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A COMPREHENSIVE REVIEW ON CANCER AND ANTICANCER HERBAL DRUGS

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ABSTRACT: Cancer is a major public health burden in both developed and developing countries. It is an abnormal growth of cells in body that can lead to death and globally the numbers of cancer patients are increasing day by day. There are several medicines available in the market to treat the various types of cancer but no drug is found to be fully effective and safe. Herbal medicines have a vital role in the prevention and treatment of cancer. With advanced knowledge of molecular science and refinement in isolation and structure elucidation techniques, various anticancer herbs has been identified, which execute their therapeutic effect by inhibiting cancer-activating enzymes and hormones, stimulating DNA repair mechanism, promoting production of protective enzymes, inducing antioxidant action and enhancing immunity of the body. Plants have been used for treating diseases since time immemorial. More than 50% of modern drugs in clinical use are of natural products. In the present review, an attempt has been made to study the plants that have been used in the treatment of cancer.

INTRODUCTION: Natural products especially plants have been used for the treatment of various diseases for thousands of years. Terrestrial plants have been used as medicines in Egypt, China, India and Greece from ancient times and an impressive number of modern drugs have been developed from them. The first written records on the medicinal uses of plants appeared in about 2600 BC from the Sumerians and Acadians [1]. According to World Health Organization, 80% of the people living in rural areas depend on medicinal herbs as primary healthcare system. The synthetic anticancer remedies are beyond the reach of common man because of cost factor.

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Herbal medicines have a vital role in the prevention and treatment of cancer and medicinal herbs are commonly available and comparatively economical. A great deal of pharmaceutical research done in technologically advanced countries like USA, Germany, France, Japan and China has considerably improved quality of the herbal medicines used in the treatment of cancer. Some herbs protect the body from cancer by enhancing detoxification functions of the body.

Certain biological response modifiers derived from herbs are known to inhibit growth of cancer by modulating the activity of specific hormones and enzymes. Some herbs reduce toxic side effects of chemotherapy and radiotherapy. Scientists all over the world are concentrating on the herbal medicines to boost immune cells of the body against cancer. By understanding the complex synergistic interaction of various constituents of anticancer herbs, the herbal formulations can be designed to attack the cancerous cells without harming normal

cells of the body [2, 3]. Today, despite considerable efforts, cancer still remains an aggressive killer worldwide. Moreover, during the last decade, novel synthetic chemotherapeutic agents currently in use clinically have not succeeded in fulfilling expectations despite the considerable cost of their development. Therefore there is a constant demand to develop new, effective, and affordable anticancer drugs [4]. From the dawn of ancient medicine, chemical compounds derived from plants have been used to treat human diseases. Natural products have received increasing attention over the past 30 years for their potential as novel cancer preventive and therapeutic agents [5, 6].

The increasing costs of conventional treatments (chemotherapy and radiation) and the lack of effective drugs to cure solid tumours encouraged people in different countries to depend more on folk medicine which is rooted in medicinal plants use. Such plants have an almost unlimited capacity to produce substances that attract researchers in the quest for new and novel chemotherapeutics. Of over 2069 anti-cancer clinical trials recorded by the National Cancer Institute as being in progress as of July 2004, over 160 are drug combinations including these agents against a range of cancers [7].

Cancer: Cancer is a general term applied of series of malignant diseases that may affect different parts of body. These diseases are characterized by a rapid and uncontrolled formation of abnormal cells, which may mass together to form a growth or tumour, or proliferate throughout the body, initiating abnormal growth at other sites. If the process is not arrested, it may progress until it causes the death of the organism. The main forms of treatment for advance stage cancer in humans are surgery, radiation and drugs (cancer chemotherapeutic agents). Cancer chemo-therapeutic agents can often provide temporary relief of symptoms, prolongation of life, and occasionally cures [8]. Many hundreds of chemical variants of known class of cancer chemotherapeutic agents have been synthesized but have a more side effects. A successful anticancer drug should kill or incapacitate cancer cells without causing excessive damage to normal cells. This ideal is difficult, or perhaps impossible, to attain and is why cancer patients frequently suffer unpleasant side effects when under-going treatment.

Synthesis of modifications of known drug continues as an important aspect of research. However, a waste amount of synthetic work has given relatively small improvements over the prototype drugs. There is a continued need for new prototype-new templates to use in the design of potential chemotherapeutic agents: natural products are providing such templates. Recent studies of tumour-inhibiting compound of plant origin have yielded an impressive array of novel structures. Many of these structures are extremely complex, and it is most unlikely that such compounds would have been synthesized in empirical approaches to new drugs [9].

Ayurvedic Concept of Cancer: Charaka and Sushruta Samhita [10,11] both described the equivalent of cancer as "granthi" and "arbuda" [12]. "Granthi" and "Arbuda" can be inflammatory or devoid of inflammation, based on the doshas involved [13]. Three doshas "Vata, Pitta and Kapha" in body are responsible for disease and the balanced coordination of these doshas in body, mind and consciousness is the Ayurvedic definition of health [14]. Tridoshicarbudas are usually malignant because all three major body humors lose mutual coordination, resulting in a morbid condition [15].

Neoplasm can be classified in Ayurveda depends upon various clinical symptoms in relation to tridoshas.

Group I: Diseases that can be named as clear malignancies, including arbuda and granthi, such as mamsarbuda (sarcomas) and raktarbuda (leukaemia), mukharbuda (oral cancer), and asadhya vrana (incurable or malignant ulcers).

Group II: Diseases that are not cancers but can be considered probable malignancies, such as ulcers and growths. Examples of these are mamsaja oshtharoga (growth of lips), asadhya galganda (incurable thyroid tumour), tridosaja gulmas, and asadhya udara roga, (abdominal tumours like carcinomas of the stomach and liver or lymphomas).

Group III: Diseases in which there is a possibility of malignancy, such as visarpa, asadhya kamala (incurable jaundice), asadhya pradara (intreatable sinusitis) [16-18].

Types of Cancers: [19]

1) Cancers of Blood and Lymphatic Systems:

a) Hodgkin's disease
b) Leukemia's
c) Lymphomas
d) Multiple myeloma
e) Waldenstrom's disease

2) Skin Cancers:

a) Malignant Melanoma

3) Cancers of Digestive Systems:

a) Esophageal cancer
b) Stomach cancer
c) Cancer of pancreas
d) Liver cancer
e) Colon and Rectal cancer
f) Anal cancer

4) Cancers of Urinary system:

a) Kidney cancer
b) Bladder cancer
c) Testis cancer
d) Prostate cancer

5) Cancers in Women:

a) Breast cancer
b) Ovarian cancer
c) Gynecological cancer
d) Choriocarcinoma

6) Miscellaneous Cancers:

a) Brain cancer
b) Bone cancer
c) Characinoid cancer
d) Nasopharyngeal cancer
e) Retroperitoneal sarcomas
f) Soft tissue cancer
g) Thyroid cancer

Causes of Cancer: Modern medicine attributes most cases of cancer to changes in DNA that reduce or eliminate the normal controls over cellular growth, maturation, and programmed cell death. These changes are more likely to occur in people with certain genetic backgrounds (as illustrated by the finding of genes associated with some cases of cancer and familial prevalence of certain cancers) and in persons infected by chronic viruses (*e.g.*, viral hepatitis may lead to liver cancer; HIV may lead to lymphoma). The ultimate cause, regardless of genetic propensity or viruses that may influence the risk of the cancer, is often exposure to carcinogenic chemicals (including those found in nature) and / or to radiation (including natural cosmic and earthly radiation), coupled with a failure of the immune system to eliminate the cancer cells at an early stage in their multiplication. The immunological weakness might arise years after the exposure to chemicals or radiation. Other factors such as tobacco smoking, alcohol consumption, excess use of caffeine and other drugs, sunshine, infections from such oncogenic virus, like cervical papilloma viruses, adenoviruses Karposis sarcoma (HSV) or exposure to asbestos. These obviously are implicated as causal agents of mammalian cancers.

