REVIEW

Medicinal Plants Combating Against Cancer - a Green Anticancer Approach

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Abstract

Cancer is the most deadly disease that causes the serious health problems, physical disabilities, mortalities, and morbidities around the world. It is the second leading cause of death all over the world. Although great advancement have been made in the treatment of cancer progression, still significant deficiencies and room for improvement remain. Chemotherapy produced a number of undesired and toxic side effects. Natural therapies, such as the use of plant-derived products in the treatment of cancer, may reduce adverse and toxic side effects. However, many plants exist that have shown very promising anticancer activities in vitro and *in vivo* but their active anticancer principle have yet to be evaluated. Combined efforts of botanist, pharmacologist and chemists are required to find new lead anticancer constituent to fight disease. This review will help researchers in the finding of new bioactive molecules as it will focus on various plants evaluated for anticancer properties *in vitro* and *in vivo*.

Keywords: Anticancer activity - anticancer agents - cancer - medicinal plants

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Introduction

Cancer is the life threatening and dreadful disease characterized by the abnormal proliferation of cells that invade the adjacent tissues and causes the destruction of these tissues (Gennari et al., 2007). Cancer spreads to distant organs through blood stream and lymphatic vessels. Cancer results when disturbance occurs in two types of genes i.e., oncogenes responsible for the growth of cancer cells, and tumor suppressor genes which prevent cancer from developing (Knudson et al., 2001). It is often impossible to evaluate the specific cause for specific cancer. However there are certain factors known to increase the risk of cancer such as tobacco use, alcohol, environmental pollutant, infectious agents, custom habits and life styles (Lrigaray et al., 2007). Approximately 10% to 15% cancer is entirely hereditary (Anand et al., 2008).

Cancers are named according to the type of cell the tumor resembles, for example carcinoma if they arise from the epithelial cell lining, sarcoma if they arise from mesodermal cell lining mean cancer of muscles, bones, cartilage and connective tissue, lymphoma if they arise from cells of immune system, leukemia if they arise from cells of bone marrow.

More than six million deaths each year occur in the world is due to cancer. In the world wide, about 12.7 million cancers were diagnosed and 7.6 million deaths were reported in 2008 (Jemal et al., 2011). Cancer is the serious health issue of both developed and developing countries.

In 2012, there were an estimated 14.1 million cases around the world, of these 7.4 million cases were in men and 6.4 million women. This number is expected to increase to 24 million by 2035 (Ferlay, 2013).

Although cancer is considered to be more of a developed world issue, in fact rate of all cancers (excluding non-melanoma skin cancer) was 1.8 times higher in more developed compared with less developed countries (Ferlay, 2013).

Chemotherapy as well as conventional treatment for the cure of cancer causes the adverse and toxic side effects therefore fails to control the cancer disease. The alternate solution for the harmful effects of synthetic agents is the use of medicinal plants (Rashid et al., 2002). The plants have been used for the cure of cancer from a prolonged period of time (Hartwell, 1982). The medicinal plants contain chemical constituents of therapeutic value (Nostro et al., 2000). These chemical substances produce physiological action on the human body. It has been shown currently by clinical studies and phytochemical

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Table 1. World Cancer Statistics for most Common Cancers in 2012

Rank	Cancer	New case diagnosed in 2012 (1000s)	Percent of all cancer excluding non melanoma of skin
1	Lung	1,825	13
2	Breast	1,677	11.9
3	Colorectum	1,361	9.7
4	Prostate	1,112	7.9
5	Stomach	952	6.8
6	Liver	782	5.6
7	Bladder	430	3.1
8	Non-hodgkin lymphoma	386	2.7
9	Leukaemia	352	2.5
10	Pancreas	338	2.4
11	Kidney	338	2.4
12	Brain	256	1.8
13	Melanoma of skin	232	1.6
14	Gall bladder	178	1.3
15	Hodgkin Lymphoma	66	0.5

Table 2. The Number of Cases in More Developed and Less Developed Countries as of the Year 2012

Cancer	Age standardized Rate per 100,000 (world)		
	World	More developed	Less developed
All cancer excluding non-melanoma skin cancer			
	182.3	268.3	147.7
Lung	23.1	30.8	20
Colorectum	17.2	29.2	11.2
Stomach	12.1	10.6	12.7
Melanoma of skin	3	9.6	0.8
Bladder	5.3	9.5	3.3
Kidney	4.4	9.2	2.6
Non-hodgkin lymphoma	5	8.6	3.6
Leukaemia	4.7	7.2	3.8
Pancrease	4.2	7.2	2.8
Liver	10.1	5.4	12
Brain	3.4	5.1	3
Gall bladder	2.2	2.1	2.2
Hodgkin lymphoma	0.9	2.1	0.6

investigation that many herbs exhibit anti tumor potential against various cancers (Sharma et al., 2011).

Medicinal plants provide outstanding contribution to modern therapeutics; approximately 100 plants based new drugs were introduced in the USA drug market during 1950 to 1970 including reserpine, deserpidine, vinblastine, vincristine. All these derived from higher plants. From 1971 to 1990 new plant based drugs came into being all over the world such as ectoposide, eguggulsterone, artemisinin and ginkgolides. During 1991 to 1995 2% drugs were introduced including pacitaxel, topotecan, gomishin, irinotecan etc. (Pandey et al., 2011). However in the middle of 20th century, the use of medicinal plants was reduced one fourth as researchers favor the use of synthetic chemicals for curing diseases. Now the trend is going to be changed and the people favor the medicinal plants as they contain natural products that are effective, chemically balanced and have fewer side effects as compared to synthetic chemicals (Hamayun et al., 2006).

