

Bioflavonoids - Cancer Bombs

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Abstract: Bioflavonoids are a group of polyphenolic compounds which are a secondary group of plant metabolites. A natural way of obtaining these bioflavonoids includes the intake of fresh fruits, citrus fruits, sweet pepper, broccoli, spinach, green tea etc., Apart from their role in anti-cancer therapy, bioflavonoids also have anti-inflammatory, anti-allergic, anti-bacterial activities, they can also induce DNA mutations. Important bioflavonoids include Catechins, EpiCatechins, EpiCatechin Gallate, Taxifolin, Quercetin etc.,. Here in this article, the role of the above mentioned bioflavonoids in anti cancer chemotherapy is reviewed.

Keywords: Bioflavonoids, Vitamin P, Polyphenols

1. Introduction

Bioflavonoids also known as "Vitamin P" (Due to the effect of permeability of vascular capillaries) are super-antioxidants which play an important role in suppressing poor cellular growth thereby playing a role in anticancer chemotherapy. Bioflavonoids also decrease the permeability and fragility of vessel walls in certain conditions. Bioflavonoids potentiate the actions of vitamin C by inhibiting its breakdown in the body. Parsley seeds, green tea, black tea, citrus fruits, blueberries etc., are some of the food substances rich in bioflavonoids. Incorporation of these dietary flavonoids regularly in our diet helps us to fight day to day stress, ageing, and also decreases the risk of many cancers.



2. Catechins

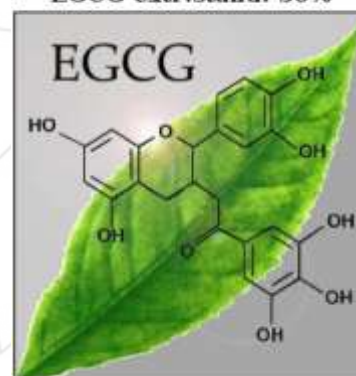
Catechins are polyphenolic flavonoids which have been isolated from many natural sources like tea leaves, grape seeds, barks of acacia. A research was conducted on the effect of Catechin hydrate (CH), a compound of Catechins in the role of anti cancer effect in breast cancer. CH targets apoptic genes in MCF-7 of the human breast cancer cells. CH kills MCF-7 cells through apoptosis. This apoptosis was confirmed TUNEL and Realtime PCR assays (1)

Green tea is a natural source of catechins. A study was conducted to assess the efficacy of green tea catechins (GTC) in preventing Prostate carcinoma in men with high grade

prostate intraepithelial neoplasia (HG PIN). 60 men with HG PIN were given GTC 200 mg tablets 3 days each. Green tea Catechins have certain important forms of Catechin like Epi Catechin gallate which inhibit 5 alpha reductase and thus the conversion of testosterone to 5 alpha dihydrotestosterone is thus prevented and there is reduced risk of prostate cell carcinoma. (2)

Green tea Catechins to a major extent can prevent the risk of pre malignant lesions of the oral cavity and oral digestive tract cancers (3)

Galatul de Epigalocatechina
EGCG extr. stand. 50%



Epigallocatechin Gallate (EGCG) is the most powerful bioflavonoid in anticancer chemotherapy. Studies have shown that EGCG playing an important role in inhibiting colon cancer. Human colorectal cancer cell lines were collected and grown in an indicated medium containing 50 IU Penicillin, 5% FBS in a humidified atmosphere. It was then plated and when it was free of contamination, cell lines were removed. Cells were seeded in 24 hr culture plates. Cell assays showed EGCG showed antiproliferative effects and was responsible for the induction of apoptosis. (4)

3. Quercetin

Quercetin is a flavonoid widely distributed in nature, it is derived from quercetum (oak forest), after Quercus. It is a naturally occurring polar auxin transport inhibitor. It also plays an important role in chemo prevention of cancer. Quercetin protects the DNA in cells because collects around the nucleus of the cell thereby providing antioxidant function. Quercetin binds to excess iron in the body, removes it from tissues, and prevents its absorption. This process is called chelation. This is critical as iron can be a

key ingredient in cancer cell growth. Quercetin has the ability to obtain the iron from cancer cells which can stop their growth and induce cell death.