However a large population of people is often exposed to these agents. Consequently cancer cells continue to divide even in situations in which normal cells will usually wait for a special chemical transduction signal. The tumour cells would ignore such stop signals that are sent out by adjacent tissues. A Cancer cell also has the character of immortality even *in vitro* whereas normal cells stop dividing after 50-70 generations and undergoes a programmed cell death (Apoptosis). Cancer cells continue to grow invading nearby tissues and metastasizing to distant parts of the body. Metastasis is the most lethal aspect of carcinogenesis [20].

Environmental factors which, from a scientist's standpoint, include smoking, diet, and infectious diseases as well as chemicals and radiation in our homes and workplace along with trace levels of pollutants in food, drinking water and in air. Other factors which are more likely to affect are tobacco use, unhealthy diet, not enough physical activity, however the degree of risk from pollutants depends on the concentration, intensity and exposure. The cancer risk becomes highly increased where workers are exposed to ionizing radiation, carcinomas chemicals, certain metals and some other specific substances even exposed at low levels. Passive tobacco smoke manifold increase the risk in a large population who do not smoke but exposed to exhaled smoke of smokers [21].

The Mechanism on Cancer Therapy: [22]

1. Inhibiting cancer cell proliferation directly by stimulating macrophage phagocytosis, enhancing natural killer cell activity.
2. Promoting apoptosis of cancer cells by increasing production of interferon, interleukin-2 immunoglobulin and complement in blood serum.
3. Enforcing the necrosis of tumour and inhibiting its translocation and spread by blocking the blood source of tumour tissue.
4. Enhancing the number of leukocytes and platelets by stimulating the hemopoietic function.
5. Promoting the reverse transformation from tumour cells into normal cells.
6. Promoting metabolism and preventing carcinogenesis of normal cells.
7. Stimulating appetite, improving quality of sleep, relieving pain, thus benefiting patient's health.

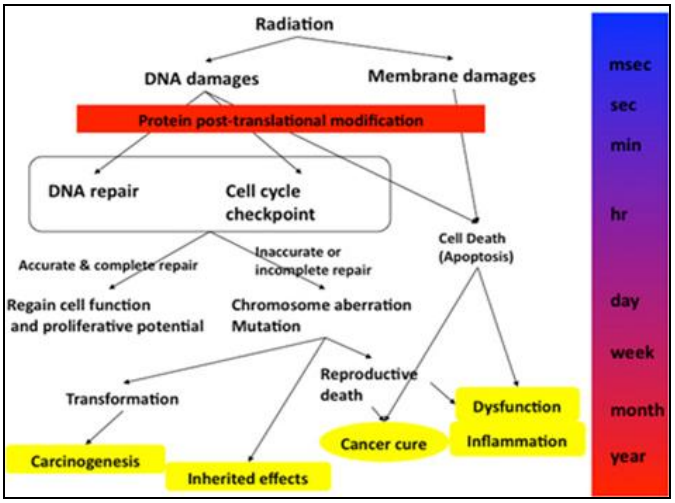

FIG. 1: THE MECHANISM ON CANCER THERAPY

Oncogenes and Tumor Suppressor Genes: Two sets of genes are controlling cancer development [7]. Oncogenes are the first set of genes and are involved in different cell activities including cell division. However, over expression of these genes transforms a normal cell into a cancer cell. On the other hand, the second set of genes (tumor suppressor genes) inhibits cancer cell formation by different mechanisms.

Tumour suppressor genes are under expressed in cancer cells while, oncogenes are over expressed [23]. Summarizes the main oncogenes and tumour suppressor genes and their role in cancer development. Oncogenes and their products represent good targets for Cancer therapy. Other targets include enzymes involved in cell division like topoisomerases that unwind the DNA during replication. The diversity of plant derived natural products can provide therapeutic products attacking different targets in cancer cells [24].

Herbs with Anticancer Activity:

***Actinidia chinensis*:** *Actinidia chinensis* root are used by the Chinese physicians in the treatment of cancer. *Actinidia chinensis* contains a polysaccharide known as "ACPSR" that possesses immune-enhancing and anticancer activities [25].

***Aegle marmelos*:** Lupeol, isolated from *Aegle marmelos*, possesses strong anticancer activity against breast cancer, malignant lymphoma, malignant melanoma, malignant ascites and leukaemia. *Aegle marmelos* possesses significant antioxidant activity and reduces side effects of chemotherapy and radiotherapy [26].

***Agave americana*:** The ethanolic extract of *A. americana* leaves has a cytotoxic and antitumor activity. Leaf contains steroidal saponin, alkaloid, coumarin, isoflavonoid, hecogenin and Vitamins (A, B, C). Therefore, this plant has potential to be utilized for the development of novel anticancer drug leads [27].

***Allium sativum*:** *Allium sativum* (garlic, lasun) is used to treat a wide variety of diseases in India. Allicin is a major component of raw garlic and ajoene is a product of the rearrangement of allicin. Its cytotoxic effect has been tested using human primary fibroblasts, a permanent, nontumorgenic cell line derived from baby hamster kidney cells and a tumorgenic lymphoid cell line derived from a Burkitt lymphoma. The cytotoxic action was in the range 2-50 μg/ml [28]. Some organo-sulfur compounds from garlic, like S-allylcysteine, are reported to retard the growth of chemically induced and transplantable tumors in several animal models [29]. Administration of garlic (250 mg/kg, p.o., thrice a week) in male wistar rats, has been significantly suppressed 4-nitro quinoline-1-oxide induced

tongue carcinogenesis as revealed by the absence by the carcinomas in the initiation phase and their reduced incidence in the post initiation phase [30].

***Aloe vera*:** *Aloe vera* contains aloe-emodin, which activates the macrophages to fight cancer. *Aloe vera* also contains acemannan, which enhances activity of the immune cells against cancer [31]. *Aloe vera* is found to inhibit metastases [32].

***Alpinia galangal*:** Acetoxy-chavicol-acetate (ACA), isolated from *Alpinia galanga*, possesses significant anticancer activity against cancers of breast, lung, stomach, colon, prostate, multiple yeloma and leukaemia. Pinocembrin isolated from *Alpinia galanga* inhibits growth and 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 [33].

***Amoora rohituka*:** Amooranin (a triterpene acid), isolated from *Amoora rohituka* inhibits growth and spread of breast and cervical cancers by arresting G2/M phase of the cell cycle and by inducing apoptosis. Amooranin and its derivatives are effective in both chemotherapy-sensitive and chemotherapy resistant cancers. Amooranin has the ability to overcome (reverse) multidrug resistance in breast cancer, colon cancer and leukaemia [34].

***Andrographis paniculata*:** Phytochemical investigation of the ethanol extract of the aerial parts of *Andographis paniculata* has been reported the isolation of 14 compounds; a majority of them are flavonoids and labdane diterpenoids. The cytotoxic activities of these compounds have been evaluated against various cell lines and found that these isolates have a potent tumour inhibitory activity against all investigated cell lines [35].

The methanol extract of *Andrographis paniculata* was fractionated, dichloromethane fraction reported to possess three active constituents which were further tested and exhibited cytotoxic activity and also potent immune stimulating activity [36]. However, there were also its adverse side effects were also reported which may include gastric upset, headache, bitter taste and fatigue. High doses of *Andographis paniculata* may have affect the normal functions of liver [37].

