



INTERNATIONAL JOURNAL OF PHARMA PROFESSIONAL'S RESEARCH



CHEMISTRY AND SIGNIFICANCE OF CHEMOPREVENTIVE NUTRACEUTICALS: A REVIEW

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Keywords:

Nutraceutical, Chemotherapy, Chemoprevention, Antitumor, Cancer

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ABSTRACT:

Nutraceutical is a food or part of food that has physiological and medical benefit and is used in the prevention of various diseases. Cancer is a serious health issue and is rarely curable that depend on its type and site. For the treatment of cancer different therapies like chemotherapy, radiotherapy, hormone therapy are used, but major disadvantage of these therapies are that they have many side effects including gastrointestinal problems, changes in skin and hair loss. According to new research, some nutraceuticals may influence the cellular and molecular steps that contribute to cancer development. Studies suggest that combination therapy can help in cancer prevention much better than a single nutraceutical. Combination strategies to chemo prevention can take various forms: two or more phytochemicals, a chemically synthesized phytochemical and an efficient drug or a chemically synthesized phytochemical and a natural nutrient. The aim of this chapter is to analyze the chemo preventive significance of the nutraceuticals.

Introduction:

According to numerous studies diet is one of the most important factor of chronic diseases like cancer, diabetes, diseases related to heart, stones in gallbladder and different diseases related to neurons. Hence, diseases and diet are directly associated with each other.[1] Cancer is the deadliest disease in which unwanted & uncontrolled growth of the cells occurs. Normally, through the process of cell division human cell grow and multiply to form new cells. When cells become old or damaged, they are replaced by new cells. But sometimes this mechanism fail, and

abnormal or damaged cells start to grow and multiply. And these cells may form malignant tumors (cancerous tumors) or benign tumor (noncancerous tumors).[2] Fatigue, lump, sudden change in weight & skin, trouble in breathing, feeling difficulty in swallowing, unexplained fevers etc. are some common symptoms of cancer.[3] Smoking, poor diet, eating too much red processed meat, heavy body weight, direct exposure of sunlight are the most common cause of cancer.[4] By surgery, chemotherapy, radiation, bone marrow transplant, immunotherapy, hormone therapy cancer is treated.[5] Risk of cancer can be reduced by

maintaining healthy body weight, avoiding alcohol & tobacco, and avoiding direct exposure of sunlight.[6] There are various factors that can help in prevention of cancer among those nutraceuticals are one of the important one that can help in the prevention of cancer.

Nutraceuticals

A nutraceutical is any substance that is contemplated as a food or part of food and is used in treatment or prevention of any disease. The word Nutraceutical is the combine of two words “nutrition” and “pharmaceutical” and was coined by Stephen DeFelice in 1989.[7] According to Stephen, “Nutraceutical is a food, food ingredients or any dietary supplement that have a specific health and medical benefits.”[8] The source of nutraceuticals are plants (e.g. Quercetin, Luteolin, Cellulose, Lutein, Gallic acid, Perillyl alcohol, Indole-3-carbonol, Pectin, Daidzein, Glutathione, Allicin, 8-Limonene, Genestein, Lycopene, Hemicellulose, Lignin, Capsaicin, Geraniol), Animals (Choline, Lecithin, Calcium, Coenzyme Q10, Selenium, Zine, Creatine) and microbes (Saccharomyces boulardii, Bifidobacterium bifidum, B. longum, B. infantis, Lactobacillus acidophilus, L. acidophilus, Streptococcus salvarius).[9] In developed countries nutraceuticals became a vicinity of the day-to-day life. It's employed in sickness condition like joint pain, insomnia, rheumatism, chronic condition, enlarged prostate, perimenopause, weight management, vas health, immunomodulators and state of mind. Nutraceuticals area unit on the market within the type of isolated nutrients, dietary supplements and specific diets to genetically designed foods, flavored merchandise and processed foods like cereals, soups and beverages. Nutraceuticals give all the essential substances that should be in healthy diet of us. Nutraceuticals provides energy and nutrient supplements to body, that area unit needed for maintaining optimum health. Nutraceuticals area unit wide employed in the food and pharmaceutical industries. Some nutraceuticals are helpful in maintaining healthy prostate perform, remedy for restlessness and sleep disorder. [10]

Cancers in the Human Body and Nutraceuticals [11]

Cancer prevention through nutraceuticals became popular in the late 1990s. Federal agencies continue to

limit the regulatory policies governing the use of nutraceuticals in cancer prevention. With the widespread victory of self-prescription and over-the-counter sale of nutraceuticals, alternative medicine ushered in a new era of safe non-prescription drugs. In the last five years, there has been a growing acceptance of nutraceuticals by both public and federal authorities. Breast, prostate, colorectal, ovarian, pancreatic, and skin cancers were identified as major health risks.