Quercetin combined with the radical polymerization of methacrylic acid around carbon nanotubes gives rise to a three functional quercetin nano composites which execute their effect as a anticancer therapeutic .Quercetin enhances the effect of mitomycin C on inhibition of tumorigenicity of mammary tumours. Quercetin arrests the MCF-7 cells in G2/Mitotic phase of the cell cycle in a dose and time dependent way (5)

Quercetin is has also shown anticancer activity against neuroblastoma. A study was conducted in vitro to determine the anticancer activity of quercetin against neuroblastoma which is a neuroendocrine tumour derived from neural crest cells. Quercetin was found to induce apoptosis in the N2a(a mouse neuroblastic cell line)(6)

Doxorubicin is commonly used in the treatment of a wide range of cancers, including hematological malignancies, many types of carcinoma and soft tissue sarcomas. Quercetin could improve therapeutic index of doxorubicin, a drug used in cancer chemotherapy, by its opposing effects on hypoxia-inducible factor-1 alpha in tumor and normal cells. Quercetin may also have anti-mutagenic properties. Quercetin serves as a chemo protectant Diethylnitrosamine (found in tobacco smoke and processed meat) is a hepatocarcinogen .The hepatocarcinogen increased malondialdehyde and decreased glutathione levels in the liver, and increased plasma levels of aspartate transaminase and alanine transaminase. Treatment with quercetin restored these levels and also reduced diethylnitrosamine induced DNA damage and apoptosis. (7)

Heat shock proteins (HSP) are a group of proteins induced by heat shock, the most prominent members of this group are a class of functionally related proteins involved in the folding and unfolding of other proteins. Their expression is increased when cells are exposed to elevated temperatures or other stress. This increase in expression is transcriptionally regulated. Heat shock proteins form a complex with mutant p53 which allows tumour cells bypass normal cell cycle arrest. Quercetin has found to inhibit heat shock proteins in many malignant cell lines including those of breast cancer, colon cancer (8)

4. Taxifolin

Taxifolin is an important bioflavonoid and it is obtained from natural sources like Siberian larch, Chinese Yew, red onions etc. It exerts its chemopreventive effect by regulating genes via ARE-dependent mechanism.(9)



Taxifolin (also known as dihydroquercetin) exerts strong chemo preventive effects against UV induced skin carcinogenesis by directly inhibiting the synthesis of Epidermal Growth Factor Receptor (EGFR) and phosphatidylinositol 3 kinase (PI-3k). Studies have shown that the EGFR and PI3-K/Akt signaling pathways are critical for UV-induced skin carcinogenesis. EGFR is activated and/or overexpressed in a variety of human cancers including UV-induced skin cancer (9–10), and AG1478, a specific inhibitor of EGFR, was shown to prevent UV-induced skin carcinogenesis (14). UV-irradiation also was reported to suppress mitochondria- and caspase-dependent apoptosis through the PI3-K/Akt pathway and PI3-k inhibitor. Taxifolin suppressed UVB-induced phosphorylation of EGFR signaling as well as the PI3-K/Akt signaling pathways (10)

Taxifolin inhibits the production of lipopolysaccharide-induced prostaglandin E, and fustin suppresses the activity of acetylcholinesterase. It controls the expression of cell cycle regulatory proteins, which blocks G1 cell cycle progression and inhibits the clonogenicity of HCT116 cells (11)

Taxifolin was found to bind at ATP-binding site of Hsp90 and stabilized the inactive "open" or "lid-up" conformation as evidenced by molecular dynamic simulation. Thus, taxifolin was found to act as an inhibitor of chaperoning process and may play a potential role in the cancer chemotherapeutics. (12)

Vascular endothelial growth factor (VEGF) is a potent growth promoter that is highly specific for vascular endothelial cells which is a strong angiogenic agent that increases vessel permeability and enhances endothelial cell growth, migration, proliferation and differentiation. Angiogenesis plays crucial role in the pathogenesis of a variety of disorders such as cancer, proliferative retinopathies, and rheumatoid arthritis. The growth promoting and angiogenic effects of VEGF are mainly mediated by two receptor tyrosine kinases (RTKs): VEGFR-1 kinase and VEGFR-2 kinase. An attempt was made to explore the potential of taxifolin to inhibit VEGFR-2 kinase. The stability of the binding complex was also demonstrated by molecular dynamics simulations. Taxifolin was found to

bind at ATP-binding site of VEGFR-2 with lowest binding energy (13)

5. Conclusion

Bioflavonoids are thus proven to be very effective chemo therapeutic agents. There are certain other bioflavonoids like hesperidin and rutin which have anticancer effects and have the power to fight ageing, reverse wrinkles and varicose veins. These powerful plant metabolites can work synergistically harmonising each other. By recognising and identifying the valuable gifts of nature one can fight cancer, ageing and even life threatening problems which can be a great revolution in the modern science and technology.

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