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Ethnopharmacological Review of Traditional Medicinal Plants for Anticancer Activity

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Abstract: Medicinal herbs have been on the forefront whenever we talk about anticancer remedies, 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. Here we covered the plants used previously and recently identified for treatment of cancer and to reduce the pains during the treatment of cancer.
Keywords: Anticancer, Medicinal herbs, Herbal medicines, Cancer treatment.

INTRODUCTION

From the earliest times, herbs have been prized for their pain-relieving and healing abilities and today we still rely largely on the curative properties of plants. 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. 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[1,2].

Medicinal herbs are also significant source of synthetic and herbal drugs. So far, pharmaceutical companies have screened more than 25,000 plants for anti-cancer drugs[2]. This should tell us that looking for single ingredients to attack cancer might be missing the point. Just as cancers are a product of disturbances in the body, so herbs can correct the disturbances as well as control many cancers. Herbal system of medicine has been practiced for thousand of years.

Phytoconstituents derived from the herbs *Vinca rosea, Taxus species, Achyranthes bidentata, Allium sativum, Aloe vera, Angelica sinensis, Astragals membranaceus, Glycine max, Glycyrrhiza glabra, Hordeum vulgare, Hydrocotyle asiatica, Medicago sativa, Morinda citrifolia, Panax pseudoginseng, Saussurea lappa, Taxus wallichiana, Tinospora cordifolia, Viscum album, Withania somnifera, Zingiber officinale* etc. have been used in various formulations to enhance activity of immune cells of the body that promotes production of cytokines including interleukin, interferon, tumor necrosis factor and colony stimulating factor. These formulations help the body to fight cancer more effectively and reduce

toxic side effects of chemotherapy and radiotherapy stages of cancer.

WHAT IS 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 tumor, or proliferate through out 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 cancer in humans are surgery, radiation and drugs (cancer chemotherapeutic agents). Cancer chemotherapeutic agents can often provide temporary relief of symptoms, prolongation of life, and occasionally cures. In recent years, a lot of effort has been applied to the synthesis of potential anticancer drugs. 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 tumor-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[3].

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 papillomaviruses, 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 tumor 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[4].

TYPES OF CANCERS[5]

1) Cancers of Blood and Lymphatic Systems:
a) Hodgkin's disease, b) Leukemias, 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) Carcinoid cancer, d) Nasopharyngeal cancer,
e) Retroperitoneal sarcomas f) Soft tissue cancer, g) Thyroid cancer

THE MECHANISM ON CANCER THERAPY[6]

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 tumor and inhibiting its translocation and spread by blocking the blood source of tumor tissue.
4. Enhancing the number of leukocytes and platelets by stimulating the hemopoietic function.

5. Promoting the reverse transformation from tumor cells into normal cells.
6. Promoting metabolism and preventing carcinogenesis of normal cells.
7. Stimulating appetite, improving quality of sleep, relieving pain, thus benefiting patients health.

Table 1: Plants with Anti-Cancer activity.

Sr. no.	Botanical name	Family	Common name	Active constituent
1	*Allium sativum*	*Liliaceae*	Garlic	Alliin ,allicin alliin, alliinase, S-allyl-cysteine (SAC), diallyldisulphide (DADS), diallyltrisulphide (DATS) and methylallyltrisuphide.
2	*Actinidia chinensis*	*Actinidiaceae*	China gooseberry, Kiwifruit	Polysaccharide known as "ACPS-R"
3	*Aloe ferox,* *Aloe barbadenis*	*Liliaceae*	Aloe vera	Aloe-emodin, emodin, aloin acemannan,
4	*Ananas comosus*	*Bromeliaceae*	Pine apple, Ananas	Bromelain
5	*Angelica sinensis*	*Umbelliferae*	Angelica	Polysaccharide fraction of known as "AR-4"
6	*Annona species*	*Annonaceae*	Monkey species	Acetogenins
7	*Arctium lappa,*	*Compositae*	Burdock	Potent anticancer factors.
8	*Astragalus membranaceus*	*Papilionaceae*	--	Swainsonine
9	*Betula utilis*	*Betulaceae*	Bhojpatra	Betulin
10	*Camellia sinensis*	*Theaceae*	Tea plant	Epigallocatechin gallate
11	*Catharanthus roseus*	*Apocynaceae*	Vinca	Vinblastine, Vincristine , Alstonine, Ajmalicine and Reserpine.
12	*Chlorella pyrenoidosa*	*Oocystaceae*	--	Lysine
13	*Colchicum luteum*	*Liliaceae*	Colchicum	Colchicines demecolcine
14	*Combretum caffrum*	*Combritaceae*	--	Combretastatin
15	*Curcuma longa Linn.*	*Zinziberaceae*	Turmeric	Tumerone, curcumine.
16	*Echinacea angustifolia*	*Asteraceae*	Black sampson	Arabinogalactan, Jucogalactoxyloglucans.
17	*Fagopyrum esculentum,*	*Polygonaceae*	Vitamin p	Amygdalin, Rutin
18	*Ginkgo biloba*	*Ginkoaceae*	Kew tree	Ginkgolide-B, A, C and J
19	*Glycine max*	*Leguminosae*	Soyabean	Zinc, selenium, vitamins (A, B_1, B_2, B_{12}, C, D, E and K), amino acids, isoflavones, protease inhibitors, saponins and phytosterols
20	*Glycyrrhiza glabra*	*Leguminosae*	Liquorice	Glycyrrhizin.
21	*Gossypium barbadense*	*Malvaceae*	Raw cotton	Gossypol
22	*Gyrophora esculenta*	*Umbilicariaceae*	Mushroom	Polysaccharides β-glucans, α-glucans, and galactomannans.
23	*Lentinus edodes*	*Agaricaceae*	--	Lentinan
24	*Linum usitatissimum*	*Linaceae*	Flax seed, Linseed	Cynogenetic glycosides, Lignans
25	*Mentha species*	*Labiateae*	Pudina	Monoterpene ketones
26	*Ochrosia elliptica*	*Apocynaceae*		Ellipticine and 9-methoxy ellipticine are pyridocarbazole (monomeric indole) alkaloids
27	*Panax ginseng*	*Aralaceae*	Ginseng	Ginsenosides, Panaxosides

