss U, Silverton JV. The structure of rohutukine, the main alkaloid of Amoorarohituka (syn. Aphanamixispolystachya) (Maliaceae). Tetrahydron. 1979; 20:721-724.

22. Cragg G, Suffness M. Metabolism of plant-derived anticancer agents. PharmacolTher. 1988; 37:425-432.
23. Losiewicz MD, Carlson BA, Kaur G, et al. Potent inhibition of cdc2 kinase activity by the flavonoid L86-8275. BiochemBiophys Res Commun. 1994; 201:589-595.
24. Worland PJ, Kaur G, Stetler-Stevenson M, et al. Alteration of the phosphorylation state of p32cdc2 kinase by the flavone L86-8275 in breast carcinoma cells. BiochemPharmacol. 1993; 46:1831-1836.
25. Kelland LR. Flavopiridol, the first cyclin-dependent kinase inhibitor to enter the clinic: current status. Ex OpinInv Drugs. 2000; 9:2903-2911.
26. Powell RG, Weisleder D, Smith CR Jr, et al. Structures of harringtonine, isoharringtonine, and homoharringtonine. TetrahydronLett. 1970; 11:815-818.
27. Zhou DC, Zittoun R, Marie JP. Homoharringtonine: an effective new natural product in cancer chemotherapy. Bull Cancer. 1995; 82:987-995.
28. Kantarjian HM, O'Brien S, Anderlini P, et al. Treatment of myelogenousleukemia: current status and investigational options. Blood. 1996; 87:3069-3081.
29. Rowinsky EK, Noe DA, Ettinger DS, et al. PhaseI and pharmacological study of the pulmonary cytotoxin 4-ipomeanol on a single dose schedule in lung cancer patients: hepatotoxicity is dose limiting in humans. Cancer Res. 1993; 53:1794-1801.
30. Rehm S, Devor DE. Acute effects of 4-ipomeanol on experimental lung tumors with bronchiolar or alveolar cell features in Syrian hamsters or C3H/HeNCr mice. J Cancer Res ClinOncol. 1993; 120:41-50.
31. Li YZ, Li CJ, Pinto AV, et al. Release of mitochondrial cytochrome c in both apoptosis and necrosis induced by β-lapachone in human carcinoma cells. Mol Med. 1999; 4:232-239.
32. Noolvi N Malleshappa, sharmarohini, Bhanotabhishek. Natural sources as potential anti-cancer agents: A review. International Journal of Phytomedicine 3 (2011) 09-26
33. Block G, Patterson B, Subar A. Fruit, vegetables, and cancer prevention: a review of the epidemiological evidence. Nutr Cancer. 1992; 18(1):1–29.
34. Steinmetz KA, Potter JD. Vegetables, fruit, and cancer prevention: a review. J Am Diet Assoc. 1996; 96(10):1027–39.
35. Reddy L, Odhav B, Bhoola KD. Natural products for cancer prevention: a global perspective. PharmacolTher. 2003; 99(1):1–13.
36. Aggarwal BB, Shishodia S. Molecular targets of dietary agents for prevention and therapy of cancer. BiochemPharmacol. 2006; 71:1397–1421.
37. Hoyoku N, Michiaki M, Harukuni T, et al. Cancer prevention by carotenoids. Arch BiochemBiophys. 2009; 483 :(2):165-168.
38. Pomponi AS. The bioprocess-technological potential of the sea. J Biotechnol. 1999; 70:5-13.
39. Schwartsmann G. Marine organisms and other novel natural sources of new anticancer drugs. Ann Oncol. 2000; 11:235-243.
40. Schwartsmann G, Rocha AB, Berlinck R, et al. Marine organisms as a source of new anticancer agents. Lancet Oncol. 2001; 2:221-225.
41. Schweitzer J, Handley FG, Edwards J, et al. Summary of the workshop on drug development, biological diversity, and economic growth. J Natl Cancer Inst. 1991; 83:1294-1298.
42. Rinehart KL. Antitumor compounds from tunicates. Med Res Rev. 2000; 20:1-27.
43. Chun HG, Davies B, Hoth D, etal.Suffness. Didemnin B The first marine compound entering clinical trials as an antineoplastic agent. Invest New Drugs. 1986; 4:279-284.