***Annona muricata*:** Graviola is known by its scientific name, *Annona muricata*. The important class of medicinal components found in graviola is acetogenins. Acetogenins was found in the fruit, seeds, leaves, and bark of the graviola plant. Preliminary research showed that acetogenins block production of adenosine triphosphate, which inhibits the pump that removes cancer drugs from the cell, allowing chemotherapy to be more effective. Furthermore, research suggested that acetogenin may have chemotherapeutic potential, especially against cancer that resistant to multiple drugs [38]. Parkinson like symptoms can occur on oral ingestion of graviola [39]. Some specific acetogenins have been reportedly identified to be toxic for various cancer cell lines like lung solid human-breast cancer, tumor carcinoma, pancreatic carcinoma, prostatic adenocarcinoma, colonic adenocarcinoma, human lymphoma, liver cancer, and multiple-drug resistant human-breast adenocarcinoma.

***Apis mellifera*:** *Apis mellifera* is the scientific name of honey bee, from which honey is produced. Honey is used to hasten healing of skin wounds, ulcerations, and burns in Indian system of medicine. A protein of the honeybee *Apis mellifera* has been reported to enhance proliferation of primary-cultured rat hepatocytes and also suppresses apoptosis [40]. It has also showed cytotoxicity in normal human lymphocytes and HL-60 cells.

Hamzaoglu *et al*., (2000) implanated cancer cell into neck wounds of mice, then divided mice into two groups. A significant decrease in wound cancer tumours were observed in the groups of mice that were treated with surgical wounds coated with honey pre and postoperatively. This finding may have some application in human surgery.

***Ananas comosus*:** *Ananas comosus* contains bromelain, which is a mixture of proteases and some other enzymes. Bromelain stimulates defence mechanism of the body against cancer by enhancing cytotoxic activity of the monocytes and

the macrophages, thus inhibiting growth of cancer. It is used in the treatment of leukaemia [41].

***Angelica sinensis*:** *Angelica sinensis* is used by the Chinese physicians to treat cancer of the cervix. The polysaccharide fraction of Angelica sinensis, known as "AR-4" possesses immune stimulating activities such as induction of interferon production, stimulation of the immune cell proliferation and enhancement of antitumour activity of the immune cell [42].

***Annona species*:** *Annona species* contain acetogenins, which possess significant cytotoxic activity against leukemia and sarcoma. Acetogenins are found to be effective in the treatment of nasopharyngeal carcinoma [43].

***Arctium lappa*:** *Arctium lappa* contains potent anticancer factors that prevent mutations in the oncogenes. It has been used in the treatment of malignant melanoma, lymphoma and cancers of the pancreas, breast, ovary, oesophagus, bladder, bile duct and the bone. A study revealed that it reduces the size of tumour, relieves the pain and prolongs the survival period [44].

***Artemisia asiatica*:** It has also been frequently used in traditional Asian medicine for the treatment of diseases involving inflammation, cancer, and microbial infection. An extract of *A. asiatica,* DA-9601, with ethanol, blocked TNF - mediated inflammatory signals by potentially modulating the p38 kinase pathway and / or a signal leading to NF-B-dependent pathways in gastric epithelial cells [45]. Another potential crude drug or crude drug element are red and white ginseng extract. Oral administration of red ginseng extracts (1% in diet for 40 weeks) in C3H/He male mice resulted in the significant suppression of spontaneous liver tumor formation. The average number of tumors per mouse in the control group and in the red ginseng extracts-treated group was 1.06 and 0.33 ($p < 0.05$), respectively. Incidence of liver tumor development was also lower in red ginseng extracts-treated group, although the difference from control group was not statistically significant. Like red ginseng extracts, white ginseng extracts have also shown anti-carcinogenic activity that is being investigated. In an ongoing study, the administration of white ginseng extracts was proven to suppress tumor promoter-induced phenomena *in vitro* and *in vivo*.

Interestingly, oral administration of a white ginseng-containing Chinese medicinal prescription known as ren-shen-yang rong-tang, resulted in the suppression of skin tumor promotion by 12-otetradecanoylphorbol-13 acetate in 7, 12-dimethylbenz[a] anthraceneinitiated CD-1 mice, suggesting the usefulness of ginseng in the field of cancer prevention [46]. Isoliquiritigenin is a natural flavonoid isolated from licorice, shallot and bean sprouts that has significantly inhibited, in a dose- and time dependent manner, the proliferation of cancer cells in the A549 human lung cancer cell line. Flow cytometric analysis demonstrated that isoliquiritigenin restrained the cell cycle progression at G2/M phase. Further examinations using cDNA arrays and real-time quantitative RTPCR revealed that isoliquiritigenin enhanced the expression of p21CIP1/WAF1, a universal inhibitor of cyclindependent kinases (CDKs).

These results suggest that isoliquiritigenin will be a promising agent for use in chemoprevention or therapeutics against lung cancer [47]. A pungent ingredient of hot chili peppers- capsaicin (8-methyl- Nvanillyl- 6- nonenamide), has been reported to possess substantial anticarcinogenic and anti-mutagenic activities; it can induce apoptosis in highly metastatic B16- F10 murine melanoma cells and, in a concentration dependent manner, inhibit their growth. A pro-apoptotic effect of capsaicin was also evidenced by nuclear condensation, internucleosomal DNA fragmentation, *in situ* terminal nick-end labeling of fragmented DNA (TUNEL), and an increased sub G1 fraction.

Treatment of B16-F10 cells with capsaicin caused, in a dose dependent manner, a release of mitochondrial cytochrome c, activation of caspase-3, and cleavage of poly (ADP-ribose) polymerase. Furthermore, Bcl-2 expression in the B16-F10 cells was slightly down-regulated by capsaicin treatment. In contrast, there were no alterations in the levels of Bax in capsaicin-treated cells. Collectively, these findings indicate that, via down regulation of the Bcl-2, capsaicin induces apoptosis of B16-F10 melanoma cells [48].

***Astragalus membranaceus*:** *Astragalus membranaceus* is used by the Chinese doctors to treat advanced cases of the liver cancer. Swainsonine, a derivative of *Astragalus membranaceus*, is known to prevent metastases. A study showed a higher survival rate in the patients of advanced stage liver cancer after administration of *Astragalus membranaceus* along with conventional treatment as compared to those patients, who were given the conventional treatment alone. *Astragalus membranaceus* protects the liver from toxic effects of chemotherapy. *Astragalus membranaceus* is often used in combination with *Panax ginseng*. Ginseng-*Astragalu*s combination (GAC) has a regulatory effect on the natural killer cells. Studies have also shown that GAC protects the body from toxic side effects of chemotherapy and enhances activity of the immune cells. GAC is found to regulate secretion of the stress hormone, cortisol. *Astragalus membranaceus* is used in China along with another herb called Ligustrum Lucidum [49].

***Autumn crocus*:** Common Names - Naked Ladies, Colchicum, and Meadow Saffron, the *Autumn Crocus*, of the Lily Family (Liliaceae), is a plant with small flowers of varying colors. This plant is indigenous to Europe, Northern African, and Asian continents. Being a plant with a history of medicinal use, records have shown that it had been used in Ancient Greece, India, and Egypt with records being stored in the oldest medical text, known as the Ebers Papyrus. At present, it is used to treat inflammatory disorders. The Colchicine content of *Autumn Crocus* is also valued for its' chemotherapeutic properties [50].

***Azadirachta indica*:** *Azadirachta indica* contains about 40 different active principles, known as liminoids, which exhibit immunoenhancing, antiinflammatory, antiulcer, antifungal, antiviral, antioxidant, hepatoprotective, antimutagenic, anticancer and antimetastatic properties. Liminoids regress growth and 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 and 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 Ês immune cells to identify and destroy cancer cells. Nimbolide also prevents metastasis of cancer. Ethanolic extract of *Azadirachta indica* inhibits growth and spread of prostate cancer by inducing apoptosis and its antiandrogenic effect. *Azadirachta indica* reduces side effects of chemotherapy and radiotherapy [51].