Plants are the effective source of anticancer agent and over 60% anticancer agents are derived from natural resources including plants, marine organisms and microorganisms (Crag et al., 2005). Although number of anticancer agents are derived from medicinal plants but still there's present a number of plants that exhibits anticancer potential but they have not yet been fully investigated. The national cancer institute has screened around 114,000 extracts for anticancer activity (Shoeb et al., 2006). Therefore, there is a need to focus to evaluate that whether these extracts will surely be the source of anticancer activity or whether these extracts can be exploited to reach cancer blocking or remedial effects in human body.

Anticancer Agents in Clinical Use

Vinblastine and vincristine are the bisindole alkaloids isolated from the Madagascar periwinkle, Catharanthus roseus G. Don. (Apocynaceae) introduced a new era of the use of plant material as anticancer agents. They were the first plant derived agents to advance into clinical use for the treatment of cancer (Cragg and Newman, 2005). Vinblastine and vincristine are primarily used in combination with other cancer chemotherapeutic drugs for the treatment of different types of cancers, including leukemias, lymphomas, testicular cancer, breast and lung cancers, and Kaposi's sarcoma (Cragg and Newman, 2005).

Camptothecin, isolated from the wood bark and fruits of Chinese ornamental tree *Camptotheca acuminate* Decne (Nyssaceae), was advanced to clinical trials by NCI in the 1970s but its use was halted because of severe bladder toxicity (Potmeisel, 1995). Topotecan and irinotecan are semi-synthetic derivatives of camptothecin and are active against ovarian and small cell lung cancers, and colorectal cancers, respectively (Creemers et al., 1996; Bertino, 1997).

Homoharringtonine is cephalotaxus alkaloid isolated from the Chinese tree Cephalotaxus harringtonia var. drupacea (Sieb and Zucc.) (Cephalotaxaceae), is another plant-derived agent in clinical use (Powell et al., 1970; Itokawa et al., 2005). A racemic mixture of harringtonine and homoharringtonine are active against acute myelogenous leukemia and chronic myelogenous leukemia (Kantarjian et al., 1996; Cragg and Newman, 2005).

Ellipticine is an antitumor alkaloid isolated from a Fijian medicinal plant Bleekeria vitensis A.C. Sm, is marketed in France for the treatment of breast cancer (Cragg and Newman, 2005).

Paclitaxel (Taxol®) derived from the bark of the Pacific Yew, *Taxus brevifolia* Nutt. (Taxaceae), is another success in natural product drug discovery. Several Native American Tribes use various parts of *Taxus brevifolia* and other Taxus species (e.g., Taxus Canadensis Marshall, *Taxus baccata* L.) for the treatment of some non-cancerous cases (Cragg and Newman, 2005) while *Taxus baccata* was reported to use in the Indian Ayurvedic medicine for the treatment of cancer. Paclitaxel is used against ovarian

cancer, advanced breast cancer, small and non-small cell lung cancer (Rowinsky et al., 1992).

Podophyllotoxin is an important anticancer liganan, which was isolated as the active anti-tumor agent from the roots of Podophyllum species, *Podophyllum peltatum* Linnaeus and *Podophyllum emodi* Wallich (Berberidaceae) (Stahelin, 1973). Etoposide and teniposide are two most successful anticancer derivatives of epipodophyllotoxin and are used in the treatment of lymphomas and bronchial and testicular cancers (Cragg and Newman, 2005; Harvey, 1997).

Anticancer Activity Of Medicinal Plants

Allium sativum

Allium sativum L. garlic is among the oldest of all cultivated plants being used as a food, having a unique taste and odor along with some medicinal qualities. Modern scientific research has revealed that the wide variety of dietary and medicinal functions of garlic can be because of the sulfur compounds present in it. The compound allicin, methyl allyl trisulfide, and diallyl trisulfide have antibacterial, antithrombotic, and anticancer activities respectively (Ariga et al., 2006). It is a remarkable plant, which has multiple beneficial health effects such as hypolipidemic, antiarthritic, antimicrobial, antithrombotic, hypoglycemic and antitumor activities. Different garlic preparations including fresh garlic extract, aged garlic, garlic oil and a number of organo sulfur compounds derived from garlic shown to have chemopreventive activity. The chemopreventive activity has been attributed to the presence of organo sulfur compounds in garlic. The two major compounds in aged garlic, S-allylcysteine and S-allylmercapto-L-cysteine possess the highest radical scavenging activity. In addition, S-allylcysteine has been found to reduce the growth of chemically induced and transplantable tumors in animal models. Therefore, the use of garlic may provide some kind of protection from cancer development (Thomson et al., 2003).

