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A Review On: Cytotoxic Activity of Indian Medicinal Plants Used Traditionally.

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ABSTRACT

The uses of ethnomedicinal plants for human healthcare still remain the most widely used medication system in developing and least developed nation. Medicinal plants remain an important source of new drugs, new drug leads and new chemical entities. The plant based drug discovery resulted mainly in the development of pharmacologically active compounds. Population rise, insufficient supply of drugs, unaffordable cost of treatments, side effects of several allopathic drugs and development of resistance to currently used drugs for a wide variety of human ailments. Anticancer agents including vinblastine, vincristine, the camptothecin derivatives, topotecan and irinotecan, etoposide, derivatives from epipodophyllotoxin, and paclitaol. Several promising new agents are in clinical development based on selective activity against cancer related molecular targets, including flavopiridol and combretastin A4 phosphate, and some agents which failed in earlier clinical studies are stimulating renewed interest.

Keywords: Cytotoxic activity, Anticancer, Dietary medicinal plants, Traditional medicine

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INTRODUCTION

India is endowed with rich wealth of medicinal plants. India recognizes more than 2500 plant species which have medicinal values[1]. Herbal medicines have become more popular in the treatment of many diseases due to popular belief that green medicine is safe, easily available and less side effects[2]. All parts of the plant are claimed to have medicinal value. The bioactive compounds like alkaloids, flavonoids, tannins and phenolic compounds are responsible for the medicinal value of the plant which produces a definite physiological action on the body[3].

Cancer is a dreadful disease caused by abnormal and uncontrolled cell division. About 6 million new incidences of cancer are reported yearly worldwide. Nature has given man a variety of useful sources of remedies to cure a number of diseases. Natural products have played a significant role in drug discovery and development, especially agents active against cancer and infectious diseases (Butler, 2008). More than 70 per cent of all cancer deaths occurred in low- and middle-income countries. The WHO noted that tobacco use, alcohol use, low fruit and vegetable intake, and chronic infections from hepatitis B virus (HBV), hepatitis C virus (HCV) and some types of human papillomavirus (HPV) are leading risk factors for cancer in low- and middle-income countries. Deaths from cancer worldwide are projected to continue rising with an estimated 12 million deaths by 2030 (Wang et al, 2007). The most frequent types of cancer worldwide in order of the number of global deaths are; among men – lung, stomach, liver, colorectal, oesophagus and prostate; and among women – breast, lung, stomach, colorectal and cervical.

Every year about 8,50,000 new cancer cases being diagnosed, India resulting about 5,80,000 cancer related death every year. India had the highest number of the oral and throat cancer cases in the world. Every third oral cancer patient in the world is from India. Compared to developed countries overall there were less cancer cases in India but that could be due to under diagnosis and under reporting. At the same time regional, ethnic, dietary and socio-economic factors might also results in difference in the cancer susceptibilities and the incidence. Also cancer was mainly a disease of old ages. Worldwide median age at diagnosis was about 60 years. Average life span was about 58 years in India compared to 75 years in the developed world.

Plants as source of anti-cancer agents:

Plants have a long history of use in the treatment of cancer and it is significant that over 60% of currently used anti-cancer agents are come from natural sources [5]. Naturally occurring drugs that includes vinca alkaloids (vincristine, vinblastine, vindesine, vinorelbine), taxanes (paclitaxel, docetaxel), podophyllotoxin and its derivative (etoposide, teniposide), camptothecin and its derivatives (topothecan, irinothecan), anthracyclines (doxorubicin, daunorubicin, epirubicin, idarubicin) and others. In fact, half of all anti-cancer drugs approved internationally were either natural products or their derivatives and were developed on the basis of knowledge gained from small molecules or macromolecules that exist in nature [6, 7]. In between 2001 to 2005, 4 new drugs derived from natural products for anti-cancer agents in 2002 doxorubicin, in 2002 estradiol, in 2004 cholorophyll and l- aspartic acid and taxol nanoparticles in 2005 [8]. Three new drugs also introduced in 2007 originate from microbial sources for the treatment of cancer is marine alkaloid trabectedin, epothilone derivative ixabepilone and temsirolimus [9]. Nature is an attractive source of new therapeutic candidate compounds as a tremendous chemical diversity is found in millions of species of plants, animals, marine organisms and microorganisms as potential anti-cancer agent [10, 11]. In this present study the potential anti-cancer agent from plants, marines, microorganisms and dietary (fruits, vegetables and spices) sources.