***Bauhinia variegate*:** Cyanidin glucoside, malvidin glucoside, peonidin glucoside and kaempferol galactoside isolated from *Bauhinia variegata* inhibit growth and spread of various cancers such as cancers of breast, lung, liver, oral cavity, larynx and malignant ascites. *Bauhinia variegata* also possesses significant hepatoprotective activity [52].

***Berberis vulgaris*:** *Berberis vulgaris* root contains berberine, berbamine, chelidonic acid, citric acid, columbamine, hydrastine, isotetrandrine, jacaranone, magnoflorine, oxycanthine and palmatine. Berberine (an isoquinoline alkaloid), possesses anticancer, immune enhancing, antioxidant and anti-inflammatory properties. Berberine arrests cancer cell cycle in G1-phase and induces apoptosis. Berberine possesses strong anticancer activity against prostate cancer, liver cancer and leukaemia. Berberine interferes with P-glycoprotein in chemotherapy-resistant cancers. Berberine also increases the penetration of some chemotherapy drugs through the blood-brain barrier, thereby enhancing their effect on intracranial tumours. *Berberis vulgaris* root bark contains three phenolic compounds, tyramine, cannabisin-G and lyoniresinol. Cannabisin-G and lyoniresinol exhibit strong antioxidant activity. Cannabisin-G protects against breast cancer. *Berberis vulgaris* also inhibits growth of stomach and oral cavity cancers [53].

***Betula alba*:** Common Name: Birch. The Birch or *Betula Alba* plant has a variety of different uses. Its medicinal use includes diuretic, anti-inflammatory, and a general pain reliever. There are currently several side effects associated with the use of the birch leaf, including chest pains, tightness in the chest or that that may cause breathing problems, and skin irritation. The Birch has sixty species throughout the world, ten of which are native to Canada and the northern part of the United States.

The effects of Betulinic Acid, as studied by Dr. Brij Saxena of Weill Cornell Medical College, has been known to kill cancerous cells, and has been especially effective in the treatment of prostate cancer patients. This compound does not cause side effects, in typical patients. However the compound is being researched further for its compatibility with patients suffering from HIV [54].

***Betula utilis*:** *Betula utilis* contains betulin that can be easily converted into betulinic acid. Studies have revealed that betulinic acid inhibits growth of malignant melanoma and cancers of the liver and the lung [55].

***Bidens pilosa*:** *Bidens pilosa* is a folk medicine reported with the presence of polyacetylenes, flavonoids, terpenoids, phenylpropanoids and others. An extensive research work on different extracts of *Bidens pilosa* and further fractionation led to the isolation and characterization of potential marker compound phenyl-1,3,5-heptatriyne. This marker compounds revealed the toxicity profile on normal blood cells in erythrocyte osmotic fragility experiments along with other extracts. Hexane, chloroform and methanol extracts of *Bidens pilosa* and their fractions were tested on various cancer cell lines. Results exhibited the antitumor activity of extracts among which hexane extract pronounced the most remarkable activity [56].

***Bolbostemma paniculatum*:** Extraction and further fractionation of Chinese herb *Bolbostemma paniculatum* (Cucurbitaceae) led to the isolation and characterization of a triterpenoid saponin Tubeimoside-V. Further investigations on tubeimoside-V revealed the apoptotic killing nature on glioblastoma cells, thus suggesting its critical role in antitumor chemotherapy. Other tubeimosides like tubeimodes-I, tubeimoside-II and tubeimoside- II also exhibited promised cytotoxic activity which may be linked to the inhibition of DNA synthesis and may induce phenotypic reverse transformation of tumor cells [57].

***Camellia sinensis* (Green Tea):** *Camellia sinensis* contains polyphenolics which are known to possess anti-mutagenic and anticancer activity. Some evidence suggests that tea has a protective effect against stomach and colon cancers [58].

Animal studies also suggest that the risk of cancer in several organs is reduced by consumption of green and black tea or their principal catechins. The tumor incidence and average tumor yield in rats with chemically induced colon cancer were significantly reduced when the rats received (-)-epigallocatechin gallate, a major polyphenolic constituent of green tea [59]. In a study conducted at the New Jersey Medical School, extracts of both black and green tea significantly inhibited leukemia and liver tumor cells from synthesizing DNA. Green and black teas are also reported to possess antifungal, antibacterial, and antiviral activity [60]. It also inhibits growth of cancer by eliminating free radicals from the body. Gallates found in green tea protect the body from damaging effects of radiation. A regular use of green tea protects the body against many cancers including those of the liver, oesophagus, stomach, intestine and the lung. It has been observed that daily consumption of 5 grams of green tea inhibits synthesis of nitrosamine (a major carcinogen) in the body [62].

***Cannabis sativa*:** *In vitro* studies of components of marijuana (*Cannabis sativa*) indicate a potential to inhibit human breast cancer cells and to produce tumor eradications. In experiments introducing marijuana to malignant brain tumors, it was found that survival of animals was increased significantly. The active components of *Cannabis sativa* are cannabinoids. Cannabinoids and their derivatives exert palliative effects in cancer patients by preventing nausea, vomiting and pain and also stimulated the appetite. These compounds have also been shown anti-tumor activity in cell culture and animal models by modulating key cell-signaling pathways [61].

***Catharanthus roseus*:** *Vinca rosea* contains vinca alkaloids, which were the first phyto-constituents ever used to treat cancer. Intense work on *Catharanthus roseus*, a folklore hypoglycaemic drug, led to isolation of more than 70 dimeric indole alkaloids, which include vinblastine, vincristine (leurocrystine), alstonine, ajmalicine and reserpine. Vinca alkaloids execute anticancer effect by binding to the tubulin (microtubule protein) thereby breaking down the microtubules, thus inhibiting formation of mitotic spindle in the metaphase that arrests division of the cancerous

cells. Although structurally closely related, vinblastine and vincristinehave significant difference in their clinical utility. Vinblastine is used in the treatment of Hodgkin's disease, non-Hodgkin's lymphoma and cancers of the kidney and the testis. Vincristine is usually given in combination with other anticancer agents to treat acute lymphocytic leukaemia, Wilm's tumour, neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma, lymphoma and cancers of the breast, lung, bladder and the cervix [62].

***Chlorella pyrenoidosa*:** *Chlorella pyrenoidosa* contains a very effective detoxifying agent, known as lysine. *Chlorella pyrenoidosa* also contains high content of albumin that neutralizes free radicals. *Chlorella pyrenoidosa* protects the body from cancer [63].

***Cinnamomum cassia* (Cinnamon Bark):** 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 [64].

***Colchicum luteum*:** *Colchicum luteum, C. autumnale* contains tropolone groups of alkaloid colchicines. Colchicine shows antimitotic activity and used in cancer for the dispersal of tumors and for treatment of various neoplastic diseases [65].

***Combretum caffrum*:** *Combretum caffrum* contains combretastatin, which has been isolated recently. Combretastatin executes its therapeutic action against cancer by inhibiting blood supply to the tumour. Camptothecin is a pyridoindole (quinoline) alkaloid, which is isolated from seeds of Camptotheca acuminate [66]. Camptothecin is a well known anticancer agent. Derivatives of camptothecin such as 18-OH-camptothecin, 11-OH-camptothecin and 10-OH-camptothecin have been found to possess a strong antileukaemic activity [67, 68].

***Coriandrum sativum* (Cilantro):** 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 [69].

***Curcuma longa*:** Curcumin (Di-feruloyl-methane) and curcuminoids isolated from *Curcuma longa* suppress cancer at every step, *i.e.* initiation, growth and metastasis. Curcumin arrests the cancer cells proliferation in G2/S phase and induces apoptosis (programmed cell death). It inhibits angiogenesis, a crucial step in the growth and metastasis of cancer. Curcumin and Genistein (isolated from *Glycine max*) act synergistically to inhibit growth and spread of oestrogen positive breast cancer. Curcumin works even in multidrug-resistant breast cancers. Curcumin suppresses adhesion of cancer cells, thus preventing metastasis. Curcumin inhibits growth and spread of various cancers including that of breast, lung, oesophagus, liver, colon, prostate, head and neck and skin.

