

DIETARY SUPPLEMENTS AS ANTI CANCER AGENTS

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ABSTRACT

In an effort to develop effective alternative strategies that increase the therapeutic efficacy and minimize the systemic toxicity of chemotherapeutic agents, more efforts are being directed towards the investigation of dietary supplements and other phytotherapeutic agents for their synergistic efficacy in combination with anticancer drugs. Cancer involves disordered cell replication that is death and disorganization of organ structure. Nutritional experts are searching for suitable naturally occurring dietary factors which are or may be anti-carcinogenic. Oncologists are trying to identify antioxidants present in consumable fruits and vegetables rich in vitamins, amino acids, and carotenes which can be utilized in the prevention and treatment of cancer. The present text aims to provide information about dietary approaches in treatment and prevention of cancer.

Keywords: Anticancer, dietary approaches, nutraceuticals, antioxidants.

INTRODUCTION

Cancer involves disordered cell replication that is death and disorganization of organ structure. Nutritional experts are searching for suitable naturally occurring dietary factors which are or may be anti-carcinogenic. Oncologists are trying to identify antioxidants present in consumable fruits and vegetables rich in vitamins, amino acids, and carotenes which can be utilized in the prevention and treatment of cancer. Present scientists are increasingly describing cancer as a disease involving excessive proliferation of cells as well as the ability to kill themselves known as apoptosis (cell suicide)³.

The present text aims to provide information about dietary approaches in treatment and prevention of cancer. Nutraceuticals include anti oxidants and immuno modulators present in natural products.

Cancer should be called a symptom rather than a disease as it indicates the abnormal uncontrolled and paired growth of cells. These cancer cells are malignant in nature. Cancer cells differ from normal biological cells mainly in two ways: they are there as long as the host is alive and can rapidly multiply themselves to form new cancer cells. They do not die until host dies. Secondly they undergo metastasis (transfer of cancer cells from one organ of the body to another which is not directly connected to it). There are more than hundred types of cancers. Broadly they are two types:

- Carcinoma: Malignant new growth made up of epithelial cells tending to infiltrate surrounding tissues and give rise to metastasis.
- Sarcoma: Cancer arising in bone, connective tissue or muscle that is the tissue mainly derived in the embryo from mesoderm and lymphatic blood vessels.

There are four methods for treatment of cancer:

- Surgery which can be practiced in case of metastasis
- Radiation Therapy which affect both normal and cancerous tissue equally
- Chemotherapy with some side effects
- Immunotherapy: the manipulation of immune response, immunotherapy is also tried in association with chemotherapy⁶.

Different natural products having Anti Cancer Property

This class comprises of plant, animal and antibiotics etc. The present text shall concentrate primarily on Podophyllotoxin, Vinca alkaloids and Taxol amongst natural products category.

Podophyllotoxin a resin isolated from Podophyllum peltatum rhizome (Fm Berberidaceae) possesses cytotoxic and anti tumor activity⁴. Etoposide, a lignan derivative is used in the treatment of small cell lung cancer and testicular cancer⁵. Vincristine and Vinblastine are dimeric indole alkaloids isolated from Madagascar periwinkle *Catharanthus roseus* (Fm. Apocyanaceae) and also acts selectively at metaphase⁶. Vinca alkaloids have been referred to as 'miracle drug' judged by their clinical acceptance by the patients.

Taxol is a naturally occurring diterpene belonging to taxane group of compounds present in genus *Taxus* Fm Taxaceae. A derivative of Taxol – Taxotere has been reported to have better bioavailability and pharmacological properties⁵.

Micro-organisms widely employed as a source of antibiotics produce a number of metabolites with anti-tumor activities. Anthracycline, bleomycin and actinomycin D derived from streptomycetes and actinomycetes sps. Respectively are clinically used as anti cancer agents. In these anthracycline and actinomycin D



are DNA intercalating agents and is believed that this DNA binding is necessary for inhibition of nucleic acid synthesis⁸.

Role of Anti-Oxidants

Anti oxidants or free radical scavengers can function as inhibitors at both initiation and promotion, propagation or transformation stages of tumor promotion or carcinogenesis and protect cells against oxidative damage and transformation^{9,10}.