Herbs produce anticancer activities:

Catharanthus roseus:

The first agents to advance into clinical use were the isolation of the vinca alkaloids, *Catharanthus roseus* (Apo-cynaceae) introduced a new era of the use of plant material as anticancer agents. Catharanthus roseus (Vinca rosea, Madagascar periwinkle) contains more than 70 alkaloids, known as vinca alkaloids such as Vinblastine, Vincristine, Vindesine, Vinorelbine. Vinca alkaloids arrest cancer cell proliferation by binding to tubulin in the mitotic spindle. Vinca alkaloids also induce apoptosis (programmed cell death) and inhibit angiogenesis (formation of new blood vessels). Vinca alkaloids inhibit growth & spread of various cancers

including that of breast, ovary, cervix, lung, colon, rectum, testis, neuroblastoma, Hodgkines disease, malignant lymphoma, multiple myeloma, various sarcomas, rhabdomyosarcoma and leukaemia. [12] They were the first agents to advance into clinical use for the treatment of cancer. Vinblastine and vincristine are primarily used in combination with other cancer chemotherapeutic drugs for the treatment of a variety of cancers.

Andrographis paniculata:

Andrographis paniculata (Acanthaceae), also known commonly as "kalmegh," is a well-known medicinal plant of Ayurveda and has been used for centuries in Asia. About 26 different polyherbal formulations of this plant are mentioned in Ayurveda as a popular remedy for the treatment of various disorders. *Andrographis paniculata* is an annual shurb grows abundantly in India. Andrographolide, active diterpine component, isolated from Andrographis paniculata, extract has shown cytotoxic activity against KB (human epidermoid carcinoma) and P388 (lymphocytic leukaemia) has immune enhancing and strong anticancer activity against cancers of breast, ovary, stomach, colon, prostate, kidney, nasopharynx malignant melanoma and leukaemia. Andrographolide exerts direct anticancer activity on cancer cells by arresting G0/G1 phase of cell-cycle and inducing apoptosis. Dichloromethane fraction of methanolic extract of Andrographis paniculata has strong anticancer activity against colon cancer.Andrographis paniculata possesses anticancer, immunostimulant, antioxidant, anti-HIV and anti-inflammatory properties. Andrographis paniculata enhances the activity of protective liver enzymes and reduces side effects of chemotherapy & radiotherapy. [13]

Azadirachta indica

Azadirachta indica contains about 40 different active principles, known as liminoids, which exhibit immune enhancing, anti-inflammatory, antiulcer, antifungal, antiviral, antioxidant, hepatoprotective, antimutagenic, anticancer and antimetastatic properties. Liminoids regress growth & spread of various cancers such as cancers of breast, lung, stomach, prostate and skin. Nimbolide, a natural triterpenoid, isolated from *Azadirachta indica* leaves and flowers inhibits growth & spread of various cancers including colon cancer, malignant lymphoma, malignant melanoma and leukaemia by inducing apoptosis (programmed cell death), a process that directs the body's immune cells to identify and destroy cancer cells. Nimbolide also prevents metastasis of cancer. Ethanolic extract of *Azadirachta indica* inhibits growth & spread of prostate cancer by inducing apoptosis and its antiandrogenic effect. *Azadirachta indica* reduces side effects of chemotherapy & radiotherapy[14].

Emblica officinalis

Emblica officinalis contains ellagic acid, gallic acid, quercetin, kaempferol, emblicanin, flavonoids, glycosides and proanthocyanidins. *Emblica officinalis*is valued for its unique tannins and flavanoids, which possess powerful antioxidant and anticancer properties. Ellagic acid isolated from *Emblica officinalis* is a powerful antioxidant and has the ability to inhibit mutations in genes. Ellagic acid also repairs chromosomal abnormalities. Quercetin, isolated from *Emblica officinalis* has hepatoprotective effect. Emblicanin A & B (tannins) possess strong antioxidant and anticancer properties. *Emblica officinalis* inhibits growth & spread of various cancers including that of the breast, uterus, pancreas, stomach, liver and malignant ascites. *Emblica officinalis* is an excellent rejuvenator and antioxidant herb. It is highly nutritious and an important source of Vitamin C, minerals and amino acids. *Emblica officinalis* protects against much cancer particularly the liver cancer. *Emblica officinalis* reduces side effects of chemotherapy & radiotherapy[15].