Breast cancer was recognized as a single major health concern mid-1990s, and it continues to be a big danger among women. Various nutraceuticals have been proven to decrease the incidence of breast cancer in both self-medications at household and health facilities. The most significant consequence of experimental animal trials was clear evidence of decreased cancer cell proliferation by nutraceutical intervention, which confirmed the function of nutraceuticals in chemoprevention. Soy genestein, isoflavones, vitamin pills as free radical scavengers, anti - oxidants, and mitochondrial oxidative phosphorylation are some examples of breast cancer protective nutraceuticals.

Prostate cancer is still considered as the single most serious health concern among men, and it is the primary target of nutraceutical supplementation to reduce risk of prostate cancer in randomized control controlled studies. Vitamin supplement antioxidants, soy isoflavones, and soy-tomato combination products are all instances of cancer-protective nutraceuticals. The majority of animal cancer research supported the reduction of prostate cancer by nutraceutical intake. It is still necessary to show the utility of nutraceuticals in medical prescription in health care facilities. A lot of academic and worldwide federal efforts are being made in this regard to establish the long-term effects of nutraceuticals in risk of prostate cancer . The rising public knowledge and self-prescription of nutraceuticals for prostate cancer benefits is a major source of worry for health officials.

Cancer of lungs and esophagus have retained underestimated health dangers, possibly due to other environmental variables acting as primary causal drivers of respiratory disorders with potential cancer risks. However, a few investigations revealed that vitamins A and E may have significant nutraceutical effects in lung cancer prevention.

IJPPR (2023), Vol. 14, Issue 1

Researches are still being made to monitor an increase in the usage of nutraceuticals in much less common malignancies. Cancer prevention by nutraceuticals has recently been demonstrated for lymphoma, skin cancer, and pancreatic cancer. Vitamins and minerals have recently been verified in chemoprevention trials for several malignancies. In other recent studies, researchers discovered a beneficial effect of several nutraceutical supplements and meals in the prevention of cancer in many organs of the body.

Different nutraceuticals and their role in chemoprevention

It is approximate that a large number of cancer death can be prevented by changing life style including by taking good nutrients.[12] Nutraceuticals play a crucial role in the prevention of cancer, they have the potency to reduce the growth of the cell and inhibit proliferation of cell. [13] Nutraceuticals, derived from soya bean, garlic, ginger, tea as well as propolis, honey and many others are helpful in prevention of cancer. [14]

Additionally, nutraceuticals also help in reducing toxicity that occur due to chemotherapy and radiation therapy and improve the weakness in cancer patients. [15]

At different cellular levels nutraceuticals have different mechanism of actions i.e. i) They affect the signaling pathway related to redox mediated transcription factors. ii) They modulate the endocrine system and inflammatory enzymes directly. iii) Some of the nutraceuticals directly affect DNA repair and cleavage process. [16]

1. Capsaicin (8-Methyl-N-vanillyl-trans-6-nonenamide)

It is an active constituent of chili peppers, a plant belonging to the genus capsicum.[17] It induce cell-cycle arrest or caspase-mediated cell death or inhibit proliferation in a variety of cancer cells, and has a potent activity in cancer prevention.[18]

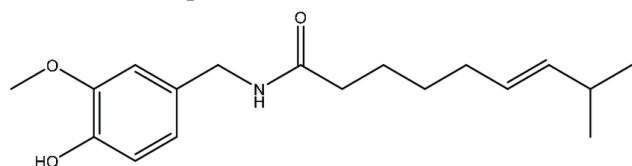


Figure 1: Molecular structure of capsaicin [19]

Review Article

- Curcumin (1E,6E)-1,7-bis (4-hydroxy-3-methoxyphenyl) -1,6- heptadiene-3,5-dione
Curcumin is a component of the spice turmeric. Curcumin has antioxidant capabilities, which means it may reduce swelling and inflammation. It is being researched as a cancer therapy since inflammation appears to have a function in cancer. Curcumin may prevent cancer, reduce its spread, make chemotherapy more efficient, and protect normal tissue from radiation treatment harm.[20]