Annona muricata L

George et al. (2012) evaluated the cytotoxic potential of n-butanolic leaf extract of Annona muricata L. on WRL-68 (normal human hepatic cells), MDA-MB-435S (human breast carcinoma cells) and HaCaT (human immortalized keratinocyte cells) lines by XTT assay. The result revealed that the extract at its lower doses exhibited a significant cytotoxicity on MDA-MB-435S and HaCaT cells with the IC50 values of 29.2 and 30.1 μg respectively, while it exhibited only a moderate cytotoxicity towards WRL-68 with a comparatively higher IC50 value of 52.4 μg, clearly indicating differential cytotoxicity, at least at the lower doses tested. On the other hand, the cytotoxic effect of the extract was similar on both normal and cancer cell lines, at the highest tested dose. This study therefore confirms the presence of therapeutically active antineoplastic compounds in the n-butanolic leaf extract of Annona muricata (George et al., 2012).

Acronychia bauer

Triterpene lupeol and the alkaloids melicopine, acronycine, and normelicopidine isolated from *Acronychia Baueri* Schott (*Bauerella australiana* Borzi) bark shown to have antitumor activity. Among three alkaloids, experimental evidence showed acronycine has the broadest antitumor spectrum. It is chemically unrelated to any of the presently utilized antitumor agents therefore represents a new lead in the search for agents effective in the chemotherapeutic management of human neoplasms (Svododa et al., 1996).

Rosa roxburghii tratt

Rosa roxburghii Tratt and *Fagopyrum cymosum* are two examples of plants which have beneficial effects in improving immune responses, enhancing digestive ability and demonstrating anti-aging effects. Some evidence shows that herbal medicine soups containing extracts of these two medicinal plants i.e *Rosa roxburghii* Tratt and *Fagopyrum cymosum* have efficacy in treating malignant tumors. The study was therefore undertaken to evaluate anticancer effects against three carcinoma cell lines (human esophageal squamous carcinoma CaEs-17, human gastric carcinoma SGC-7901 and pulmonary carcinoma A549) by MTT assay and flow cytometry. IC30 of *Rosa roxburghii* Tratt and *Fagopyrum cymosum* were obtained by MTT assay. Combination of *Rosa roxburghii* Tratt and *Fagopyrum cymosum* showed significant inhibition of cell growth and increase in apoptosis; the mRNA and protein expression levels of Ki-67 and Bcl-2 in *Rosa roxburghii* Tratt and *Fagopyrum cymosum* group were all greatly decreased, while the expression of Bax was markedly increased. These results therefore show that the synergistic antitumor effects of combination of *Rosa roxburghii* Tratt and *Fagopyrum cymosum* are related to inhibition of proliferation and induction of apoptosis (Liu et al., 2012).

Artemisia capillaries

Artemisia capillaries is a major food and medicinal resource plan found in Korea. The methanol extracts of *Artemisia capillaries* were used for the evaluation of DPPH(2,2-diphenyl- 1-picrylhydrazyl) scavenging, total phenolic content, total flavonoid content, hydroxyl radical (OH) scavenging, reducing power assay as antioxidant activity, as well as anticancer activities using MTT assay. As a result, the *Artemisia capillaries* extracts exhibited potential antioxidant activity and anticancer activity in vitro. These results suggest that the *Artemisia capillaries* extracts have a potential alleviated oxidation process, cell motility activity, and tumorigenesis (Jung et al., 2008).

Derris scandens

The ethanolic extract of the medicinal plant, Derris scandens Benth has been identified as a potent radiosensitizer of human colon cancer HT29 cells. Cell death mechanisms underlying radiosensitization activity of *D. scandens* extract was further identified. The study showed that treatment of HT-29 cells with *D. scandens* extract in combination with gamma irradiation synergistically sensitizes HT-29 cells to cell lethality by apoptosis and mitotic catastrophe. Moreover, the extract was found to decrease Erk1/2 activation. This

study concludes that *D. scandens* extract mediates radiosensitization via at least two distinct modes of cell death and silences pro-survival signaling in HT-29 cells (Arunee et al., 2014).

Goniothalamus macrophyllus

Goniothalamus is a medicinal plant belonging to the Annonacae family; contains substances which possess anticancer properties towards several tumor cell lines. Goniothalamin, a natural compound extracted from Goniothalamus sp. Apoptosis induction by goniothalamin in the Hela cervical cancer cell line was observed by MTT assay method. The IC50 value of goniothalamin was 3.2±0.72 μg/ml. It was concluded that morphological changes and biochemical processes associated with apoptosis were evident on phase contrast microscopy and fluorescence microscopy. DNA damage, DNA fragmentation, caspase-9 activation and a large increase in the sub-G1 and S cell cycle phases confirm the happening of apoptosis in a time-dependent manner. The study there showed that goniothalamin possesses a promising cytotoxicity effect against cervical cancer cells (Hela) and the cell death mode induced by goniothalamin was apoptosis (Aied et al., 2013).

Angelica sinensis

Angelica sinensis polysaccharide, a major active component in Dong quai (Chinese *Angelica sinensis*), effectively inhibited human acute myelogenous leukemia CD34+CD38 cell proliferation *in vitro* culture in a dose-dependent manner. Moreover, *Angelica sinensis* polysaccharide exerted cytotoxic affects on acute myelogenous leukemia K562 cells, especially LSC-enriched CD34+CD38 cells. Colony formation assays further showed that acute myelogenous leukemia significantly suppressed the formation of colonies derived from acute myelogenous leukemia CD34+CD38 cells but not those from normal CD34+CD38 cells. *Angelica sinensis* polysaccharide induced CD34+CD38– cell senescence, which was strongly related with a series of characteristic events, including up-regulation of p53, p16, p21, and Rb genes and changes of related cell cycle regulation proteins P16, P21, cyclin E and CDK4, telomere end attrition as well as repression of telomerase activity. On the basis of these findings, it was concluded that *Angelica sinensis* polysaccharide represents a potentially important agent for leukemia stem cell-targeted therapy (Jun et al., 2013).