Curcumin is particularly effective in radiotherapy-resistant prostate cancer. Curcumin is effective even in advanced stages of cancer. Curcumin also protects from stomach cancer and colon cancer. *Curcuma longa* also possesses antimutagenic, antioxidant, immuno-stimulant, antiinflammatory, hepatoprotective and radioprotective properties [70].

***Daphne mezereum*:** *Daphne mezereum* is a plant widely used as afolklore remedy for treating cancer like symptoms. A hydro alcohol extract of *Daphne mezereum* has exhibited a potent antileukemic activity against lymphocytic leukemia in mice. Further fractionation studies on the extract resulted in the isolation and characterization of mezerein as a potent antileukemic compound [71].

***Echinacea angustifolia*:** *Echinacea angustifolia* contains arabinogalactan, which protects the body from cancer by activating the macrophages.

Echinacea angustifolia is used to treat metastatic carcinoma of the oesophagus and the colon [72].

***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 and B (tannins) possess strong antioxidant and anticancer properties.

Emblica officinalis inhibits growth and 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 and radiotherapy [73].

***Fagopyrum esculentum*:** *Fagopyrum esculentum* contains amygdalin which has been used by the Chinese physicians for more than 3,500 years to treat various tumours. Ernest Krebs, a noted biochemist, has confirmed the anticancer activity of Amygdalin, which is derived from *Fagopyrum esculentum*. Amygdalin is one of the nitrilosides (natural cyanide-containing substances), which consists of two molecules, *i.e.* benzaldehyde and cyanide. In the body, these two molecules split off in the liver by an enzyme, called beta-glucosidase to form glucuronic acid. Another enzyme known as glucuronidase that is present in higher concentrations in the cancerous cells breaks glucuronic acid to produce cyanide that kills the cancerous cells. It is worth mentioning that cancerous cells do not contain rhodanase (sulphur transferase), an enzyme, which is found in normal cells of the body. Rhodanase protects normal cells of the body from the killing effects of cyanide by converting free cyanide into relatively harmless substance known as thiocyanate [74].

***Ginkgo biloba*:** Ginkgetin and Ginkgolides (A and B), isolated from *Ginkgo biloba* inhibits growth and 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 and radiotherapy [75].

***Glycine max*:** Isoflavones (such as genistein and daidzein) and saponins isolated from *Glycine max* inhibit growth and spread of various cancers such as cancers of the breast, uterus, cervix, ovary, lung, stomach, colon, pancreas, liver, kidney, urinary bladder, prostate, testis, oral cavity, larynx, and thyroid. Glycine max is also effective in nasopharyngeal carcinoma, skin cancer, malignant lymphoma, rhabdomyosarcoma, neuroblastoma, malignant brain tumours and leukaemia. Isoflavones and saponins isolated from *Glycine max* possess wide ranging anticancer properties such as inhibition of cancer cell proliferation, promotion of cell differentiation and induction of apoptosis. Genistein works by blocking angiogenesis (formation of new blood vessel), acting as a tyrosine kinase inhibitor (the mechanism of action of many new cancer drugs) and inducing apoptosis.

Genistein is an excellent intracellular antioxidant. Genistein also blocks the supply of oxygen and nutrients to cancer cells, thus killing them by starving. Genistein and quercetin have synergistic anticancer effect against ovarian carcinoma. Saponins isolated from *Glycine max* decrease invasiveness of the glioblastoma cells. Anthocyanins isolated from Glycine max induce apoptosis in leukaemic cells. *Glycine max* protects against many cancers including that of the colon, lung and ovary [76].

***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 and 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 [77].

***Gossypium barbadense*:** *Gossypium barbadense* contains gossypol. Recent studies have revealed that gossypol possesses selective toxicity towards cancerous cells [78].

***Gossypium hirsutum*:** *Gossypium hirustum* or *Gossypium herbaceum* also called as Gossypol or cottonseed oil and used as a male contraceptive, in the treatment of metastatic carcinoma of endometrium or ovary and also used in HIV. Some *in vivo* and *in vitro* studies revealed the antitumor properties of gossypol on many cytosolic and mitochondrial enzyme systems that is fundamental for tumor cell growth, including melanoma, endometrial, colon, lung, prostate, breast, brain, and adrenocortical cancer [79]. However no typical dose is yet suggested for the treatment of cancer and self-medication with gossypol is not safe because of its potential toxicity [80].

***Gunnera perpensa*:** Pure Z-venusol, previously isolated from the roots of *G. perpensa*, was incubated with human breast (the MCF-7 s) cancer cells and human mammary epithelial cells (HMECs). Proliferation was assessed using the sulforhodamine B (SRB) assays. The fluorescein isothiocyanate (FITC) Annexin V and the lactate dehydrogenase (LDH) activity assays were conducted to determine whether cell death, if any, was apoptotic or necrotic. The drugs used as positive controls included cisplatin and camptothecin. Re-Joovena™, a concoction claiming to contain *G. perpensa* (0.3 mg/ml) and *Ocotea bullata* (0.3 mg/ml), was also investigated [81].

***Gyrophora esculenta*:** *Gyrophora esculenta* is a mushroom that inhibits growth of cancer by enhancing activity of the natural killer cells. A study reveled that it inhibits carcinogenesis and metastases [82].

***Indigofera tinctoria*:** The present study has been under taken with an objective to determine the antibacterial, antioxidant and cytotoxic activity of the leaf extract *Indigofera tinctoria*. Determination of cytotoxic activity of leaf extract was carried out on lung cancer cell line. The compound present in the extract were identified by GC-MS analysis. The extract screened for photochemical analysis was found to contain bioactive compounds like flavonoids, saponins, tannins, steroidal terpens, phenols and anthroquinone [83].

***Justicia procumbens*:** Numerous efforts have been conducted in searching for effective agents against cancer, in particular from herbal medicines. *Justicia procumbens* is a traditional herbal remedy which was produced in the south-western and southern provinces of China and Taiwan province used to treat fever, pain, and cancer. Here, we identified a new compound 6′-hydroxy justicidin A (JR6) from *Justicia procumbens*, which showed obvious anti-cancer effects [84].

***Lentinus edodes*:** Lentinan, a β-glucan found in shiitake mushrooms, has been shown to have antitumor activity; it was active against lung carcinoma [85]. It is thought that lentinan has its effects by activating the host immune system. Lentinan stimulates increased production and activity of natural killer cells and macrophages, which destroy tumor cells [86]. Preliminary studies also suggest that shiitake extracts possess hypolipidemic and antithrombotic activity [87]. Screening tests on fungi belonging to the Polyporaceae family have identified several compounds with antitumor activity, including a variety of terpenoids and steroids, polysaccharides, and an organic germanium compound [88].

***Linum usitatissimum*:** *Linum usitatissimum* (Flaxseed) contains a rich supply of lignans. These plant lignans are converted to mammalian lignans (enterolactone and enterodiol) by bacterial fermentation in the colon [89] and they can then act as

estrogens. Mammalian lignans appear to be anticarcinogenic; lignan metabolites bear a structural similarity to estrogens and can bind to estrogen receptors and inhibit the growth of estrogen-stimulated breast cancer [90, 91]. Urinary excretion of lignans is reduced in women with breast cancer, whereas the consumption of flaxseed powder increases urinary concentration of lignans several-folds [92].

Mentha species: Mentha species such as *Mentha piperita, Mentha longifolia* and *Mentha aquatica* contain phenolic antioxidants that prevent recurrence of cancer. The essential oils of exhibited OH-radical scavenging activity, reducing OH-radical generation in the Fenton reaction by 24%. [93] The most powerful scavenging compounds in *Mentha piperita* oil were monoterpene ketones. Spearmint tea causes inhibition of carcinogen activation by direct effects on the activated metabolites [94, 95].

