REVIEW ARTICLE

HERBS AGAINST CANCER: AN UPDATE

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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.

Key Words: Anticancer, Medicinal herbs, Cancer treatment.

INTRODUCTION

From the ancient time, 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 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[1]. Herbal formulations help the body to fight cancer more effectively and reduce toxic side effects of chemotherapy and radiotherapy stages of cancer.

HERBS WITH ANTICANCER ACTIVITY

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, Sallyl cytokine (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*[2]. Recent studies revealed presence of bioflavonoid quartering and cyaniding 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-allylcysteine, found in *Allium sativum*, have ant carcinogenic properties. Diallyltrisulphide prevents metastases in the lung cancer [3]. 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[4].

Camellia sinensis

It contains polyphenolics which are known to possess antimutagenic and anticancer activity. Some evidences suggest that tea has a protective effect against stomach and colon cancers[5]. Animal studies also suggest that the risk of cancer in several organs is reduced by consumption of green and black tea or their principal catech The 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[6]. 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 [7].

Catharanthus roseus

It 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 andreserpine. Vinca alkaloids execute anticancer effect by binding to the tubulin (microtubule

protein) therebybreaking down the microtubules, thus inhibitingformation of mitotic spindle in the metaphase that arrests division of the cancerous cells. Although structure is closely related vinblastine and vincristinehave have significant difference in their clinical utility. Vinblastine is used in the treatment of Hodgkin' 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 [8].

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* [9]. 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 [10,11].

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 [12] 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 [13]. Its activity is largely due to the antioxidant curcumin (a diferuloylmethane), which has been shown to be an effective anti-inflammatory agent in humans [14].

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 moleules split off in the liver by an enzyme, called beta-glucosidase to form glucuronic acid. Another enzyme known a 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 [15].

Glycine max

Glycine max (Soya bean) is rich in zinc, selenium ,vitamins (A, B, B2, B12, 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 [16].

Glycyrrhiza glabra

The liquorice plant contains about 8% of glycoside called glycyrrhizin.which 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 has stop 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 [17].

Lentinus edodes

Lentinan, a β-glucan found in shiitake mushrooms, has been shown to have antitumor activity; it was active against lung carcinoma [18]. 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. Preliminary studies also suggest that shiitake extracts possess hypolipidemic and antithrombotic activity.

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Screening tests on fungi belonging to the *Polyporaceae* family have identifiedseveral compounds with antitumor activity, including a variety of terpenoids and steroids, polysaccharides, and an organic germanium compound [19].

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[20] 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 [21, 22]. Urinary excretion of lignans is reduced in women with breast cancer, whereas the consumption of flaxseed powder increases urinary concentration of lignans several-folds[23].

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, reducing24%OH-radical generation in the Fenton reaction.[24] 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 [25, 26].

Panax ginseng

Studies suggest that ginseng may lower the risk of cancer in humans [27]. 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 [28]. Other active constituents that may help reduce cancer risk include flavonoids, polysaccharides, and polyacetylenes, essential oils, phytosterols, amino acids, peptides, vitamins and minerals [29]. *Panax ginseng* regenerates the natural killer cells, which are damaged by chemotherapy and radiotherapy, stimulate the macrophages and promote production of the antibodies [30]. Ginseng seemed to be most protective against cancer of the ovaries, larynx, pancreas, esophagus, and stomach and less effective agains breast, cervical, bladder, and thyroid cancers [31].

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 [32].

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 [33]

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 t treat leukaemia and cancers of the breast, ovary, colon and the lung [34].

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*.[35].

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OTHER HEARBS HAVING ANTICANCER ACTIVITY

Aloe Vera also contains acemannan, which enhances activity of the immune cells against cancer[37] and is found to inhibit metastases. *Ananas comosus* contains bromelain, which 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. *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. *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. *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. *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 [38]. Berberine obtained from berberidaceae family is an selective lung cancer agent. barberine or its salt or derivatives are identified as the active compound for selectively inhibiting breast cancer and lung cancer [39]. Ellipticine and 9-methoxy ellipticine are pyridocarbazole (monomeric indole) alkaloids that have been isolated from *Ochrosia elliptica*, which act 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 [40]. *Gossypium barbadense* contains gossypol that has found to selective toxicity towards cancerous cells[41]. *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 [42]. *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 [43]. *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 [44, 45]. *Chlorella pyrenoidosa* contains a very effective detoxifying agent, known as lysine.It is found to contains high content of albumin that neutralizes free radicals. *Chlorella pyrenoidosa* protect the body from cancer [46]. *Colchicum luteum*, *Colchicum autumnale* contains tropolone groups of alkaloid showing antimitotic activity colchicines. Colchicine used in cancer for the dispersal of tumors and for treatment of various neoplastic diseases [47].

CONCLUSION

The above review on plants having potantial anticancer activities along with other medicinal effects.These medicinal plants possess good immunomodulatory and antioxidant properties, leading to anticancer activities. The antioxidant phytochemicals protect the cells from oxidative damage. Thus, consuming a diet rich in antioxidant plant foods (e.g. fruits and vegetables) will provide health-protective effects. In conclusion, this article provides the knowledge about anticancer medicinal plants of foreign origin, which are used by the people all over the world. Also, it is of significance to exploit novel anticancer drugs from these medicinal plants. Future research on this topic would help to identify safe and effective anticancer drugs and will further the exploration of their mechanism of action. Practitioners and researchers in medical sciences can help to improve this medicine by increasing their involvement and contribution.

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