Atractylis lancea (Thunb.) DC. an important medicinal herb in Asia, has been shown to have anti-tumor effects on cancer cells. The potential effects and molecular mechanisms of *Atractylis lancea* was evaluated *in vitro* on the proliferation of the Hep-G2 liver cancer cell line. Cell viability was determined by MTT test in Hep-G2 cells incubated with an ethanol extract of Atractylis lancea. Then, the effects of *Atractylis lancea* on apoptosis and cell cycle progression were investigated by flow cytometry. Results show that *Atractylis lancea* effectively inhibits proliferation in Hep-G2 cells in a concentration- and time-dependent manner. Apoptosis was induced by *Atractylis lancea* via arresting the cells in the G1 phase. Moreover, *Atractylis lancea* effectively reduced telomerase activity through inhibition of mRNA and protein expression. The study therefore, demonstrated that *Atractylis lancea* exerts anti-proliferative effects in Hep-G2 cells (Wei et al., 2013).

Phyllanthus emblica

Phyllanthus emblica is known to exhibit various pharmacological properties. Antimetastatic potential of a *Phyllanthus emblica* aqueous extract was evaluated. Cytotoxicity to human fibrosarcoma cells, HT1080, was assessed by viability assay using the 3-(4,5-dimethylthiazol,2-yl)-2,5-diphenyltetrazolium bromide (MTT) reagent. Cell migration, cell attachment onto normal surfaces of cell culture plates, the molecular mechanism of antimetastatic activity were investigated using chemotaxis chambers containing membranes pre-coated with collagen IV, measuring the gene expression of matrix metalloproteinases, MMP2, and MMP9, using reverse transcription-polymerase chain reaction (RT-PCR) assay respectively. The result of the study showed that *Phyllanthus emblica* extract reduces cell proliferation, migration, invasion, and adhesion in both dose- and time-dependent manners, especially growth arrest with low IC50 value (Waraporn et al., 2013).

Astragalus membranaceus

Astragalus membranaceus, a commonly used Chinese medicinal plant, has been shown to restore the impaired T cell functions in cancer patients. The *in vitro* and *in vivo* anti-tumor effects of root of *A. membranaceus* were investigated. Five bioactive fractions were isolated, the fraction designated as AI was found to be the most active among the five fractions with respect to its mitogenicity on murine splenocytes. Its cytostatic activities, macrophage function, tumor necrosis factor production, induction of lymphokine-activated killer cell and tumor cell differentiation were examined. Cytostatic activity of AI against the macrophage-like tumors and the myeloid tumors were found to be more sensitive, whereas the fibroblast-like tumors and the mouse Ehrlich ascites tumor appeared to be relatively resistant. Moreover, AI could effectively suppress the *in vivo* growth of syngeneic tumor in mice. Collectively, the results showed that *A. membranaceus* could exhibit both *in vitro* and *in vivo* anti-tumor effects, which might be due to the anti-tumor immune mechanism of the host (William et al., 2007).

Beta vulgaris

In vitro inhibitory effect of *Beta vulgaris* (beet) root extract on Epstein-Barr virus early antigen (EBV-EA) was evaluated. The result showed high order of activity compared to capsanthin, cranberry, red onion skin and short and long red bell peppers. An *in vivo* anti-tumor activity evaluated against the mice skin and lung bioassays. Result also revealed a significant tumor inhibitory effect. The combined findings suggest that *Beta vulgaris* (beetroot) ingestion can be one of the useful means to prevent cancer (Kapadia et al., 1996).

Camellia sinensis

Green tea is an aqueous infusion of dried unfermented leaves of Camellia sinensis (Family Theaceae) possesses numerous biological activities including antimutagenic, antibacterial, hypocholesterolemic, antioxidant, antitumor and cancer preventive activities. It has been reported that green tea leaves contains six compounds (+)-gallocatechin (GC), (-)-epicatechin (EC), (-)-epigallocatechin (EGC), (-)-epicatechin gallate (ECG), (-)-epigallocatechin gallate (EGCG) and caffeine. These compounds were tested against four human tumor cells lines such as (MCF-7 breast carcinoma, HT-29 colon carcinoma, A-427 lung carcinoma and UACC-375 melanoma). EGCG, GC and EGC found to be most potent against all four tumor cell lines. In view of these extensive *in vitro* studies, it would be of considerable interest to evaluate all three of these components in animal tumor model systems before final decisions are made concerning which of these potential chemopreventive agent should be taken into broad clinical trials (Valcis et al., 1996).

Camptotheca acuminate

Camptothecin (CPT) is an anticancer and antiviral alkaloid isolated from Chinese tree Camptotheca acuminata (Nyssaceae). Several attempts have been made to produce CPT from cell suspensions. The hairy roots of Camptotheca acuminata produce and secrete Camptothecin as well as the more potent and less toxic natural derivative, 10- hydroxycamptothecin, into the medium (Lorence, 2004).