Curcuma longa

Turmeric is promoted mainly as anti-inflammatory herbal remedy, some scientists believe that the anti-oxidant curcumin present in turmeric may prevent or slow the growth of many cancers including tumor of esophagus, stomach and intestine, breast cancer and also skin cancer in experimental animals. However clinical research is needed to determine its efficacy in cancer prevention and treatment in human beings. The laboratory studies have confirmed the cucumin interferes with several molecular pathways involved in cancer development, growth and spread. Further, a study found that ethanolic extract of turmeric produces remarkable symptomatic relief in patients with external cancerous lesions. Other than paclitaxel (Taxol), quite a few natural compounds from fruit and vegetables are being investigated for its potential medicinal qualities.

For example, curcumin (from the plant Curcuma longa) used in Chinese medicine and in the Indian traditional food of curry as the yellow coloring agent in turmeric is known for its antioxidant, anti-inflammatory, antiviral, antibacterial, antifungal, and anticancer activities and potentially combat various other disorders including diabetes, allergies, arthritis, and Alzheimer's disease. [16] Goel et al. [17] reported on curcumin and posited that because most cancers are caused by dysregulation of as many as 500 different genes, agents, such as curcumin, that target multiple genes are needed for the prevention and treatment of cancer. In studies to date, curcumin has been shown to interact with a wide variety of proteins and modify their expression and activity. These proteins include inflammatory cytokines and enzymes, transcription factors, and gene products linked with cell survival, proliferation, invasion, and angiogenesis. [17] As of 2007, 22 Phase I or II cancer-related clinical trials [18] involving curcumin have been ongoing. Several of these trials indicate that curcumin is safe and may exhibit therapeutic efficacy. For example, curcumin has inhibited the spread of various tumor cells in culture, prevented carcinogen induced cancers in rodents, and inhibited the growth of human tumors in xenotransplant or orthotransplant animal models either alone or in combination with chemotherapeutic agents or radiation. [16]

Glycyrrhiza glabra

Flavonoids (flavones, flavonals, isoflavones, chalcones, licochalcones and bihydrochalcones), derived from *Glycyrrhiza glabra* possess strong anticancer, antioxidant, antimutagenic, antiulcer, anti-HIV and hepatoprotective properties. Licochalcone-A isolated from *Glycyrrhiza glabra*, inhibits growth and spread of various cancers particularly the androgen-refractory prostate cancer by inducing apoptosis and arresting cancer cells division. Licoagrochalcone, possesses strong anticancer activity against cancers of breast, lung, stomach, colon, liver, kidney and leukaemia. Glycyrrhizin isolated from *Glycyrrhiza glabra* inhibits growth & spread of lung cancer and fibrosarcomas. Glycyrrhizic acid isolated from *Glycyrrhiza glabra* protects against aflatoxins (powerful fungal carcinogens of the liver).*Glycyrrhiza glabra* stimulates immune system response of the body and protects against colon cancer and oestrogen-positive breast cancer[19].

Ocimum sanctum

Ocimum sanctum contains eugenol, eugenol derivatives, linolenic acid, rosmarinic acid and flavonoids such as orientin, vicenin, cirsilineol, cirsimaritin, isothymusin, isothymonin and apigenein. Eugenol, orientin and vicenin inhibits growth and spread of various cancers such as breast cancer, liver cancer and sarcomas particularly fibrosarcoma by blocking supply of oxygen and nutrients to the cancer cells and killing them by starving. Ursolic acid isolated from *Ocimum sanctum* has immune enhancing and tissue-protective properties. Polysaccharides isolated from *Ocimum sanctum* have antioxidant and radio protective properties. *Ocimum sanctum* protects against various cancers particularly the breast cancer and reduces side effects of chemotherapy and radiotherapy[20].