***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, hepato-protective and immune enhancing properties [96].

***Nervilia fordii*:** *Nervelia fordii* is a drug used in China as a folklore remedy. Petroleum ether and ethyl acetate extracts of *Nervilia fordii* has been screened out for its anticancer properties using mice models. Both extracts have shown prominent anticancer effects when administered to S-180 mice and H-22 mice models; also prolong the life of cancer bearing mice. This study suggests, *Nervilia fordii* can exploit as cancer inhibiting agent and further research work is required to isolate active constituent/s present in drug [97].

***Nigella sativa*:** Thymoquinone and dithymo-quinone 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 and radiotherapy [98.]

***Nothapodytes foetida*:** Common Name: Nothapodytes Tree. The Nothapodytes Tree has its medicinal use whose wood-extract is used in treating diseases. This tree is found in Western Ghats, India, which have become important because of it being an anticancerous compound containing plant with medicinal properties similar to the camptothecin plant, due to their remarkably similar chemical makeup. Compound - Acetylcamptothecin, Camptothecin, Scopolectin Camptothecin found in the Nothapodytes tree is an inhibitor of the DNA topoisomerase found in cancerous cells.

This halts the process of mutation and development of the cancer cells that render them useless and as a result, they die. This means of cancer curation makes use of the property of inhibition that the camptothecin compound has with the DNA of the cancerous cells. Some side effects in using this compound include diarrhea and anemia [99].

***Ochrosia elliptica*:** Ellipticine and 9-methoxy ellipticine are pyridocarbazole (monomeric indole) alkaloids that have been isolated from *Ochrosia elliptica*, which acts as potent anticancer agent. Ellipticine and its derivatives are used to treat cancers of the breast and the kidney. Lipophilic derivatives of ellipticine act by binding to the DNA [100].

***Ocimum basilicum* (Basil):** Basil is well known for its medicinal value. Apart from having anti inflammatory, blood pressure lowering, and nervous system stimulating properties, this popular herb has been found to have chemoprotective potential for colon cancer. In fact, a study found that basil played a significant role in reducing colon tumors in experimental animals. However, no human clinical trials have been conducted to confirm this experiment [101].

***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 radioprotective properties. *Ocimum sanctum* protects against various cancers particularly the breast cancer and reduces side effects of chemotherapy and radiotherapy [102].

***Oldenlandia diffusa*:** *Oldenlandia diffus*a (Bai Hua She She Cao) contains oldenlandosides, stigmasterol, ursolic acid, oleanolic acid, betasitosterol, p-coumaric acid and flavonoid glycosides. Ursolic acid inhibits growth and spread of various cancers such as cancers of lung, ovary, uterus, stomach, liver, colon, rectum, brain, malignant melanoma, malignant as cites, lymphosarcoma and leukaemia. Ursolic acid works by a typical cytotoxic effect on cancer cells and by inducing apoptosis [103].

***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 rodents. 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 [104].

***Panax ginseng*:** Studies suggest that ginseng may lower the risk of cancer in humans [105]. *Ginseng* inhibits growth of cancer by interfering with the DNA synthesis. *Panax ginseng* contains several active constituents; the main active ingredients in ginseng root are thought to be a family of 6 triterpene saponins called ginsenosides [106]. Other active constituents that may help reduce cancer risk include flavonoids, polysaccharides, and polyacetylenes, essential oils, phytosterols, amino acids, peptides, Vitamins and minerals [105]. *Panax ginseng* regenerates the natural killer cells, which are damaged by chemotherapy and radiotherapy, stimulate the macrophages and promote production of the antibodies [107]. *Ginseng* seemed to be most protective against cancer of the ovaries, larynx, pancreas, esophagus, and stomach and less effective against breast, cervical, bladder, and thyroid cancers [108].

***Pfaffia paniculata*:** Roots of *Pfaffia paniculata* have been well documented for multifarious therapeutic values and have also been used for cancer therapy in folk medicine. Study has been performed in a human breast tumor cell line, the MCF-7 cells. These are the most commonly used model of estrogen-positive breast cancer, and it has been originally established in 1973 at the Michigan Cancer Foundation from a pleural effusion taken from a woman with metastatic breast cancer. Butanolic extract of the roots of *P. paniculata* showed cytotoxic effect MCF-7 cell line, as determined with crystal violet assay, cellular death with acridine orange / ethidium bromide staining, and cell proliferation with immunocytochemistry of bromodeoxyuridine (BrdU). Subcellular alterations were evaluated by electron microscopy. Cells treated with butanolic extract showed degeneration of cytoplasmic components and profound morphological and nuclear alterations. The results show that this butanolic extract indeed presents cytotoxic substances, and its fractions merit further investigations [109].

***Picrorrhiza kurroa*:** *Picrorrhiza kurroa* (Kutki) has shown to reduce formation of liver cancer due to chemical exposures. Kutki is a combination of active herbal constituents, picrosides-I, II and III and kutkoside. *Picrorrhiza kurroa*, has been shown to decrease levels of lipid peroxidases and hydroperoxidases, free radical producing agents, and help facilitate the recovery of a powerful antioxidant in the liver needed to prevent oxidative damage [110].

***Plumbago zeylanica*:** Plumbagin isolated from *Plumbago zeylanica* inhibits growth and spread of breast cancer, liver cancer, fibrosarcoma, malignant

ascites and leukaemia by inhibiting cancer cell proliferation. *Plumbago zeylanica* also possesses strong antioxidant, hepatoprotective, neuro-protective and immunoenhancing properties [111].

***Podophyllum hexandrum*:** Podophyllotoxin and podophyllin (lignans) isolated from *Podophyllum hexandrum* (Himalayan May Apple) inhibit growth and spread of various cancers including that of the breast, ovary, lung, liver, urinary bladder, testis, brain, neuroblastoma, HodgkinÊs disease, non-HodgkinÊs lymphoma and leukaemia. Podo-phyllotoxin is the most active among all the natural anticancer compounds. *Podophyllum hexandrum* also possesses potent radioprotective and haemopoietic properties [112].

***Prunella vulgaris*:** Ursolic acid and oleanolic acid, isolated from *Prunella vulgaris* (Xiaku- cao/Self heal), inhibit growth and spread of various cancers such as cancers of the breast, cervix, lung, oral cavity, oesophagus, stomach, colon, thyroid, malignant lymphoma, intracranial tumours and leukaemia. *Prunella vulgaris*, is traditionally used in China to treat sores in mouth and throat. *Prunella vulgaris* also possesses immune enhancing, hepatoprotective, antioxidant, anti-HIV and anti-Herpes properties. *Prunella vulgaris* has normoblastic effect on the bone marrow [113].

***Psoralea corylifolia*:** Bavachinin, corylfolinin and psoralen isolated from *Psoralea corylifolia* (Bu Gu Zhi), 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 and 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, immunomoenhancing and hepatoprotective properties [114].

***Rubia cordifolia*:** Rubidianin, rubiadin, RA-7, RA-700 and RC-18 isolated from *Rubia cordifolia* inhibit growth and spread in cancers of breast, ovary, cervix, colon, lung, malignant ascites, malignant lymphoma, malignant melanoma sarcoma and leukaemia. Rubiadin also possesses hepatoprotective activity [115].

***Salvia miltiorrhiza*:** Tanshinone-I was isolated from traditional herb *Salvia miltiorrhizae*, was investigated on the expression of intercellular adhesion molecule. The study revealed a potential anticancer effect of tanshinone-I on breast cancer cells, suggesting that tanshinone-I may serve as an effective drug for the treatment of breast cancer [116]. Tanshinone II-A, isolated from *Salvia miltiorrhiza*, induced apoptosis which was linked to proteolytic cleavage of a major component in apoptotic cell death mechanism [117].