The dietary antioxidants having anti carcinogenic property are in demand. Nutritional oncologists are concentrating on this topic and active research is being done. Identification and characterization of these anti carcinogens in the diet can be used for reducing the risk of human cancer. Any agent which can block the metabolic activation step or enhance detoxification would be a potential chemopreventive agent¹¹⁻¹³. Because dietary approach for cancer prevention is economical and cost effective¹. Some of the vitamins and mineral supplements show chemopreventive effect, but act harmful or not shown clear benefit¹⁴. Therefore to consume plenty of fruits, vegetables having rich antioxidants are beneficial¹.

Human diet contains a complex mixture of phenols. These natural phenols distributed in plant kingdom because of their strong anti oxidant activity and free radical scavenging potency¹⁵⁻¹⁸. The two main classes of plant phenols are flavinoids and anthraquinones¹⁹⁻²¹. Fourteen plant phenols having 5 different structural groups – flavones, flavanals, flavon – 3-ol, isoflavones and phenyl propanoids demonstrated concentration dependant inhibitory or modulatory effect on various types of cell culture model- lymph, human umbellical vein, endothelial cell and osteoclasts^{22,23}. Quercitin the most common flavanal is non- mutagenic and lacks DNA damaging activity²⁴. Alizarin, a plant phenolic anthraquinone has radical scavenging activity²⁵.

Caffeine belongs to a group of compounds known as methylxanthine that has proved carcinogenic²⁶⁻²⁸ and has been reported to antagonize the carcinogenic effect in vitro²⁹. In vivo condition, it alters chemically induced tomorigenesis³⁰.

Amino acids rich foods have been used as a source to discover new compounds having anticancer and antimicrobial properties. N-acetylcysteine is at present considered to be one of the most promising second generation chemopreventive agents³¹.

Fruits and Vegetables: Green leafy vegetables exhibits higher antioxidant activity followed by nutritive whole grains, however cooking reduces this activity³². Antimutagenic effect of ethanolic extracts of fruits and vegetables against N-nitrosamines was demonstrated as Liquorice>Kinu>Carrot>Broccoli>Pineapple

Without amines:

Onion>Liquorice=Garlic>green pepper>Carrot³³

Citrus fruits: There is a considerable evidence that the antioxidant nutrients like Vitamin C, D, E and β carotene present in fresh fruits. Vegetables and their seeds help to maintain human health and protect various organs from free radical injury and diseases^{34,37}. 27 different citrus flavanoids are believed to be active against tumor cells a how weak antiproliferative activity against normal human cell lines³⁶. Lemon fruit coumarins(8-gera ploxypsoralen-5-geranyloxy-7-methoxy coumarins etc) isolated from lemon fruit (Citrium limon) acts as in vitro inhibitor of tumor promotion in mouse macrophage cells by inhibiting superoxide and NO generation³⁷.

Figs (Ficus carica;Moraceae): Figs are widely used both as food and medicine in the middle east. The latex released on picking the fruits is used to treat skin tumors and warts³⁸.Primary palmitoyland Linoleyl with minor amounts of stearyl and oleyl has been isolated as a potent cytotoxic agent³⁹. Latex of the fruit is used to treat skin tumors and warts⁴⁴. Mixture of 6-o-acyl- β -D glucosyl- β -sitosterol, acyl moety primarily palmitoyl and linoleyl with minor amounts of stearyl and Oleyl has potent cytotoxic action⁴⁵.

Grapefruit: Coumarins and limonoids isolated from grape fruit(Citrus paradisica) have shown antimicrobial and antitumor activity⁴⁰.

Grapes: Aromatase(especially tumor aromatase) is known to play an important role in promoting breast cancer in post menopausal women by converting androgens to estrogens. Grape juice (Vitis vitefera, Family Vitaceae) has been found to contain relavant phytochemicals which inhibit estrogen biosynthesis by competing for the substrate androstenedione chemicals in grape juice and simultaneouslyactm as weak agonist of estrogen receptor⁴¹.Resveratrol produced in the skin of red grapes protect against cancer by acting as powerful antioxidants. This natural phytoalexin is a remarkable inhibitor of ribonucleated reductase and DNA synthesis in mammalian cells. Thus it might act as antiproliferative agent in humans⁴².In vitro and in vivo studies authenticate that free radical scavenging activity, cytochrome p450 inhibitory activity, antinecrotic anti-apoptotic, anticarcinogenic, modulatory, antioxidant activity in grapes⁴³.