Solanum nigrum

Solamargine and solasonine, isolated from *Solanum nigrum* (Lo-ing-kue) inhibit growth and spread of various cancers including that of the breast, liver and lung. Steroidal glycosides (spirostane, furostane, spirosolane and pregnane), isolated from *Solanum nigrum* inhibit growth and spread of colon cancer and pheochromocytoma. Glycoproteins isolated from *Solanum nigrum* have antiproliferative and apoptotic effects on colon and breast cancers. Polysaccharides isolated from *Solanum nigrum* have significant inhibitory effect on growth of cervical cancer. *Solanum nigrum* inhibits growth & spread of liver cancer by two distinct anticancer activities, i.e. apoptosis (programmed cell death) and autophagy (autophagocytosis). Higher doses of *Solanum nigrum* induce apoptotic cell death while lower doses lead to autophagocytic death of cancer cells. Lunasin, isolated from *Solanum nigrum* is a cancer-preventive peptide. *Solanum nigrum* and *Solanum lyrati* (Shu-yang-quan) inhibit growth & spread of stomach cancer, sarcomas, malignant ascites and leukaemia[21].

Withania somnifera

Withanolides isolated from *Withania somnifera*, are similar to ginsenosides (the active principles of *Panax ginseng*) in both structure and activity. Withanolides (including Withaferin A, Sitoindoside IX, Physagulin D, Withanoside IV and Viscosalactone B) inhibit growth & spread of various cancers such as cancers of the breast, lung, colon and central nervous system due to their antiproliferative and antiangiogenic properties.

Withaferin-A (the most important withanolides) inhibit growth & spread of various cancers including that of the breast, cervix, colon, prostate, nasopharynx, larynx, malignant ascites and sarcomas by inducing apoptosis. Withaferin A is effective in both androgen-responsive and androgen-refractory prostate cancers. Sitoindosides VII-X and Withaferin A have strong antioxidant, antistress, immunomodulatory, anti-inflammatory and antiaging properties. Withanolide D inhibits the metastatic colony formation in the lungs by malignant melanoma. Ashwagandhanolide, a new dimeric withanolide, isolated from *Withania somnifera,* inhibits growth and spread in cancers of breast, stomach, colon, lung and central nervous system. *Withania somnifera* also possesses immune enhancing, haemopoietic and neuroprotective properties and reduces side effects of radiotherapy & chemotherapy[21].

Zingiber officinale

Gingerols isolated from *Zingiber officinale* inhibit growth & spread of various cancers including that of the ovary, cervix, colon, rectum, liver, urinary bladder, oral cavity, neuroblastoma and leukaemia by inducing apoptosis. The most active individual component, 6-shogaol, isolated from *Zingiber officinale*, inhibit growth & spread of many cancers particularly the ovarian cancer by blocking formation of new blood vessels and by inducing apoptosis & autophagy. It is effective even in chemotherapy resistant ovarian cancer. *Zingiber officinale* also possesses antioxidant, antimutagenic and anti-inflammatory properties and reduces side effects of chemotherapy & radiotherapy[22].

Cannabis Sativa

Cannabis Sativa is an annual herb that may reach 5 meters in height with leaves that form a fan-like structure with jagged edges. This plant is native to central Asia and as a result of importation, has expanded toward Europe and the Americas. This plant has many uses, some of which are furnishing fiber, oil, in medicine, and narcotics. Commonly referred to as Cannabis, Hemp is a very versatile material and is frequently used to relieve cancer pain, treat depression, and hypothermia, it also works as an appetite suppressant. A controversial plant in the field of medicine, it has been up for the debate of its use being an abused or medically prosperous drug. Compound – Delta-9- Tetrahydrocannabinol. Research has shown that the administering of smoked marijuana helped treated the nausea that was caused by cancer chemotherapy, thereby being an aid to the cancer treatment process. Side effects of this compound are not often seen in the physical aspect, rather in the mental or cognitive domain such as inability to distinguish space distances and time intervals, vigilance, and memory processes.[22]