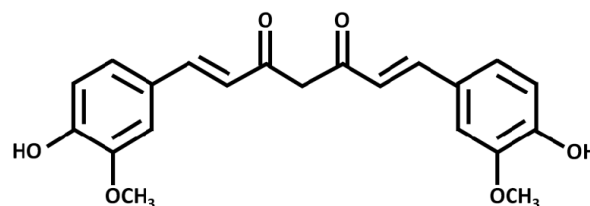


Figure 2: Molecular structure of Curcumin [19]

- Enterolactone (3R,4R)-3,4-bis[(3-hydroxyphenyl)methyl]oxolan-2-one

A mammalian lignan produced from diet lignans is called enterolactone. Multiple studies have shown that it has strong anti-cancer and/or preventive capabilities against many malignancies, including liver cell malignancy, breast, prostatic, colo-rectal, lung, ovarian, endometrium, and cervical malignancies. The anti-proliferative, pro-apoptotic, anti-inflammatory, anti-angiogenic, and anti-metastatic properties of enterolactone have been primarily linked to these actions.[21]

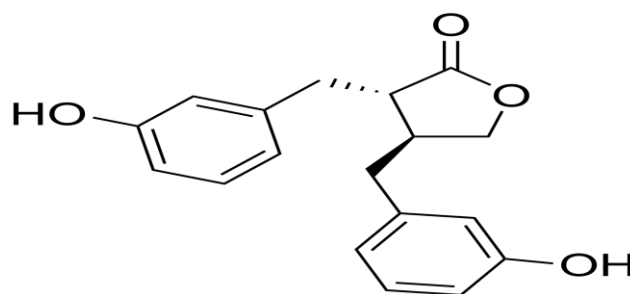


Figure 4: Molecular structure of Genistein

- Genistein** 5,7-Dihydroxy-3-(4-hydroxyphenyl)-4H-1-benzopyran-4-one:

Genistein is a phytoestrogen and isoflavone generated from soy that has antineoplastic action. Genistein binds to and suppresses protein-tyrosine kinase, causing signal transduction to be disrupted and cell differentiation to occur. This drug also

suppresses topoisomerase-II, causing DNA breakage and death, as well as causing G2/M cell cycle arrest.[23]

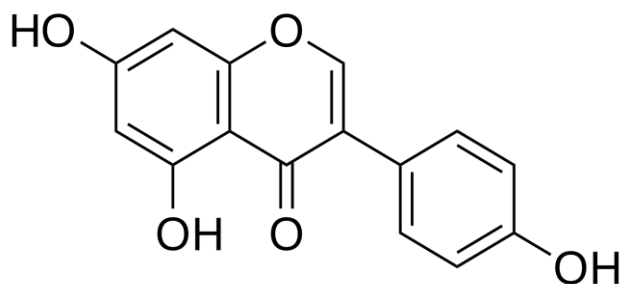


Figure 4: Molecular structure of Genistein

5. Gingerol (5*S*)-5-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)decan-3-one

Gingerol is an active constituent of ginger. It is obtained as pungent yellow oil from the rhizome of ginger. It is present in all plants belonging to family Zingiberaceae .[25] It has the potential to reduce tumour necrosis factor alpha (TNF-alpha) expression by inhibiting I-kappaB alpha (IkappaBalph) phosphorylation and nuclear factor kappa B nuclear translocation. Additional antiproliferative effects of gingerol involve Cytochrome c release, Caspases activation, and a rise in proteolytic protease-activating factor-1 (Apaf-1) as such an apoptosis induction process.[26]

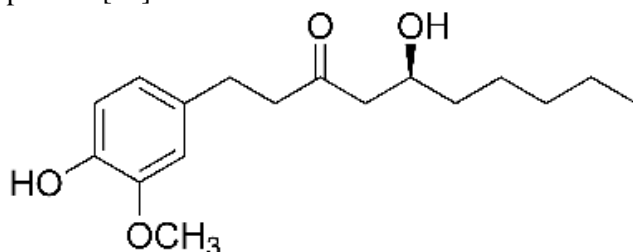


Figure 5: Molecular structure of Gingerol [27]