28	*Picrorrhizia kurroa*	*Scrophulariaceae*	Picrorrhizia (kutki)	Picrosides I, II, III and kutkoside
29	*Podophyllum hexandrum*	*Berberidaceae*	Podophyllum	Podophyllin,astragalin
30	*Taxus brevifolia*	*Taxaceae*	Pacific yew	Taxanes, taxol cepholomannine
31	*Withania somnifera*	*Solanaceae*	Ashwagandha	Withanolides, *Withaferin*
32	*Zingiber officinale*	*Zingiberaceae*	Ginger	Curcumin,gingerenoneA,Gingeols, shogaols, zingerone

HERBS WITH ANTICANCER ACTIVITY

The list of plants along with their chemical constituents responsible for anticancer activity is given Table No. 01, and the plants are discussed below-

01. *Allium sativum*

Garlic has been used for thousand of years to treat various diseases. Hippocrates was the first to recommend its use for cancer. *Allium sativum* contains more than 100 biologically useful secondary metabolites, which include alliin, alliinase, allicin, S-allyl-cysteine (SAC), diallyldisulphide (DADS), diallyltrisulphide (DATS) and methylallyltrisuphide. Garlic oil contains an amino acid known as alliin, which is converted to allicin when its bulbs are crushed. Allicin is a precursor to several sulphur-containing compounds that are responsible for the flavour, odour and pharmacological properties of *Allium sativum*[7]. Recent studies revealed presence of bioflavonoids quercetin and cyanidin are responsible for antioxidant properties of garlic. Ajoene, a sulphur-containing compound, found in garlic oil, inhibits mutagenesis. Garlic oil prevents prostaglandin-dependent cancers by inhibiting lipoxygenase and cyclo-oxygenase enzymes. Garlic contains a rich content of selenium, which is a cellular antioxidant. Diallyltrisulphide, diallyldisulphide and S-allyl-cysteine, found in *Allium sativum*, have anticarcinogenic properties. Diallyltrisulphide prevents metastases in the lung cancer[8]. Garlic has shown significant therapeutic effect in cancers of the stomach and the intestines. The Chinese Academy of Medical Sciences has reported inverse relationship between garlic consumption and incidence of the stomach cancer[10]. *Allium sativum* inhibits genesis as well as growth of cancer by enhancing activity of the natural killer cells and the macrophages. Studies have revealed that *Allium sativum* increases count of the suppressor T cells and makes the lymphocytes more cytotoxic to cancerous cells. *Allium sativum* also inhibits metastases by preventing adhesion of the circulating cancerous cells to the blood vessels. The Garlic extract protects DNA from the damaging effect of carcinogens, increases activity of detoxifying enzymes, speeds up excretion of chemical carcinogens and enhances immunity of the body. The Garlic extract is found to inhibit growth of many cancers including those of the breast, bladder, skin, colon, oesophagus, stomach and the lung[11]. The research done at National Medical Centre and Hospital in Japan has revealed that the Garlic extract reduces side effects of radiotherapy and chemotherapy.

02. *Actinidia chinensis*

Actinidia chinensis root are used by the Chinese physicians in the treatment of cancer. *Actinidia chinensis* contains a polysaccharide known as "ACPS-R" that possesses immune-enhancing and anticancer activities[12].

03. *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[13]. *Aloe vera* is found to inhibit metastases[14].