44. Geldof AA, Mastbergen SC, Henrar REC, et al. Cytotoxicity and neurocytoxicity of new marine anticancer agents evaluated using invitro assays. Cancer ChemotherPharmacol. 1999; 44:312-318.
45. Demetri G, Garcia-Carbonero R, Harmon D, et al. Ecteinascidin-743 (ET-743) induces objective responses and disease control in patients with advanced non-osseous sarcomas: results from phaseII trials. Ann Oncol. 2000; 11(Suppl 4):126.
46. Erba E, Bergamaschi D, Bassano L, et al. Ecteinascidin-743 (ET-743), a natural marine compound, with a unique mechanism of action. Eur J Cancer. 2001; 37:97-105.
47. Damia G, Silvestri S, Carrassa L, et al. Unique pattern of ET-743 activity in different cellular systems with defined deficiencies in DNA-repair pathways. Int J Cancer. 2001; 92:583-588.
48. Poncet J. The dolastatins, a family of promising antineoplastic agents. Curr Pharm Des. 1999; 5:139-162.
49. Bai R, Pettit GR, Hamel E. Dolastatin10, a powerful cytostatic peptide derived from a marine animal. Inhibition of tubulin polymerization mediated through the vinca alkaloid binding domain. BiochemPharmacol. 1990; 39:1941-1949.
50. Pathak S, Multani AS, Ozen M, et al. Dolastatin10 induces polyploidy, telomeric associations and apoptosis in a murine melanoma cell line. Oncol Res. 1998; 5:373-376.
51. Pettit GR. The bryostatins. FortschrChem Org Naturst. 1991; 57:153-195.

52. Pagliaro L, Daliani D, Amato R, et al. Phase II trial of bryostatin-1 for patients with metastatic renal cell carcinoma. Cancer. 2000; 89:615-618.
53. Varterasian ML, Mohammad RM, Shurafa MS, et al. PhaseII trial of bryostatin1 in Patients with relapsed low-grade non-Hodgkin's lymphoma and chronic lymphocytic leukemia. Clin Cancer Res. 2000; 6:825-828.
54. Zonder JA, Shields AF, Zalupski M, et al. A phase II trial of bryostatin 1 in the treatment of metastatic colorectal cancer. Clin Cancer Res. 2001; 7:38-42.
55. Ahmad I, Al-Katib AM, Beck FW, et al. Sequential treatment of a resistant chronic lymphocytic leukemia patient with bryostatin1 followed by 2-chlorodeoxyadenoside: case report. Clin Cancer Res. 2000; 6:1328-1332.
56. Mayer A and Gustafson KR. Marine pharmacology in 2002–2004: Anti-tumour and cytotoxic compounds. Eur J Cancer. 2006; 42:2241–2270.
57. Mayer A and Gustafson K R. Marine pharmacology in 2005–2006: Anti-tumour and cytotoxic compounds. Eur J Cancer. 2008; 44: 2257–2287.
58. Binaschi M, Farinosi R, Borgnetto ME, et al. In vivo site specificity and human isoenzyme selectivity of two topoisomerase II poisoning anthracyclines. Cancer Res. 2000; 60:3770-3776.
59. Patrick Y. Major microbial diversity initiative recommended. Am SocMicrobiol News. 1997; 63:417-421.
60. Alberts MW, Williams RT, Brown EJ, et al. KBP-Rapamycin inhibits a cyclin-dependent kinase activity and a cyclin D1-Cdk association in early Gl of an osteosarcoma cell line. J Biol Chem. 1993; 268:22825-22829.
61. Schulte TW, Neckers LM. The benzoquinone ansamycin17-allylamino-17 demethoxygeldanamycin binds to HSP90 and shares important biologic activities with geldanamycin. Cancer ChemotherHarmacol. 1998; 42:273-279.
62. Cadenas ME, Sandfrison A, Cutler NS, et al. Signal transduction cascades as targets for therapeutic intervention by natural products. Trends Biotechnol. 1998; 16:427-433.
63. Adjei AA. Signal transduction pathway targets for anticancer drug discovery. CurrPharmaceut Design. 2000; 6:361-378.
64. www.Wikipedia, the free encyclopedia.htm