***Saussurea lappa*:** Sesquiterpenes and costunolide dehydrocostuslactone, isolated from *Saussurea lappa* inhibit growth and 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 and 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 and spread of cancers by arresting cancer cell division in G2 phase and inducing apoptosis [118].

***Solanum nigrum*:** Solamargine and solasonine, isolated from *Solanum nigrum* (Loing-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 and 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 and spread of stomach cancer, sarcomas, malignant ascites and leukaemia [119].

Taxus species: *Taxus brevifolia, Taxus yunnanensis, Taxus baccata* and *Taxus wallichiana* contain taxanes, which include paclitaxel (Taxol) and docetaxel (Taxotere). Taxanes have a different mode of action on the cancerous cells than that of the podophyllin and the vinca alkaloids. Taxanes arrest multiplication of cancerous cells by cross-linking the microtubules. Taxanes are used to treat leukaemia and cancers of the breast, ovary, colon and the lung [120].

***Terminalia Chebula*:** *Terminalia chebulais* a source of hydrolysable tannis and its antimutagenic activity in Salmonella typhimurium has been documented [121]. Phenols like chebulinic acid, tannic acid, ellagic acid are the cancer growth inhibitors found in the fruits of *Terminalia chebula* [122]. *Terminalia chebula* fruits powder and its acetone extract of bark have been reported with promising antimutagenic and anticarcinogenic activity [123].

***Thymus vulgaris* (Thyme):** Thyme is sweeter and milder than oregano. Thyme as a dried herb contains very high levels of anti-oxidants in the form of rosmarinic acid and phenolic compounds such as thymol and carvacrol. A Turkish study supported by Hacettepe University Research Foundation suggested that these phenolic compounds at concentrations below 0.2 mM and 0.1 mM respectively can significantly reduce the oxidative DNA damage and thus prevent the development of any type of cancer [124].

***Tinospora cordifolia*:** Sesquiterpenes and diterpenes isolated from *Tinospora cordifolia* inhibit growth and 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 and B) isolated from Tinospora cordifoliapossesses significant immune enhancing activity. *Tinospora cordifolia* also possesses neuroprotective, hepatoprotective, antistress, antiulcer and antipyretic properties. *Tinospora cordifolia* reduces side effects of radiotherapy and chemotherapy [125].

***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 immune stimulating 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 [126].

***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 and 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 and 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 and chemotherapy [127].

***Zingiber officinale*:** *Zingiber officinale* ethanol extract was investigated to find out its antitumor effects in skin tumorigenesis model. Pre-application of *Zingiber officinale* ethnol extract onto the skin of mice resulted in significant inhibition of 12-0-tetradecanoylphorbol- 13-acetate (TPA)-caused induction of epidermal ODC, cyclo oxygenase, and lipoxygenase activities and ODC mRNA expression in a dose dependent manner.

Pre application of *Zingiber officinale* ethanol extract to mouse skin also resulted in a significant inhibition of TPA caused epidermal edema and hyperplasia. In prolonged time studies, topical application of *Zingiber officinale* ethanol extract thirty minute prior to that of each TPA application to 7, 12-dimethylbenz (a) anthracene initiated mice caused a marked protection against skin tumor incidence its multiplicity [128].

Ginger's natural bio-actives, specifically ginger extract and 6-gigerol, have also been investigated for their *in vitro* inhibition of two key aspects of colon cancer biology, cancer cell proliferation and angiogenic potential of endothelial cell tubule formation. These active ginger constituents linked to a direct effect on cancer cells. Among other compounds, 6-gingerol was found more effective even at lower doses resulted in inhibition of endothelial cell tube formation [129]. The suggested mechanism of action of Ginger extract on colon cancer cells may be its suppression and arresting the G0/G1-phase, reducing DNA synthesis and inducing apoptosis [130].

TABLE 1: LIST OF ANTICANCER PLANT

S. no.	Plant	Family	Active constituent	Use
1.	*Actinidia chinensis*	(Actinidiaceae)	Polysaccharide known as "ACPSR"	immune-enhancing and anticancer
2.	*Aegle marmelos*	(Rutaceae)	Lupeol	Breast cancer, malignant lymphoma, malignant melanoma, leukaemia
3.	*Agave americana*	(Agavaceae)	Steroidal saponin, alkaloid, coumarin, isoflavonoid, hecogenin and Vitamins (A, B, C)	cytotoxic and antitumor
4.	*Allium sativum*	(Amaryllidaceae)	Allicin	Cytotoxic and anticancer
5.	*Aloe vera*	(Asphodelaceae)	aloe-emodin	Anticancer
6.	*Alpinia galangal*	(Zingiberaceae)	Acetoxy-chavicol-acetate (ACA), Pinocembrin, Galangin	breast, lung, stomach, colon, prostate, multiple yeloma leukaemia, antioxidant and antimutagenic
7.	*Amoora rohituka*	(Meliaceae)	Amooranin (a triterpene acid)	Breast and cervical cancers, colon cancer and leukaemia
8.	*Andographis paniculata*	(Acanthaceae)	flavonoids and labdane diterpenoids	Cytotoxic and potent immune stimulating activity
9.	*Annona muricata*	(Annonaceae)	Acetogenins	Anticancer
10.	*Apis mellifera*	(Apideae)	Protein	Cytotoxicity in normal human lymphocytes and HL-60 cells
11.	*Ananas comosus*	(Bromeliaceae)	bromelain	Cytotoxic activity and leukaemia
12.	*Angelica sinensis*	(Apiaceae)	polysaccharide known as "AR-4"	Antitumour activity and cervix cancer
13.	Annona species	(Annonaceae)	acetogenins	Cytotoxic activity against leukemia and sarcoma
14.	*Arctium lappa*	(Asteraceae)	Arctigenin	Lymphoma and cancers of the pancreas, breast, ovary, oesophagus, bladder, bile duct and the bone
15.	*Artemisia asiatica*	(Asteraceae)	Isoliquiritigenin	Inflammation, cancer, and microbial infection
16.	*Astragalus membranaceus*	(Fabaceae)	Swainsonine,	Liver cancer
17.	*Autumn Crocus*	(Liliaceae)	Colchicine	Chemotherapeutic properties
18.	*Azadirachta indica*	(Meliaceae)	Liminoids and Nimbolide	Antimutagenic, anticancer and antimetastatic properties