6. Ajoene (4,5,9-trithiadodeca-1,6,11-triene-9-oxide) Ajoene is one of the active constituents generated when crushed garlic is heated. Ajoene has a wide range of biological actions, including anticancer properties. Its cytotoxicity against cancer cells is thought to be caused by an apoptotic mediated pathway that involve activation of the mitochondrial-dependent signaling cascade. [28]

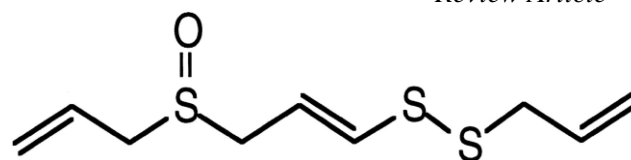


Figure 6: Molecular structure of Ajoene [29]

7. Epigallocatechin-3-gallate [(2*R*,3*R*)-5,7-dihydroxy-2-(3,4,5-trihydroxyphenyl)chroman-3-yl] 3,4,5-trihydroxybenzoate The epigallocatechin-3-gallate (EGCG) is an active constituent of green tea. This green tea compound's anti-cancer role has been acknowledged in different types of cancer and is now being researched. EGCG has been shown to have chemopreventive properties by inhibiting carcinogenesis processes like initiation, promotion, and progression. Furthermore, this catechin has demonstrated its role in cancer management by modulating various cell signalling pathways including controlling proliferation, programmed cell death, angiogenesis, and cancerous cells killing.[30]

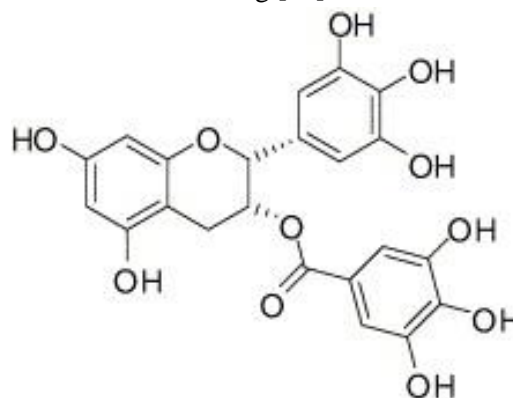


Figure 7: Molecular structure of Epigallocatechin-3-gallate [31]

8. **Lycopene** (6*E*,8*E*,10*E*,12*E*,14*E*,16*E*,18*E*,20*E*,22*E*,24*E*,26*E*)-2,6,10,14,19,23,27,31-Octamethyldotriacont-2,6,8,10,12,14,16,18,20,22,24,26,30-tridecaene] : Lycopene is a constituent of ripe tomatoes. It is also found in many red fruits as well as in vegetables e.g. red carrot, watermelon, papaya etc. It has anti-inflammatory and chemopreventive properties. Lycopene absorbs oxidative stress, scavenges free radical damage, and protects DNA from oxidative damage. As a result, it inhibits normal cells from developing into cancerous cells. It also influences genetic mutations, cancer enzymes, cytotoxicity, and defense function.[32]

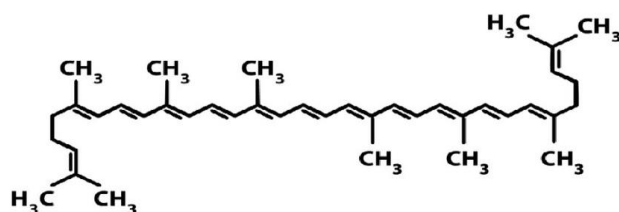


Figure 8: Molecular structure of Lycopene [33]

Conclusion:

Cancer is a deadliest disease, and it has many types. Many of them including breast cancer, prostate cancer, thyroid cancer etc. may be cured but cancer of liver, lung, pancreas and gallbladder are not curable easily. Avoiding alcohols and cigarettes, having good diet, maintaining a proper body weight, avoiding direct exposure of sunlight are the various factors that reduce risk of cancer. Uses of nutraceuticals in the prevention of cancer are a novel approach because generally they have no side effects and are inexpensive. Many of the nutraceuticals have shown their good response in the prevention of cancer, but still there is more need for research on chemopreventive mechanism of nutraceuticals.

Conflict of Interest

The authors declare that the review was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgement

The authors are thankful to their parents.

Funding

None

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