Boerhaavia diffusa

Boerhaavia diffusa (Linn.) (Syn. *B. repens* L.; *B. procumbens Roxb*) commonly known as "Punarnava" in indian system of medicine is a perennial creeping herb belong to family Nyctaginaceae. Its ethanol extract showed cytotoxic effect against Hela cell lines and inhibit the S-phase of the cell cycle. It also inhibits the growth of cancer cells in DMBA- induced cancer carcinogenesis in mice through free radical scavenging mechanism (Bharali et al., 2003).

Solanum nigrum

Solanum nigrum Linn. belongs to family Solanaceae commonly known as black nightshade, Makoy and deadly night shade. It possesses no. of medicinal properties like antimicrobial, anti-oxidant, cytotoxic properties, antiulcerogenic, and hepatoprotective activity. *Solanum nigrum* is a potential herbal alternative as anti-cancer agent and its one of the active principle Diosgenin reported to be responsible for this action.

A Hela cell is an immortal cell line used in medical research. The cell line was derived from cervical cancer cells of Henrietta Lacks, who died from her cancer in 1951. At first, the cell line was said to be named after a "Helen Lane" in order to preserve Lacks's anonymity. Anticancer activity of *Solanum nigrum* was evaluated. The methanol extract of the fruit of *Solanum nigrum* was tested for its inhibitory effects on the Hella cell line and vero cell line by SRB assay and MTT assay in concentration range between 10mg/ml to 0.0196mg/ml. Both the assay shows significant cytotoxic effects on the Hella cell line and little effect on Vero cell line (Patel et al., 2009). This shows that *Solanum nigrum* may indeed have potential as an anticancer herb.

Woodfordia fruticosa

The *in vitro* cytotoxic activity of the 95% ethanol extract, 50% ethanol extract and hot water extract of *woodfordia fruticos*a at 100ug/100ml was evaluated by SRB assay against six human cancer cell lines viz ., lung cancer cells (A-459, NCI-H23), colon cancer cells (COLO-205, SW-620), Liver cancer cells (HEP-2) and Neuroblastoma cancer cells (SK-N-MC). It was demonstrated by the result that the 95% ethanol extract from the flowers of plants showed cytotoxicity against two cancer cell lines viz., HEP-2 and SK-N-MC and did not give any significant activity against other four human cancer cell lines. While the other two extract 50% ethanol and hot water extract did not give any cytotoxic activity against human cancer cell lines (Sharma et al., 2011). The study shows that *Woodfordia fruticos*a possess the cytotoxic potential.

Glochidion zeylanicum

The plant *Glochidion zeylanicum* (Euphorbiaceae) commonly named as Neeru in traditional system of medicine plays an important role in curing many diseases like cancer, stomachic, diabetes, refrigerant. The previous studies have shown that potential anti-tumor activity of lupane type triterpinoids from stem bark of Glochidion zeylanicum, and Glochidionisides A-D, Megastigmane glycosides from the leaves of Glochidion zeylanicum. The *in vitro* cytotoxic activity of the methanol extract of the roots of *Glochidion zeylanicum* was evaluated against human cancer cell lines Hep G2, HT-29 and PC-3. The study shows that the methanol extract of root of Golichidion zeylanicum possess cytotoxic potential in a concentration dependent manner and give significant cytotoxic activity on PC-3 cell lines (Sharma et al,2011). However, further study may still be necessary to evaluate the chemical nature and the active principle of the root which is responsible for its activity.

Acanthus ilicifolius

In vivo anticancer activity of the whole plant of Acanthus ilicifolius was evaluated using different extract and fractioned by comet assay against Hela and KB cell lines. The extracts were fractioned with ethyl acetate, acetone and water. The data demonstrated that ethylacetate extract of the whole plant of Acanthus ilicifolius has a potential cytotoxic activity on Hela cell and KB cell lines (Kajure et al., 2011).

Cucurbita maxima

In vivo methanol extract of the aerial part of *Cucurbita maxima* was studied for anticancer activity against Ehrlich ascities carcinoma cells in mice. Oral administration of the methanol extract of the *Cucurbita maxima* at a dose of 200mg/kg and 400mg/kg give the cytotoxicity against the Ehrlich ascities carcinoma cells in mice in dose dependent manner (Saha et al., 2011).

Parthenium hysterophorus

The methanol and acetone extract of the flowers of *Parthenium hysterphorus* were studied for *in vitro* anticancer activity against the A-549 (Lung adenocarcinoma) cell lines by MTT assay and Tryphan blue exclusion assay. In this study result shows that acetone extract of *Parthenium hysterphorus* give greater anticancer activity compare to methanol extract (Kumar et al., 2011).