04. *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[15].

05. *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 immunostimulating activities such as induction of interferon production, stimulation of the immune cell proliferation and enhancement of antitumour activity of the immune cell[16]

06. *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[17]

07. *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[18]

08. *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-Astragalus 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*[19].

09. *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[20].

10. *Camellia sinensis* (green tea)

Camellia sinensis contains polyphenolics which are known to possess antimutagenic and anticancer activity. Some evidence suggests that tea has a protective effect against stomach and colon cancers[21]. 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[22]. 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[23]. 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.

11. *Catharanthus roseus*

Vinca rosea contains vinca alkaloids, which were the first phytoconstituents 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 vincristine have 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[24.]

12. *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[25].

13. *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[26].

14. *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 acuminata*[27]. 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[28,29].

15. *Curcuma longa*

Curcuma longa contains curcumin, which inhibits the growth of cancer by preventing production of harmful eicosanoid such as PGE-2. The anticancer effect of curcumin has been demonstrated in all the steps of cancer development, i.e. initiation, promotion and progression of cancer. Data obtained from several studies suggest that curcumin inhibits the genesis of cancer as well as promotes the regression of cancer[30]. Curcumin suppresses mutagenic effect of various mutagens including cigarette smoke condensates, 7, 12-dimethylbenz (a)anthracene (DMBA) and benzopyrene. Curcumin is found to decrease levels of urinary mutagens. It also possesses anti-inflammatory and antioxidant properties. The protective effects of *Curcuma longa* and its derivatives are partially due to direct antioxidant effect. Studies have revealed that *Curcuma longa* inhibits production of nitrosamine that enhances natural antioxidant functions of the body. *Curcuma longa* increases levels of glutathione and other non-protein sulphahydryls. It acts directly on several enzymes. Curcumin is used to treat squamous cell carcinoma of the skin and the ulcerating oral cancer. *Curcuma longa* also prevents malignant transformation of leukoplakia. Its active phenolic constituents inhibit cancer and also have antimutagenic activity. Turmeric has been shown to suppress the development of stomach, breast, lung, and skin tumors[31]. Its activity is largely due to the antioxidant curcumin (a diferuloylmethane), which has been shown to be an effective anti-inflammatory agent in humans[32].

16. *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[33].

17. *Fagopyrum esculentum*

*Fagopyrum esculentum contains a*mygdalin 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[34].

18. *Ginkgo biloba*

Ginkgo biloba contains Ginkgolide-B, which protects the body against cancer. It inhibits growth of cancer by regulating activity of the platelet-activating factor. A recent study done on the workers of nuclear power station at Chernobyl in Russia has shown that *Ginkgo biloba* protects the DNA from damaging effects of nuclear radiation[35,36].

19. *Glycine max*

Glycine max (Soya bean) is rich in zinc, selenium, vitamins (A, B_1, B_2, B_{12}, C, D, E and K), amino acids, isoflavones, protease inhibitors, saponins and phytosterols. Studies have shown that isoflavones convert the cancerous cells to normal cells by inducing cell-differentiation. Genistein, one of the isoflavones found in higher concentrations in soya products, is known to induce apoptosis (programmed cell death) in the cancerous cells. Genistein also prevents platelet aggregation by inhibiting tyrosine kinase inhibitor enzyme. It is worth mentioning that platelet aggregation promotes the spread of cancer. It has been observed that genistein blocks the synthesis of DNA in the cancerous cells, thus inhibiting the growth of cancer. Genistein also inhibits growth of hormone dependent cancers of the breast and the prostate. Studies have revealed that genistein and other isoflavones prevent growth of cancer by inhibiting angiogenesis (formation of new blood vessels). It enhances immunity of the body and prolong survival period in the liver and the stomach cancer patients. A clinical study done by Chinese doctors on various cancers patients including those of the lung, stomach, oesophagus, intestines and the lymphatic system, has revealed that it improves quality of life and physical functioning by improving appetite, strengthening immune system of the body and reducing toxic effects of chemotherapy and radiotherapy[37].

20. *Glycyrrhiza glabra*

The liquorice plant contains about 8% of glycoside called glycyrrhizin. Glycyrrhizin specifically reduces the activity of two enzymes that break down prostaglandin E. Liquorice shows anti-infective and anticancer properties. In laboratory and animal studies, it have stopped or slowed the growth of certain bacteria, fungi, and parasites. Chemicals derived from liquorice have shown anticancer activity in animal studies and in laboratory cultures of human cancer cells. Additionally, true liquorice may have some ability to improve functioning of the immune system[38].

21. *Gossypium barbadense*

Gossypium barbadense contains gossypol. Recent studies have revealed that gossypol possesses selective toxicity towards cancerous cells[39].

22. *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[40].