19.	*Bauhinia variegata*	(Caesalpiniaceae)	Cyanidin glucoside, and kaempferol galactoside	Cancers of breast, lung, liver, oral cavity
20.	*Berberis vulgaris*	(Berberidaceae)	berberine, berbamine, chelidonic acid, oxycanthine and palmatine	Anticancer, immune enhancing, antioxidant and anti-inflammatory properties
21.	*Betula alba*	(Betulaceae)	Betulinic Acid	Prostate cancer, diuretic, anti-inflammatory
22.	*Betula utilis*	(Betulaceae)	betulin	Liver and the lung cancer
23.	*Bidens pilosa*	(Asteraceae)	phenyl-1,3,5-heptatriyne	Anticancer
24.	*Bolbostemma paniculatum*	(Cucurbitaceae)	Tubeimoside-V	Cytotoxic activity
25.	*Camellia sinensis*	(Theaceae)	(-)-epigallocatechin gallate	Anti-mutagenic and anticancer activity
26.	*Cannabis sativa*	(Cannabaceae)	Cannabinoids	Anti-tumor activity
27.	*Catharanthus roseus*	(Apocynaceae)	vinblastine, vincristine	Hodgkin's disease, breast, lung, bladder and the cervix cancer
28.	*Chlorella pyrenoidosa*	(Chlorellaceae)	Lysine and albumin	Anticancer
29.	*Cinnamomum cassia*	(Lauraceae)	coumarin	Antticancer
30.	*Colchicum luteum*	(Liliaceae)	colchicines	Antimitotic activity, neoplastic diseases
31.	*Combretum caffrum*	(Combretaceae)	combretastatin	Anticancer
32.	*Coriandrum sativum*	(Apiaceae)	beta-carotene, quercetin and rutin	Anti-cancer properties
33.	*Curcuma longa*	(Zingiberaceae)	Curcumin (Di-feruloyl-methane) and curcuminoids	Stomach cancer, colon cancer and antimutagenic
34.	*Daphne mezereum*	(Thymelaeaceae)	mezerein	Antileukemic activity
35.	*Echinacea angustifolia*	(Asteraceae)	arabinogalactan	Anticancer activity
36.	*Emblica officinalis*	(Phyllanthaceae)	Emblicanin A and B, quercetin	Hepatoprotective and anticancer properties
37.	*Fagopyrum esculentum*	(Polygonaceae)	amygdalin	Anticancer activity
38.	*Ginkgo biloba*	(Ginkgoaceae)	Ginkgetin and Ginkgolides (A and B)	Antioxidant and anticancer activity
39.	*Glycine max*	(Fabaceae)	genistein and daidzein	Skin cancer, malignant brain tumours and leukaemia
40.	*Glycyrrhiza glabra*	(Fabaceae)	Licochalcone-A and Glycyrrhizin	breast, lung, stomach, colon, liver, kidney cancer and leukaemia
41.	*Gossypium barbadense*	(Malvaceae)	Gossypol	Anticancer activity
42.	*Gossypium hirustum*	(Malvaceae)	Gossypol	Colon, lung, prostate, breast, brain cancer
43.	*Gunnera perpensa*	(Gunneraceae)	Z-venusol	Anticancer activity
44.	*Gyrophora esculenta*	(Umbilicariaceae)	-	Carcinogenesis and metastases
45.	*Indigofera tinctoria*	(Fabaceae)	flavonoids, saponins, tannins, phenols and anthroquinone	Antibacterial, antioxidant and cytotoxic activity
46.	*Justicia procumbens*	(Acanthaceae)	6′-hydroxy justicidin A (JR6)	Anti-cancer effects
47.	*Lentinus edodes*	(Polyporaceae)	Lentinan, terpenoids and steroids	Antitumor activity, and antithrombotic activity
48.	*Linum usitatissimum*	(Linaceae)	Lignans	Anticarcinogenic
49.	Mentha species	(Lamiaceae)	monoterpene ketones, phenolic compound	Anticancer activity
50.	*Morinda citrifolia*	(Rubiaceae)	Damnacanthol, NB10 and NB11	Anticancer activity and hepato protective
51.	*Nervelia fordii*	(Orchidaceae)	required to isolate active constituent/s present in drug	Anticancer properties
52.	*Nigella sativa*	(Ranunculaceae)	Thymoquinone and dithymoquinone	Anticancer activity, anti-inflammatory properties
53.	*Nothapodytes Foetida*	(Icacinaceae)	Acetylcamptothecin, Camptothecin, Scopolectin Camptothecin	Anticancerous
54.	*Ochrosia elliptica*	(Apocynaceae)	Ellipticine and 9-methoxy ellipticine	Breast and the kidney cancer
55.	*Ocimum basilicum*	(Lamiaceae)	-	Anticancer, anti inflammatory, blood pressure lowering
56	*Ocimum sanctum*	(Lamiaceae)	Eugenol, orientin, cirsilineol, Ursolic acid cirsimaritin,	Breast cancer, liver cancer, tissue-protective

57.	*Oldenlandia diffus*a	(Rubiaceae)	oldenlandosides, stigmasterol, ursolic acid,	Ovary, lung uterus, stomach, liver, colon, rectum, brain and leukaemia.
58.	*Origanum vulgare*	(Lamiaceae)	Rosmarinic acid	Colon cancer-bearing, anti-oxidant activity
59.	*Panax ginseng*	(Araliaceae)	flavonoids, polysaccharides, and polyacetylenes	Breast, cervical, bladder, and thyroid cancers
60.	*Pfaffia paniculata*	(Amaranthaceae)	presents cytotoxic substances	Estrogen-positive breast cancer
61.	*Picrorrhiza kurroa*	(Plantaginaceae)	picrosides-I, II and III and kutkoside	Liver cancer and antioxidant
62.	*Plumbago zeylanica*	(Plumbaginaceae)	Plumbagin	Anticancer and neuroprotective
63.	*Podophyllum hexandrum*	(Berberidaceae)	Podophyllotoxin and podophyllin	Breast, ovary, lung, liver, urinary bladder, testis, brain, neuroblastoma, HodgkinÊs disease, lymphoma and leukaemia
64.	*Prunella vulgaris*	(Lamiaceae)	Ursolic acid and oleanolic acid	Breast, cervix, lung, oral cavity, stomach, colon, thyroid cancer, anti-HIV
65.	*Psoralea corylifolia*	(Fabaceae)	Bavachinin, Psoralidin corylfolinin and psoralen	lung cancer, liver cancer, osteosar-coma, fibrosarcoma, and leukaemia
66.	*Rubia cordifolia*	(Rubiaceae)	Rubidianin, rubiadin, RA-7, RA-700 and RC-18	breast, ovary, cervix, colon, lung, malignant ascites and leukaemia
67.	*Salvia miltiorrhizae*	(Lamiaceae)	Tanshinone-I and Tanshinone II-A	anticancer effect (breast cancer)
68.	*Saussurea lappa*	(Asteraceae)	Sesquiterpenes costunolide Cynaropicrin, and dehydrocostuslactone	Anticancer property
69.	*Solanum nigrum*	(Solanaceae)	Solamargine and solasonine	Anticancer property
70.	Taxus species	(Taxaceae)	taxanes	Leukaemia and cancers of the breast, ovary, colon and the lung
71.	*Terminalia chebulais*	(Combretaceae)	chebulinic acid, tannic acid, ellagic acid	antimutagenic and anticarcinogenic activity
72.	*Thymus vulgaris*	(Lamiaceae)	rosmarinic acid and phenolic compounds	Anticancer
73.	*Tinospora cordifolia*	(Menispermaceae)	Sesquiterpenes and diterpenes	Lung, cervix, throat and malignant ascites
74.	*Viscum album*	(Santalaceae)	Lectins (such as viscumin), and phenolic compounds (such as digallic acid)	Breast, cervix, ovary, lung, stomach, colon, rectum, kidney, urinary bladder, testis
75.	*Withania somnifera*	(Solanaceae)	Withanolides (including Withaferin A, Sitoindoside IX, Physagulin D, Withanoside IV and Viscosalactone B)	Anticancer, antiproliferative and antiangiogenic properties
76.	*Zingiber officinale*	(Zingiberaceae)	6-gigerol	Anticancer

CONCLUSION: Medicinal plants maintain the health and vitality of individual and also cure various diseases including cancer without causing toxicity. Natural products discovered from medicinal plants have played an important role in treatment of cancer. Cancer is an abnormal malignant growth of body tissue or cell. A cancerous growth is called a malignant tumour or malignancy. A noncancerous growth is called benign tumour. The process of cancer metastasis is consisting of series of sequential interrelated steps, each of which is rate limiting. Plants with loaded with chemical with chemo protective activities of some of them are undergoing clinical trial. Inhibition of angiogenesis is a novel process of cancer therapy. The selected and careful use of this plant may definitely in anti angiogenic therapy and thus in cancer management.

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. In this review some anti cancer plants have been presented. These plants possess good immunomodulatry and antioxidant properties leading to anticancer activity. In conclusion this article provides the knowledge

about anticancer medicinal plants of foreign origin, which are used by people all over the world. Also it is of significance to exploit novel anticancer drugs from medicinal plants.

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