Inonotus obliquus

The Chaga mushroom (*Inonotus obliquus*) has been used traditionally as a medicine to treat cancers. It is hypothesized that the pure compounds (3β-hydroxy-lanosta-8, 24-dien-21-al, inotodiol and lanosterol, respectively) isolated from *I. obliquus* would inhibit invivo tumor growth in Balbc mice bearing Sarcoma-180 cells (S-180) and growth of human carcinoma cells in vitro. To test this hypothesis, the growth inhibition of each subfraction isolated from *I. obliquus* were tested *in vitro* against human carcinoma cell lines (lung carcinoma A-549 cells, stomach adenocarcinoma AGS cells, breast adenocarcinoma MCF-7 cells, and cervical adenocarcinoma HeLa cells). The study showed that all of the subfractions isolated from *I. obliquus* possessess significant cytotoxic activity against the selected cancer cell lines. However *in vivo* results showed subfraction 1 at concentrations of 0.1 and 0.2 mg/mouse per day significantly decreased tumor volume by 23.96% and 33.71%, respectively, as compared with the control. Subfractions 2 and 3 also significantly slow down tumor growth in mice as compared with the control mouse tumor. The overall result of the study showed that Subfraction 1 from *I. obliquus* exhibited greater inhibition of tumor growth than subfractions 2 and 3, which agrees well with the *in vitro* results. The results suggest that *I. obliquus* could be used as natural anticancer ingredients in the food and/or pharmaceutical industry (Mijachung et al., 2010).

Citrus maxima

The methanol extract of the leaves of the Citrus maxima was evaluated for its anticancer activity at a dose of 200-400mg/kg against Ehrlich Ascities carcinoma cell lines in Swiss albino mice. Oral administration of the methanol extract of the leaves of Citrus maxima reverses the tumor parameters such as tumor volume, viable tumor cell count, and increase body weight, hematological parameters and life span. Therefore study show that methanol extract of the aerial part of Citrus maxima possess antitumor activity in a dose dependent manner (Kundusen et al., 2011).

Amaranthus paniculatus

Amaranthus paniculatus (Amaranthaceae) is commonly known as "Rajgira" in India and "Amaranth" in English. This plant is cultivated by Native Americans for several thousand years and now cultivated worldwide. It is the world's most nutritious plant and used traditionally for respiratory infections, vision defects, tuberculosis, fleshy tumors, liver complaints and inflammations. Sreelatha et al. (2012) investigate the antioxidant capacity and the possible protective effects of *Amaranthus paniculatus* leaves on the antioxidant defense system in Ehrlich's ascites carcinoma (EAC) -treated mice. The results of this study demonstrated the indirect inhibitory effect of the extract in EAC bearing group, which is probably mediated by the enhancement and deactivation of either macrophages or cytokine production. In addition, the result of the study had shown the anticancer effect of the ethanolic extract of *Amaranthus paniculatus* against EAC in swiss albino mice. Moreover a significant enhancement of mean survival time and decrease in tumor volume suggest the delaying impact of *Amaranthus paniculatus* in cell division. Cytological studies of Leishman-stained tumor cell smear also have revealed a decrease in the number of mitotic cells following *Amaranthus paniculatus* extract treatment when compared with that of EAC control (Sreelatha et al., 2012).

Curcuma longa

Anticancer potential of the rhizomes of turmeric (Curcuma longa) was evaluated *in vitro* using tissue culture methods and *in vivo* in mice using Dalton's lymphoma cells grown as ascites form. *C. longa* extract inhibited the cell growth in Chinese Hamster Ovary (CHO) cells at a concentration of 0.4 mg/ml and was cytotoxic to lymphocytes and Dalton's lymphoma cells at the same concentration. Cytotoxic effect was happened within 30 min at room temperature (30°C). Curcumin was found to be the active constituents of *C. longa* which showed cytotoxicity to lymphocytes and Dalton's lymphoma cells at a concentration of 4 mg/ml. Initial experiments indicated that *C. longa* extract and curcumin reduced the growth of animal tumours (Kuttan et al., 1985).

Cynara syriaca and Cynara cardunculus: Apoptotic and cytotoxic activity of plant extracts obtaining from *Cynara syriaca* in and *Cynara cardunculus* (artichoke species) against DLD1 colorectal cancer cells was determined. This paper was the first report, concerning with, positive effects of plant extracts obtained from two different artichoke species against to colorectal cancer cell line. In this study, their results demonstrated that artichoke extracts had inhibitory effects on the proliferation of human colorectal cancer DLD1 cells. Extracts not only hold back cell proliferation but also induce apoptotic pathway on DLD1 cells (Simsek et al., 2013).

Withania somnifera

Withania somnifera (L.) family (Solanaceae) Dunal (also known as ashwagandha), is a medicinal plant having antitumor, anti-aging, anti-stess, anti-oxidant and immunomodulatory properties. *In vitro* cytotoxicity of the ethanol extracts of root, stem and leaves of *Withania somnifera* was evaluated against five human cancer cell lines of four different tissues i.e, Pc-3, DU-145(Prostrate), HCT- 15(colon), A-549(Lung) and IMR-32(Neuroblastoma).50% ethanol extract showed the significant anticancer activity of different parts of *Withania somnifera*. But the 50% ethanol extract of the leaves of *Withania somnifera* give the maximum activity against the cell lines compare to other two parts i.e, root and stem (Yadav etal., 2010).

Melissa officinalis

Melissa officinalis L. commonly known as lemon balm is one of the most used medicinal plants in Europe and the Mediterranean region, as a herbal tea for its aromatic, digestive and antispasmodic properties in nervous disturbance of sleep and functional gastrointestinal disorders. Saraydin. et al (2012) investigated the antiproliferative properties of *Melissa officinalis* from Turkey on breast cancer. *Melissa officinalis* showed cytotoxicity against three cancer cell lines, inducing increase in Annexin-positive cells. Furthermore, study showed that mean tumor volume inhibition ratio in *Melissa officinalis* treated group was 40% compared with the untreated rats. This study confirmed that *Melissa officinalis* extracts have antitumoral potential against breast cancer (Saraydin et al., 2012).