Aloe vera

Acemannan (a polysaccharide), isolated from *Aloe vera*, stimulates the immune system, accelerates wound healing and possess significant anticancer property. Emodin and Lectins isolated from *Aloe vera* exhibit strong anticancer and immune enhancing activities. Aloe-emodin inhibits growth & spread of stomach cancer and various sarcomas by inducing apoptosis. Aloe-emodin has selective anticancer activity against neuroectodermal tumours (PNET). Alexin B isolated from *Aloe vera* possesses strong anticancer activity against leukaemia. Polysaccharides isolated from *Aloe vera* have strong immune enhancing and anticancer properties. *Aloe vera* contains “super carbohydrates” that protect against many cancers, particularly the liver cancer. *Aloe vera* prevents genesis of cancer, regresses growth of cancer and prevents metastasis of cancer. *Aloe vera* stimulates immune system response of the body by activating macrophages and releasing cytokines such as interferon, interleukin and tumour necrosis factor. *Aloe vera* has an extraordinary antioxidant profile and reduces side effects of chemotherapy & radiotherapy.[23]

Alpinia galangal

Acetoxy-chavicol-acetate (ACA), isolated from *Alpinia galanga*, possesses significant anticancer activity against cancers of breast, lung, stomach, colon, prostate, multiple myeloma and leukaemia. Pinocembrin isolated from *Alpinia galanga* inhibits growth & spread in colon cancer by arresting cell proliferation and inducing apoptosis. Galangin, a flavonoid isolated from *Alpinia galanga*, possesses strong anticancer, antioxidant, antimutagenic and anti-inflammatory properties. Galangin protects against breast and prostate cancers.[24]

Tinospora cordifolia

Sesquiterpenes and diterpenes isolated from *Tinospora cordifolia* inhibit growth & spread of various cancers including cancers of lung,cervix, throat and malignant ascites. Polysaccharide fraction isolated from *Tinospora cordifolia* inhibits lung metastasis. Arabinogalactan, syringine, cordiol, cordioside, cordifoliosides (A & B) isolated from *Tinospora cordifolia* possesses significant immune enhancing activity. *Tinospora cordifolia* also possesses neuroprotective, hepatoprotective, antistress, antiulcer and antipyretic properties. *Tinospora cordifolia* reduces side effects of radiotherapy & chemotherapy.[27]

Allium Sativum

The National Cancer Institute (affiliated to the NIH) recognizes garlic to have potential anticancer properties. The sulphydryl compounds in garlic have the ability to block the formation of cancer -causing substances. Several population studies have shown an association between increased garlic consumption and reduced risk of cancers of the stomach, colon, esophagus, pancreas, and also breast cancer. A study has found that garlic intake of 10 g per day could reduce the risk of prostate cancer by 50 percent. [28]

Zingiber officinale

Some pungent substances present in ginger rhizome have antioxidant and anti-inflammatory activities. The anticancer properties of ginger are attributed to phenolic substances such as 6-gingerol and 6-paradol and other constituents such as shogaols and zingerone. A study published in the journal Biochemical and Biophysical Research Communications reported that 6-gingerol can reduce viability of gastric cancer cells and limit the spread of cancer. Gingerols isolated from Zingiber officinale inhibit growth & spread of various cancers including that of the ovary, cervix, colon, rectum, liver, urinary bladder, oral cavity, neuroblastoma and leukaemia by inducing apoptosis. The most active individual component, 6-shogaol, isolated from Zingiber officinale, inhibit growth & spread of many cancers particularly the ovarian cancer by blocking formation of new blood vessels and by inducing apoptosis & autophagy. It is effective even in chemotherapy resistant ovarian cancer. Zingiber officinale also possesses antioxidant, antimutagenic and anti-inflammatory properties and reduces side effects of chemotherapy & radiotherapy. [29]

Cinnamomum cassia

Cinnamon has antioxidant properties that can significantly decrease lipid peroxidation that lead to cancer. Further, cinnamon bark oil has been found by researchers to be one of the most effective inhibitors of bacteria, such as Helicobacter pylori, that facilitate the invasion and progression of cancer. However, high amount of coumarin present in cinnamon can damage liver tissues. Although there are no reports of coumarin related tumor formation, high levels of coumarin did trigger cancer in experimental rodents. [30]

