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DIETARY HERBS AS ANTICANCER DRUGS

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ABSTRACT

Cancer is a major community health trouble in both urban and rising countries. Plant derivative are being used for the action against cancer. Worldwide effects are ongoing to identify new anticancer compounds from plants. Current available molecular entities are not sufficient so the the pharmaceutical industry are in search of novel anticancer agents from traditional medicines. In recent years people desire more use of natural plant products due to the fear of side effects for treatment of cancer. An anti-cancer agent could be useful at any of the classically defined stages of carcinogenesis initiation, promotion and progression. These agents are found in fruits, vegetables and herbs etc. Consumption of fruits and vegetables helps in the prevention of cancer. Citrus fruits, allium vegetables, Cruciferous vegetables are few agents which prevent cancer. This article has been made to review important dietary herbs in cancer which will be useful to treating cancer disease. The plant sources of India are likely to provide effective anticancer agents. Herbs have a vital role in the prevention and treatment of cancer.

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INTRODUCTION

The term “cancer” was coined first time by father of medicine Hippocrates, who used Greek words “carcinoma” and “Karakinos” to describe tumor⁽¹⁾ Cancer is abandoned growth of abnormal cells in the body⁽²⁾. Normally, meiosis and cell death are the procedure occurs in body to protect stable condition of tissues in balanced state⁽³⁾. Carcinogenesis is a multi mechanism procedure which have multistage. The first stage is irreversible cell changes, second is The promotion phase i.e clonal proliferation of cells and third stage is progression phase includes aggressive and metastatic phase of disease. In case of insitu cancer Deformed cell mass could remain inside of tissue from which it has been originated when it can be distributed to adjacent tissues, is called malignant form. There are More than 100 types of cancer have been predicted. Cancer is classified according to cell type involved at first. According to

National Cancer Institute (NCI) classification, different types of cancer are classified as follows:⁽²⁾

- **Sarcomas** -- Cancers arising from connective or supporting tissues, such as bone or muscle.
- **Carcinomas** -- Cancers arising from the body's glandular cells and epithelial cells, which line body tissues.
- **Lymphomas** -- Cancers of the lymphoid organs such as the lymph nodes, spleen, and thymus, which produce and store infection-fighting cells. These cells also occur in almost all tissues of the body, and lymphomas therefore may develop in a wide variety of organs.

Nowadays cancer is considered as a human trouble and causality occurrence resulting from cancer is increasing. WHO has predicted that number of cancer new cases will reach 15 million until 2020⁽⁴⁾

Common Treatment Methods of Cancer

The most common methods of cancer treatment are Surgery, chemotherapy and radiotherapy although all of these treatment methods are not always useful and the clinical results are not acceptable⁽⁵⁾.

Hormonal therapy, targeted therapy (including immunotherapy such as monoclonal antibody therapy) and synthetic lethality are the other methods used for treating the cancer. Depending upon the location and grade of the tumor and the stage of the disease, general state of the patient method is selected.

Limitations of Modern Treatment Methods

Chemotherapy and radiotherapy are highly effective methods of cancer treatment but these methods have severe side effects⁽⁶⁾. Gradual resistance of cancer cells against treatment is One of the main problems in cancer treatment⁽⁷⁾. Hence, there is need to achieve a new approach is reason for most of immuno pharmacological studies to improve cancer treatment results⁽⁸⁾. From 1980 to 2000, following Aristotle and Galenos doctrine, indicating cancer as a result of black bile coagulation, up to now during which with the start of new treatment methods, cancer mortalities have been reduced for 25%, plants have played an important role in controlling cancer symptoms and treatments⁽⁴⁾

Relationship of Nutrient's and Cancer

So much has been written about using diet and supplements to lower the risk of developing cancer. But if person, have already been diagnosed with cancer, recovery is naturally. Unfortunately, finding tips on what to do *after* a diagnosis isn't nearly as easy. But there's actually plenty people can do to cut down on the side effects of conventional cancer treatments, to speed up recovery, and improve odds of long-term survival. Conventional oncologists know very little about nutrition, so they rarely make any dietary recommendations. Even worse, some oncologists tell patients there's no relationship between their diet and cancer. But The truth is, diet can make all the difference between recovering or succumbing to this ugly disease. And when it comes to supplements, oncologists tend to be downright hostile, believing that vitamins and herbs will interfere with conventional treatments or have no benefit. Nothing could be further from the truth. After surgery individuals at a higher risk for nutritional deficiencies, particularly when it comes to vitamins C and B12. And there's plenty of research showing that both during and after chemo, supplements are beneficial. The research on taking supplements during radiation therapy is less clear, but still valuable for clinical experience^(29,30,31)