Curcuma zedoaria

Curcuma zedoaria belonging to the family Zingiberaceae has been used in the traditional system of medicine in treating many human ailments and is found to possess many biological activities. Isocurcumenol was characterized as the active compound of *C. zedoaria* and was found to inhibit the proliferation of cancer cells without inducing significant toxicity to the normal cells. *In vivo* tumour reduction studies of *C. zedoaria* revealed that a dose of 35.7mg/kg body weight significantly reduced the ascitic tumour in DLA-challenged mice and increased the lifespan with respect to untreated control mice (Lakshmi et al., 2011).

Daucus carota

Three constituents, epilaserine, β-sitosterol and laserine were obtained from the lipophilic fraction of *Daucus carota*. Among the 3 constituents, epilaserine showed significantly inhibitory activity against leukemia cell, HL-60 (Jing et al., 2008).

Rubia cordifolia

Rubia cordifolia Linn, which belongs to the Rubiaceae family, is a well-known herb used in Ayurvedic medicine. Shilpa. et al (2012) investigated the influence of a methanolic extract of *Rubia cordifolia* on the induction of apoptosis in HEp-2 (human laryngeal carcinoma) cell line. *Rubia cordifolia* extract decrease the viability of HEp-2 cell lines in a dose- dependent manner and induced apoptosis. Antiproliferative effect was confirmed by, cell viability quantified by MTT assay. A dose and time dependent fall in mitochondrial activity was noted in HEp-2 cell line showing IC50 at 10mg/ml. Further studies are needed to confirm this effect as the present work opens new perspectives for cancer treatment based on ethnopharmacological studies (Shilpa et al., 2012).

Avicennia officinalis

Avicennia officinalis is an ever green tree found infrequently on the banks of river and rarely found near the sea. Fruits are used to treat boils and tumours. Poultice of unripe seed stop inflammation, roots used for its aphrodisiac, bark is used to treat skin especially scabies, resins for snake bite and contraceptive by women, seed for ulcers. Research revealed that plant contains pentacyclic triterpenoids such as lupeol, betulin, betulinaldehyde, betulinicacid, beta-sitosterol and Iridoid glucosides having c-11 carboxylic acid group were also present and other compounds present are flavanoids, alkaloid, steroids, tannins, wax esters are the most considerable compounds.

The *in vivo* cytotoxic activity of the methanol extract of the leaf of Avicennia officinalis was studied against Ehrlich Ascties Carcinoma cell lines in Rodents. Result demonstrated that the oral administration of the methanol extract of the leaf of Avicennia officinalis at a dose of 200mg/kg and 400mg/kg give the anticancer activity and reverse the hematological changes induced by cell lines. Therefore result show the cytotoxic potential in the methanol extract of the leaves of Avicennia officinalis in dose dependent manner (Sumithra et al., 2011)

Glycyrrhiza glabra

Licochalcone (LA) is a novel estrogenic flavonoid isolated from *Glycyrrhiza Glabra* showed significant antitumor activity in various malignant human cell lines. Evaluation of its anti-cancer activities were carried out in LA-elicited growth control and induction of apoptosis using androgen- independent p53-null PC-3 prostate cancer cells. Licochalcone induced modest level of apoptosis but had more pronounced effect on cell cycle progression arresting cells in G2/M, accompanied by suppression of cyclin B1 and cdc2. It also inhibited phosphorylation of Rb, decreased expression of transcription factor E2F concurrent with reduction of cyclin D1, down-regulation of CDKs 4 and 6, but increased cyclin E expression. These findings provide mechanistic explanation for Licochalcone activity and suggest that it possess chemopreventive potential and its anticancer effect should be further explored (Yue fu et al., 2009).

Nigella sativa

Anticancer activity of the methanol extract of the seeds of *Nigella sativa* was evaluated by MTT assay on different cancer and normal cell lines such as HL-60, U-973 AND HEK 293T. It was demonstrated by the result that methanol extract of the *Nigella sativa* seeds possess potent inhibitory activity against Hl-60 and U-937 cell lines (Raval et al., 2010).

Hydrastis canadensis

Ethanolic extract of Hydrastis canadensis has been evaluated for its anti-cancer potentials against p-dimethylaminoazobenzene (p-DAB) induced hepatocarcinogenesis in mice. Analysis of results of this study shows anti-cancer potentials of the drug and suitable for use as a supportive complementary medicine in liver cancer (Karmakar et al., 2010).

Larrea divaricata

The aqueous extract of *Larrea divaricata* has an antiproliferative activity on T lymphoma (BW 5147) cells in culture. Moreover the effect of an extract of *Larrea divaricata* was studied on a mammary carcinoma chemically induced with N-nitrosomethylurea in female rats. The extract was administered at a dose of 250

mg/kg three times each week by two different routes, subcutaneous (s.c.) and intratumoral (i.t.). The result showed that the aqueous extract of this plant possess an *in vivo* antitumor activity with the intratumor route being most effective in tumor regression (Anesini et al., 2011).