Viscum album

Lectins (such as viscumin), polypeptides (viscotoxins) and phenolic compounds (such as digallic acid) isolated from *Viscum album* inhibit growth and spread of various cancers including that of the breast, cervix, ovary, lung, stomach, colon, rectum, kidney, urinary bladder, testis, malignant melanoma, sarcomas, fibrosarcoma, malignant ascites, lung metastasis and leukaemia by inducing apoptosis and anti-angiogenesis activity. Lectins isolated from *Viscum album* possess both anticancer and immunostimulating activities. Viscumin, responsible for most of the biological activities of *Viscum album*, works by bringing together immune system effector cells and cancer cells. Lectin-II induces apoptosis in cancer cells via activation of caspase cascades.[25]

Rubia cordifolia

Rubidianin, rubiadin, RA-7, RA-700 and RC-18 isolated from *Rubia cordifolia* inhibit growth & spread in cancers of breast, ovary, cervix, colon, lung, malignant ascites, malignant lymphoma, malignant melanoma sarcoma and leukaemia. Rubiadin also possesses hepatoprotective activity.[26]

Plumbago zeylanica

Plumbagin isolated from *Plumbago zeylanica* inhibits growth & spread of breast cancer, liver cancer, fibrosarcoma, malignant ascites and leukaemia by inhibiting cancer cell proliferation. *Plumbago zeylanica* also possesses strong antioxidant, hepatoprotective, neuroprotective and immunoenhancing properties.[26]

Psoralea corylifolia

Bavachinin, corylfolinin and psoralen isolated from *Psoralea corylifolia* possess strong anticancer activity against lung cancer, liver cancer, osteosarcoma, fibrosarcoma, malignant ascites and leukaemia. Psoralen enhances immunity of the body by stimulating natural killer cell activity. Psoralidin isolated from *Psoralea corylifolia* inhibits growth & spread of stomach and prostate cancers by inhibiting G2/M phase of cell cycle. Psoralidin induces apoptosis in both androgen-responsive and androgen refractory prostate cancers. *Psoralea corylifolia* also possesses strong antioxidant, immunomo enhancing and hepatoprotective properties.[27]

Green tea

Polyphenols in green tea and sometimes black tea, help kill cancerous cells and stop their progression. Mayo Clinic studies have revealed that a substance called epigalloacatechin gallate (EGCG) in green tea reduces the number of leukemia cells in patients with CLL (chronic lymphocytic leukemia), a form of blood cancer. Similarly, another study found that women who drank powdered green tea were less likely to develop bladder cancer. Again, men who drank the most green tea were 37 percent less likely to develop pancreatic cancer. A large Chinese clinical study found that the risk of prostate cancer declined with increasing frequency and quantity of green tea consumption. However, scientists found that green tea could reduce the chances of recurrence of breast cancer but it could not prevent or improve breast cancer.[28]

Coriandrum sativum

Cilantro or, more commonly, coriander is another potent herb that has anti-cancer properties. The prevalent antioxidants in cilantro are beta-carotene, quercetin and rutin. This herb, normally used in chelation therapy for people suffering from lead poisoning, helps remove free radicals by getting rid of the heavy metals in your body. Dr. Yoshiaki Omura from the Heart Disease Research Foundation, New York, NY, USA, has actually found that fresh cilantro removes heavy metals and with it the free radicals too from the body in less than 2 weeks. [28]

Origanum vulgare

Amongst the dried herbs, oregano has perhaps the highest antioxidant levels. Rosmarinic acid is the compound in oregano that has the strong anti-oxidant activity. An Indian study reported that oregano supplementation of 40 mg per kg of body weight had a modulatory role on tissue lipid peroxidation in colon cancer-bearing experimental odents. The dosage for human beings has not yet been determined, but then, how much of oregano would you need to flavor your dish it depends. [28]

Saussurea lappa

Sesquiterpenes and costunolide dehydrocostuslactone, isolated from *Saussurea lappa* inhibit growth & spread of breast cancer. Cynaropicrin, isolated from *Saussurea lappa* possesses strong anticancer activity against malignant lymphoma and leukaemia. Costunolide, isolated from *Saussurea lappa* inhibits growth & spread of intestinal cancer. Mokkolactone isolated from *Saussurea lappa* induces apoptosis in leukaemic cells. Shikokiols isolated from *Saussurea lappa* exhibit anticancer activity against cancers of the ovary, lung, colon and central nervous system. *Saussurea lappa* inhibits growth & spread of cancers by arresting cancer cell division in G2 phase and inducing apoptosis.[29]