Herbal compound with anti-cancer activity

Curcumin

Curcumin (Diferuloyl methane) is a phenol compound derived from rhizome of curcuma specie.⁽⁹⁾ Using curcumin, pre-clinical cancer research has shown that this plant inhibits carcinogenic procedure in the most cancers including colorectal, pancreas, gastric, and prostate. It is also effective on different stages of carcinogens, proliferation, angiogenesis and metastasis. Moreover, curcumin acts as a chemo-sensitizer, and results in increased activity of other anticancer factors in treating multi-drug resistant and chemotherapy-resistant resistant cancers^(6,10). NF-K β Signaling pathway is involved in cytotoxic doxorubicin effects and its analogues; hence, curcumin increases response of tumor cells to doxorubicin through blocking NF-K β signaling pathway.⁽¹¹⁾ Phase II clinical trial studies have shown that curcumin is not toxic to human to a dose of 8000 mg/day.⁽¹²⁾

Ginger

Ginger is a phenol complex whose rhizome is used widely in traditional medicine. Phenol compounds of this plant show cytotoxic activity through apoptosis in cancer cells⁽⁹⁾

Some pungent substances present in ginger rhizome have anti-oxidant and anti-inflammatory activities. The anticancer properties of ginger are attributed to phenolic substances such as 6-gingerol and 6-paradol and other constituents such as shogaols and zingerone. A study published in the journal *Biochemical and Biophysical Research Communications* reported that 6-gingerol can reduce viability of gastric cancer cells and limit the spread of cancer.

Grapes

Resveratrol is a phytoalexin found in grapes. It was shown that resveratrol causes apoptosis in HL60 cells and T47D (breast carcinoma cells)⁽¹⁰⁾. It induces apoptosis through CD95 signaling-dependent apoptosis in HL60 and T47D cells. Moreover, it was shown that such complex enhances CD95L expression on HL60 and T47D cells.⁽¹³⁾

Green Tea

There are a stack of studies showing green tea's ability to fight cancer including breast, prostate, esophagus, stomach, colon, lung, skin, liver, bladder, ovary, mouth, and blood cancers. A Japanese study found that five or more cups of green tea a day could slash the risk of blood and lymph-based cancers by about 50%.⁽¹⁴⁾ Green tea contains a powerful group of antioxidants known as polyphenols that prevent free radicals (unstable molecules) from damaging cell DNA and tissues of the body. If individual undergoing chemotherapy or radiation check with their oncologist about the most recent research on green tea to make sure it's compatible with individual therapy.

Vitamin D

Vitamin D is a real cancer-fighting superstar. This vital vitamin can help cut individual cancer risk and support them to recover after a diagnosis. Researcher find that most cancer patients are deficient in D and a medical history often reveals that they were likely deficient before their diagnosis as well.

In a recent study researchers found that leukemia and lymphoma patients were deficient in vitamin D before their diagnosis, and their deficiencies became worse after being treated with chemotherapy⁽¹⁵⁾ In another study, scientists found that low D levels can raise persons chances of being diagnosed with breast cancer.⁽¹⁶⁾ And a brand new report in the journal *Anticancer Research* found that breast cancer survivors with the highest vitamin D levels had HALF the death rate of those with low levels.⁽¹⁷⁾ But the benefits of vitamin D go so much further. More than 60 studies have found that high levels of vitamin D are associated with a lower risk of certain cancers, including those of the breast, prostate, colon, and lung, as well as leukemia and myeloma^(18,19,20,21,22). Researcher typically recommend 5,000 IU of vitamin D daily with food, and more if individual levels are below 50. Aim for a blood level of vitamin D of at least 50 ng/ml.