Lycopersicum esculentum

The cytotoxicity effect of methanol extract of leaves of tomato (*Lycopersicum esculentum*) was evaluated on cancer cells (MCF-7 breast cancer cell lines and Vero cells using *in vitro* cytotoxicity assay to indicate its active fractions and its half maximal inhibitory concentration (IC50). Purified sample gave a potential effect towards MCF-7 breast cancer cells with IC50 value of 5.85 µg mL- (Chick et al., 2010)

Panax ginseng

Panax ginseng (Ginseng) is traditionally used in most of the parts of world as a popular remedy for various diseases including cancer. It was reported that the ginsenoside Rp1, a compound isolated from ginseng, reduces cancer cell proliferation through inhibition of the insulin-like growth factor 1 receptor (IGF-1R)/Akt pathway. Its efficacy was first tested against human breast cancer cell lines. The result showed treatment with Rp1 significantly inhibited breast cancer cell proliferation and inhibited both anchorage dependent and independent breast cancer cell colony formation. In addition, to this treatment with 20 µM Rp1 causes cycle arrest and apoptosis- mediated cell growth suppression. Findings suggested that Rp1 reduced the stability of the IGF- 1R protein in breast cancer cells. Therefore, it is concluded that Rp1 has potential as an anticancer drug and that IGF-1R is an important target for treatment and prevention of breast cancer (Kang et al., 2011).

Pfaffia paniculata

Roots of *Pfaffia paniculata* have been well documented for several therapeutic effects and have also been used for cancer therapy in folk medicine. It anticancer activity was evaluated against human breast tumor cell line and the MCF-7 cells. Butanolic extract of the roots of *P. paniculata* showed cytotoxic effect against MCF-7 cell line. The results show that this butanolic extract indeed presents cytotoxic substances; further investigations are required to explore the active principle and its mechanism of action (Nagamine et al., 2009).

Polygonum multiflorum

Three anthraquinones, physcion, emodin, and questin were isolated from the methanolic extract of the roots of Polygonum multiflorum Thunb. (Polygonaceae). Research revealed emodin and questin strongly inhibited the growth of human colon cancer cells (Choi et al., 2007).

Ricinus communis

Ricin A is a newly isolated lectin from Ricinus communis which has a strong inhibitory effect on the growth of tumor cells. By using cell cultures, it was found that the tumor cells were more sensitive to lectin than non-transformed cells, and that this could be due to higher binding affinity of lectin to tumor cells than to non- transformed cells (Lin et al., 1986).

Barley and wheat

A unique 43 amino acid, Lunasin, 4.8 kDa isolated from barley and wheat is a cancer-chemopreventive peptide. It has been shown to be cancer- chemopreventive in mammalian cells and in a skin cancer mouse model against oncogenes and chemical carcinogens (Jeong et al., 2007).

Tabebuia avellanedae

The DNA topoisomerase inhibitor β-lapachone is a quinone isolated from the bark of the lapacho tree (*Tabebuia avellanedae*) in South America. It has been reported to possess a numerous of biological activities, and is a promising cancer chemopreventive agent. The effects of β- lapachone on the growth of the human hepatoma cell line HepG2 were investigated. The results showed that β-lapachone inhibits the viability of HepG2 by inducing apoptosis, as evidenced by the formation of apoptotic bodies and DNA fragmentation. Reverse transcription-polymerase chain reaction and immunoblotting results suggested that treatments of cells with β-lapachone resulted in down-regulation of anti-apoptotic Bcl-2 and Bcl-XL and up-regulation of pro-apoptotic Bax expression. β-Lapachone- induced apoptosis was associated with a proteolytic activation of caspase-3 and -9 and degradation of poly (ADP-ribose) polymerase protein. The study therefore indicated that β-lapachone possess potential chemopreventive effect for liver cancer (Hyun et al., 2006).

Vitis vinifera

Proanthocyanidins (PAs), also known as condensed tannins, are naturally occurring oligomers and polymers of flavan-3-ol monomer units widely found Grape seeds (*Vitis vinifera* L.) which have been used as nutritional supplements and, as antioxidants, to prevent atherosclerosis and cardiovascular diseases. Proanthocyanidins shows the anti mutagenic activity (De Rezender et al., 2009). Antitumor and antioxidant activity of ethanolic extract of *Vitis vinifera* L. leaves were evaluated against Ehrlich ascites carcinoma (EAC) induced in Swiss albino mice. The antitumor effect and antioxidant role was determined by using tumor volume, packed cell volume and estimation of liver LPO and antioxidant enzymes such as SOD, CAT. Treatment with extract at a dose of 200 and 400 mg/kg increased mean survival time, decreased the levels of LPO and increased the levels of superoxide dismutase, catalase. The results suggest that ethanolic extract of *Vitis vinifera* exhibited significant antitumor, antioxidant response in EAC tumor bearing mice (Mahadik et al., 2011).

Conclusion

Medicinal plants have been used for the cure of different ailments including cancer for thousands of years. Large numbers of medicinal plants having anticancer properties are available in nature but they are not fully phytochemially investigated. It should be of particular

interest to explore the anticancer potential of the medicinal plants extracts for isolation and characterization of the active anticancer principles so that better, safer and cost effective drugs can be developed for treating cancer.

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