Vital Vegetables:

Broccoli and Cauliflower: A bacterium named Helicobacterium pylori has been responsible for the vast majority of stomach cancers a leading cause of cancer deaths. Sulphoraphane, indole-3 compound found in broccoli sprouts and in cauliflower kills the bacterium in vitro studies⁴⁶.

Garlic (Allium sativum): Garlic has been used as medicinal plant for thousands of years and shown to have antimicrobial and antitumor properties. These effects have been linked to their influence on eicosanoid metabolism that influences immune functions. Epidemiological studies suggest that rich garlic content in



the diet might reduce the proliferation of tumors in humans. Garlic extract supplemented with garlic powder (to 10% final concentration, there is a concentration dependent clear inhibition of tumor cell growth. Upon mixing the two preparations no potentiation occurred. The antiproliferative activity of garlic may be due to breakdown product of allicin. Allicin also exerts immunosuppressive effect.

Tea: Drinking some types of tea and coffee is a part of everyday life. Tea (*Camellia thea*) an evergreen plant contains antioxidants which prevent and repair cellular damage caused by reactive free radicals. Both green and black teas have shown to inhibit lung tumor genesis in vitro investigation studies performed on laboratory models during carcinogenesis treatment⁴⁹. Epicatechin gallate (ECg), Epigallocatechin gallate (EGCg) and Theaflavin suppressed strongly the invasion of HT 1080 cells into the monolayer of human umbilical vein endothelial cells. They also invade the metalloproteinase (MMP) activity on human fibrosarcoma cells without cytotoxicity against normal cells. Herbal products like Essiae and flor essence sold as nutritional supplements are used by patients suffering chronic conditions even in cancer.

Ginger (*Zingiber officinale*): belonging to family Zingiberaceae contains pungent ingredients in which gingerol and piperone have shown antitumor promotional and antiproliferative effects.

Green Tea (*Camellia sinensis*): contains epigallocatechin gallate which protects cancer by preventing covalent bonding of carcinogens to the DNA. It also acts through another mechanism i.e by eliminating free radicals from the body. Gallates found in green tea protects the body from damaging effects of radiation. A regular use of green tea protects the body against many cancers including liver, oesophagus, stomach and lung. Studies have shown that there is lower incidence of stomach cancer in habitual tea drinkers as compared to those who do not drink tea. It has been said that daily consumption of 5gms of green tea inhibits synthesis of nitrosamine (major carcinogen) in the body.

Aloe: Aloe vera and other species of aloe contain aloe emodin which activates the macrophages to fight cancer. Aloe vera also contains acemannan which enhances the activity of immune cells against cancer.

Betula vitilis (White barked Birch tree): 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 lungs.

Milk Thistle (*Silybum marianum*): Milk thistle specially protects the body against liver cancer by accelerating regeneration of liver cells. Bioflavonoids found in *Silybum marianum* such as silymarin and silybin are known to protect the liver tissue. It also contains cytotoxic compounds.

Echinea angustifolia: It contains arabinogalactan which protects the body from cancer by activating macrophages. It is used to treat metastatic carcinoma of the oesophagus and the colon⁴⁶.

Others: Supervitamin drinks containing a combination of *Hordeum vulgare*, *Medicago sativa* and *Spirulina* enhances the activity of immune cells against cancer. *Mentha* species containing antioxidants prevent recurrence of cancer.

CONCLUSION

Neutraceuticals are having their own importance amongst all natural products. In an effort to develop effective alternative strategies that increase the therapeutic efficacy and minimize the systemic toxicity of chemotherapeutic agents, more efforts are being directed towards the investigation of dietary supplements and other phytotherapeutic agents for their synergistic efficacy in combination with anticancer drugs. The present review summarises plant-derived botanical and dietary supplements which are widely prescribed world wide and are considered natural, safe, and beneficial.

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