Omega-3 Fatty Acid

Like vitamin D, omega-3s (found in fish oils) are cancer fighters. They are anti-inflammatory, which means they essentially dampen down the biological craziness of cancer cells. And recent research revealed that omega-3s could cut the risk of breast cancer by up to one-third—as well as play an important role in treatment.^(23,24)

In another study of women treated for metastatic breast cancer, researchers discovered that large amounts of docosahexaenoic acid (DHA)—one of the fatty acids found in fish oil—led to a significant increase in survival.⁽²⁵⁾ In other words, DHA literally saved lives!

Other studies have found that high-dose omega-3s combined with chemotherapy have significant benefits for patients with non-small cell lung cancer (NSCLC).²⁶ This is important because NSCLC has such a poor prognosis with conventional treatment alone. The omega-3s also help cancer patients maintain their weight^(27,28)

For breast cancer patients, Researcher typically recommend taking 1,800 mg of DHA daily. For non-small cell lung cancer, they suggest taking approximately 2.2 grams of EPA and 240 mg of DHA daily. And for other types of cancer, it is suggested to taking 1,000 mg of eicosapentaenoic acid (EPA) and 1,000 mg of DHA.

Fermented wheat germ extract

Researcher often recommend fermented wheat germ extract (FWGE) to patients with cancer. A solid stack of human research—more than 100 studies published in over 20 peer-reviewed medical journals—has shown that FWGE helps fight cancer. The benefits in these studies were crystal clear. FWGE improves quality of life, overall survival and disease free survival. FWGE fights cancer in several ways. It reduces the supply of glucose (sugar) to cancer cells making it harder for the tumors to survive. It also reduces a certain protein found on cancer cells making it easier for individual immune system to find and target the tumor. And, finally, it enhances person's immune system response against tumors. Research has revealed that FWGE is beneficial in fighting colorectal, breast, melanoma, lung, and oral cancers^(32,33,34,35). It has also been shown to reduce infections in kids and teens undergoing chemotherapy⁽³⁶⁾

Allium Sapium

The members of *Allium sapium* (garlic, onions and chives) play a vital role as anti-cancer agent because of the chemoprotective phytochemicals present in these herbs⁽³⁷⁾

Several phytochemicals inhibit tumor formation by stimulating the protective phase II enzyme, glutathione transferase. GT is a detoxifying enzyme that catalyzes the reaction of glutathione with electrophiles to form compounds that are less toxic, more water-soluble, and can be excreted easily. The phytochemicals that stimulate glutathione transferase activity include sulfides, found in garlic and onions⁽³⁸⁾. Garlic is known to have antitumor properties, owing to its content of a wide variety of organic sulfides and polysulfides. Various studies have shown that garlic can slow the development of bladder, skin, stomach, and colon cancers⁽³⁹⁾. Risk of cancer in the distal colon was 50% lower in women with the highest consumption of garlic than that of women who did not consume garlic⁽⁴⁰⁾. Garlic can inhibit the formation of nitrosamines, which are potent carcinogens, and can also inhibit the formation of DNA adducts⁽⁴¹⁾. A study conducted in Greece has shown that high consumption of onions, garlic, and other *Allium* species is protective against stomach cancer⁽⁴²⁾.

Folic Acid

Folate, a water soluble B-vitamin, is required for a variety of methylation-related processes. Although the terms “folate” and “folic acid” are sometimes used synonymously, the latter refers to the synthetic oxidized form that is commonly used in fortification and supplements, whereas naturally occurring folates are reduced molecules that exist in nature in several different forms with various degrees of polyglutamation. The association of folate and folic acid with cancer risk has been most intensely studied with regard to colorectal neoplasia. Although it has been proposed that synthetic sources of folate might confer greater protection than natural forms⁽⁴³⁾, results of one meta-analysis of observational studies⁽⁴⁴⁾ of colorectal cancer showed that total folate (dietary plus synthetic sources) did not provide greater protection than dietary folate.

Oregano

Amongst the dried herbs, oregano has perhaps the highest anti-oxidant 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!

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.

Turmeric

Although turmeric is promoted mainly as anti-inflammatory herbal remedy, some scientists believe that the anti-oxidant curcumin present in turmeric may prevent or slow the growth of many cancers including tumor of esophagus, stomach and intestine, breast cancer and also skin cancer in experimental animals. However, clinical research is needed to determine its efficacy in cancer prevention and treatment in human beings. But, the laboratory studies have confirmed that curcumin interferes with several molecular pathways involved in cancer development, growth and spread. Further, a study found that ethanolic extract of turmeric produces remarkable symptomatic relief in patients with external cancerous lesions. There was a reduction in smell in 90 percent of cases and reduction in itching in almost all cases.