23. *Lentinus edodes*

Lentinan, a β-glucan found in shiitake mushrooms, has been shown to have antitumor activity; it was active against lung carcinoma[41]. 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[42]. Preliminary studies also suggest that shiitake extracts possess hypolipidemic and antithrombotic activity[43]. 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[44]. Several other edible mushrooms are reported to have antitumor activity and other useful medicinal properties such as hypotensive action, antithrombotic activity, antiinflammatory effects, and ability to improve hyperlipidemia .

24. *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[46] 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[47,48]. Urinary excretion of lignans is reduced in women with breast cancer, whereas the consumption of flaxseed powder increases urinary concentration of lignans several-folds[49].

25. *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%[50]. 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[51,52].

26. *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[53].

27. *Panax ginseng*

Studies suggest that ginseng may lower the risk of cancer in humans[54]. 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[55]. Other active constituents that may help reduce cancer risk include flavonoids, polysaccharides, and polyacetylenes, essential oils, phytosterols, amino acids, peptides, vitamins and minerals[54]. *Panax ginseng* regenerates the natural killer cells, which are damaged by chemotherapy and radiotherapy, stimulate the macrophages and promote production of the antibodies[56]. 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[57].

28. *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[58]

29. *Podophyllum*

Podophyllum peltatum and *P. hexandrum* contain podophyllin, which has similar therapeutic action on the dividing cancerous cells as that of the vinca alkaloids. Podophyllin arrests multiplication of cancerous cells by breaking down the microtubules into smaller subunits, thus inhibiting the cell division. Podophyllotoxin, an active principle of podophyllin, is used in the treatment of Hodgkin's disease, non-Hodgkin's lymphoma, leukaemia, bronchogenic carcinoma and cancers of the ovary and the testis[59]

30. *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[60].

31. *Withania somnifera*

Withania somnifera contains withanolides, which possess immuno-modulatory activity. Withaferin A and withanolide D found in *Withania somnifera* are known to inhibit growth of cancer[61]. The other alkaloids presents in *Withania somnifera* are ashwagandhine, cuscohygrine, anahygrine, tropine, steroidal compounds, including ergostane type steroidallactones, withasomniferin-A, withasomidienone, withasomniferols A-C, and withanone[62]. Other constituents include saponins containing an additional acyl group (sitoindoside VII and VIII), and withanolides with a glucose at carbon 27 (sitoindoside IX and X)[63,64]. Apart from these contents plant also contain chemical constituents like withaniol, acylsteryl glucosides, starch, reducing sugar, hantreacotane and ducitol, Studies have revealed that *Withania somnifera* enhances the therapeutic effect of radiotherapy. The chemopreventive activity is thought to be due in part to the antioxidant / free radical scavenging activity of the extract[65]. An *in vitro* study showed withanolides from *Withania somnifera* inhibited growth in human breast, central nervous system, lung, and colon cancer cell lines comparable to doxorubicin[66].

32. *Zingiber officinalis*

Zingiber officinalis (ginger) rhizomes offer a rich package of gingerols-phenolic antioxidants that possess pronounced anti-inflammatory activity-that inhibit various cancers. Ginger also contains curcumin, which assists in the elimination of cancer causing substances from the body. The anticancer properties of ginger are attributed to the presence of certain pungent vallinoids, viz. [6]-gingerol and [6]-paradol, as well as some other constituents like shogaols, zingerone etc. A number of mechanisms that may be involved in the chemopreventive effects of ginger and its components have been reported from the laboratory studies in a wide range of experimental models[67,68].

DISCUSSION

Science has long acknowledged the value of healing substances found in nature, such as digitalis, aspirin, penicillin, insulin, steroids, etc. There has been a resurgence of interest, both scientifically and popularly, in the utilization of natural approaches. Experiments on cell lines and in animals demonstrated that herbal drugs anticancer role by inducing apoptosis and differentiation, enhancing the immune system, inhibiting angiogenesis and reversing multidrug resistance[69]. However, the mechanism of the anticancer role has not yet been fully elucidated. Further research is needed to explore the molecular mechanism of herbal drugs. Although the clinical trials showed that herbs were helpful against cancer, these outcomes require further confirmation with rigorously controlled trials, many clinical trials focusing on the anticancer effects of herbal formulas have been conducted. Though many of them demonstrated that herbs are helpful against cancer, especially useful in improving survival and quality of life in patients suffering from advanced cancer, the lack of controls and reporting bias have been severe flaws. Researchers must pay attention to the scientific rigor of studies of herbal drugs in the future to improve the status. Some herbs may be harmful to the human body if they are used improperly. Some herbs may cause serious toxicity when taken excessively or under inappropriate circumstances. Also, potential herb-drug interactions should be taken into consideration if multiple drugs are prescribed simultaneously[70]. In future research is required to determine which ingredients are effective which will provide valuable clues for researching and developing anticancer drugs in the future.

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