Nigella sativa

Thymoquinone and dithymoquinone isolated from *Nigella sativa* have strong anticancer activity against various cancers including cancers of the colon, prostate, pancreas, uterus, malignant ascites, malignant lymphoma, malignant melanoma, sarcomas and leukaemia. Thymoquinone is effective in both hormone-sensitive and hormone refractory prostate cancer. *Nigella sativa* kills cancer cells by binding to the asialofeutin (lectin) on the surface of cancerous cells, causing their aggregation and clumping. *Nigella sativa* also possesses immune enhancing and anti-inflammatory properties. It protects against liver cancer. *Nigella sativa* enhances immune function of the body and reduces side effects of chemotherapy & radiotherapy.[30]

Ginkgo biloba

Ginkgetin and Ginkgolides (A & B), isolated from *Ginkgo biloba* inhibits growth & spread of various aggressive cancers such as invasive oestrogen-receptor negative breast cancer, glioblastoma multiforme, hepatocellular carcinoma and cancers of ovary, colon, prostate and liver by inducing apoptosis.*Ginkgo biloba* extract is well known for its antioxidant activity. *Ginkgo biloba* also reduces side effects of chemotherapy & radiotherapy.[31]

Morinda citrifolia

Damnacanthol, NB10 and NB11 isolated from *Morinda citrifolia* possess strong anticancer activity against various cancers particularly lung cancer and sarcomas. *Morinda citrifolia*, possesses strong antioxidant, hepatoprotective and immunoenhancing properties.[31]

Plant-derived anticancer agents for future development:

A large number of bioactive compounds have been isolated from plant sources. Several of them are currently in clinical trials or preclinical trials or undergoing further investigation. Flavopirido is a synthetic flavone, derived from the plant alkaloid rohitukine, which was isolated from *Dysoxylum binectariferum*. It is currently in phase I and phase II clinical trials against a broad range of tumors, including leukemia, lymphomas and solid tumors. Synthetic agent roscovitine (which is derived from natural product olomucine, originally isolated from *Raphanus sativus* L. (Brassicaceae), is in Phase II clinical trials in Europe. Combre-tastatins were isolated from the bark of the South African tree *Combretum caffrum* Kuntze (Combretaceae). Combretastatin A-4 is active against colon, lung and leukemia cancers and it is expected that this molecule is the most cytotoxic phyto-molecule isolated so far. Betulinic acid a pentacyclic triterpene, is a common secondary metabolite of plants, primarily from *Betula* species (Betulaceae). Pervilleine-A was isolated from the roots of *Erythroxylum pervillei* Baill. (Erythroxylaceae). Pervilleine A was selectively cytotoxic against a multidrug resistant (MDR) oral epidermoid cancer cell line (KB-V1) in the presence of the anticancer agent vinblastine. Pervilleine A is currently in preclinical development . Silvestrol was first isolated from the fruits of *Aglaila sylvestre* (M. Roemer) Merrill (Meliaceae). Silvestrol exhibited cytotoxicity against lung and breast cancer cell lines. Biological studies are ongoing to determine the mechanism(s) of action for silvestrol. Two novel alkaloids, schischkinnin and montamine have been isolated from the seeds of *Centaurea schischkinii* and *Centaurea montana*. Both of the alkaloids exhibited significant cytotoxicity against human colon cancer cell lines. The unique structural features of schischkinnin and montamine can be exploited as a template for generating com-pounds with enhanced anticancer activity. However, further investigations are necessary for their use as anticancer agents.

CONCLUSION

Natural products have been a prime source for the treatment of many forms of cancer, many of which are consumed daily with the diet. They provide significant protection against various cancers and many other diseases. The medicinal plants and their products prevent from the cancer and other diseases by protecting cells from damage. Thus, consuming a diet rich in antioxidant fruits, vegetables, herbs etc. will provide health-protective effects. Microbes and marine organisms also have been offering the great role in the prevention and treatment of cancer. Medicinal plants have contributed a rich health to human beings. Plant extracts and their bioactive compounds present in them which are responsible for anticancer activity have to be screened for their valuable information. 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.

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