Garlic

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

Maitake Mushroom

Maitake is an edible mushroom native to the mountains of northeast Japan. Its active ingredient is a polysaccharide called beta glucan. Maitake mushroom extract is said to limit or even reverse tumor growth. It also enhances the benefits of chemotherapy and lessens the side effects of anti-cancer drugs. It acts by activating certain cells and proteins that attack cancer, T-cells and interleukin-1 and interleukin-2. The daily dose of dried mushroom is between 3 to 7 g. Maitake may not be suitable for those on hypoglycemic medication.

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.

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 & 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 & spread of various cancers including that of breast, lung, oesophagus, liver, colon, prostate, head & 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, immunostimulant, anti-inflammatory, hepatoprotective and radioprotective properties.

Tomato

Tomatoes (*Solanumlycopersicum*) are a member of the nightshade vegetable family called Solanaceae, which also includes veggies like peppers, eggplant and potatoes. They are considered a high-antioxidant food and one of the best sources of the phytonutrient called lycopene in the world, which is closely tied to enhanced immunity and cancer risk reduction. Although most people correlate lycopene with deeply colored red tomatoes, it's believed to present in equally high quantities in organic yellow, green or orange tomatoes.

Research has shown that when lycopene supplements are given to men who already have existing prostate cancer, the lycopene helps to reduce the size of the tumors and stop the spreading of cancerous cells⁽⁵⁶⁾

Broccoli & Cruciferous Vegetables

The link between cruciferous vegetables and their components to cancer prevention is relatively well-studied. AICR/WCRF's expert report and its updates group cruciferous vegetables – and most green vegetables – as non-starchy. (Corn and potatoes, on the other hand, are examples of starchy vegetables.). The greater consumption of cruciferous vegetables and lower risk of lung, colorectal, stomach, breast, prostate and other cancers. Among more recent, well-designed studies, the specific link between cruciferous vegetables and reduced cancer risk is not as consistent or strong⁽⁵⁷⁾

Somediary food

Sr.no. and Reference	Dietary herbs	Active Constituents	Activity	Type of cancer treated
1 ^[6,9,10]	Curcumin	Di-feruloyl-methane	chemo-sensitizer	colorectal, pancreas, gastric, and prostate cancer
2 ^[9]	Ginger	6-gingerol and 6-paradol	cytotoxic activity through apoptosis	stomach cancer
3 ^[10,13]	Grapes	Resveratrol	apoptosis in HL60 cells and T47D	breast cancer
4 ^[14]	Green tea	polyphenols	prevent free radicals (unstable molecules) from damaging cell DNA	breast, prostate oesophagus, stomach, colon lung, skin, liver, bladder, ovary, mouth, and blood
5 ^[32,33,34,35]	fermented wheat germ extract (FWGE)	Certain protein	reduces the supply of glucose (sugar) to cancer cells making it harder for the tumors to survive	fighting colorectal, breast, melanoma, lung, and oral cancers
6 ^[38,39,41]	garlic, onions and chives	organic sulfides and polysulfide's	inhibit the formation of nitrosamines	bladder, skin, stomach and colon cancers
7	Oregano	Rosmarinic acid	strong anti-oxidant activity	colon cancer
8	Cilantro (coriander)	beta-carotene, quercetin and rutin	anti-cancer properties	
9	Maitake mushroom	polysaccharide called beta glucan	limit or reverse tumor growth.	-
10	cinnamon bark	Coumarin	decrease lipid peroxidation that lead to cancer	
11	Tomato	lycopene	high-antioxidant food	prostate cancer
12	Broccoli & Cruciferous Vegetables			lower risk of lung, colorectal, stomach, breast, prostate cancer

CONCLUSION

Herbs are very cheap source of medicine which is easily available. This herbs contributed a rich health to human beings. Edible herbs and their bioactive compounds present in them which are responsible for anticancer activity have to be screened for their valuable information. This review had given some of the dietary herbs possessing anticancer activity for various types of cancer. This review can help others to explore herbs to further extent and its use in various other disease.

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