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Review Article

Pleiotropic Effects of Green Tea: An Overview

Gurfateh Singh, Hardeep Kaur and S.L.Harikumar
Rayat and Bahra Institute of Pharmacy, Sahauran, Dist. Mohali-140104, Punjab, India

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Abstract

In response to the increased popularity and greater demand for medicinal plants, a number of conservation groups are recommending that wild medicinal plants be brought into cultivation. Over the past decade many scientific and medical studies have focused on green tea for its long-purported health benefits. There is convincing evidence that tea is a cup of life. Green Tea is one of the most ancient and popular therapeutic beverages consumed worldwide. This product is made from the leaf of the plant called "Camellia sinensis". It can be prepared as a drink, which can have many systemic health effects or an "extract" can be made from the leaves to use as medicine. Green tea is reported to contain thousands of bioactive ingredients which are almost contributed by polyphenols which plays a key role in prevention and treatment of many diseases. The aim of this literature review was to illustrate therapeutic properties of the plant "Green tea".

1. INTRODUCTION

Various linkages have been established between health and nutrition diverting the human trend towards plant based natural products to cure various diseases. Besides their health promoting potential, medication cost in developing countries is also high, which is a contributory factor for the popularity of diet based regimen. Functional foods or beverages are important in this scenario because of easy accessibility, low cost and maximum health benefits. In this context, some fruits, vegetables, whole grains, cereals, nuts etc are important showing therapeutic potential owing to their rich phytochemistry. Among the functional foods, green tea is becoming popular due to its health promoting potential besides consuming as traditional beverage. Health benefits of green tea are due to its polyphenolic components known as catechins, including epicatechin, epicatechin gallate, epigallocatechin and epigallocatechin gallate (EGCG)[1]. However, EGCG is the most promising component. Catechins possess anti-oxidant[2], Antiobesity[3], antihypercholesterolemic[4], antihyperglycemic[5] and anticancer properties[6]. Hence, the present review is designed to explore the possible pleiotropic effects of green tea with special reference to catechins and EGCG against lifestyle-related and drugs induced disorders.

2. GREEN TEA

Green tea (GT) is one of the most popular beverages consumed worldwide after water. Tea which is obtained from the plant *Camellia sinensis* (Theaceae) is consumed in different parts of the world as green, black, or Oolong tea[7]. Among all of these, the most significant effects on human health have been observed with the consumption of green tea[8]. GT is processed differently during manufacturing. To produce green tea, freshly harvested leaves are immediately steamed to prevent fermentation, yielding a dry, stable product. This steaming process destroys the enzymes which are responsible for breaking down the color pigments in the leaves and allows the tea to maintain its green colour during the subsequent processes like rolling and drying. These processes preserve natural polyphenols with respect to the health promoting properties. As GT is fermented to Oolong and then to black tea, polyphenol compounds (catechins) in green tea are dimerized to form a variety of thea flavins, such that these teas may have different biological activities.

Corresponding Author:
Gurfateh Singh,
Asst. Professor,
Rayat and Bahra Institute of Pharmacy,
Sahauran, Mohali-140104, Punjab, India.
Email : dr_sugga@yahoo.co.in

3. COMPOSITION OF GT

GT contains useful compounds like polysachharides, flavanoids, vitamin B-complex, vitamin C and fluoride in its natural state. The tea leaf contains poly phenols such as catechins, flavonols, flavandiols and phenolic acids, epigallocatechin gallate (EGCG), enzyme polyphenol oxidase. The major tea catechins are EGCG, (-) epigallocatechin (EGC), (-)-epicatechin-3-gallate (ECG), (-)-epicatechin (EC) and (-) catechin[4]. The chemical composition of GT is complex structure contains proteins (15-20% dry weight), whose enzymes constitute an important fraction like amino acids, carbohydrates, minerals and trace elements, trace amounts of lipids, sterols, vitamins, caffeine, theophylline, pigments (chlorophyll, carotenoids), and volatile compounds[9]. In addition, they have phenolic acids such as gallic acids and characteristic amino acids such as theanine[1]. GT contains polyphenols, which include flavanols, flavandiols, flavonoids, and phenolic acids; these compounds may account for up to 30% of the dry weight. Most of the green tea polyphenols (GTPs) are flavonols, commonly known as catechins. Products derived from green tea are mainly extracts of GT in liquid or powder form that vary in the proportion of polyphenols (45-90%) and caffeine content (0.4-10%). The major flavonoids of green tea are various catechins, which are found in greater amounts in GT than in black or Oolong tea[1]. The preparation methods influence the catechins both quantitatively and qualitatively; the amount of catechins also varies in the original tea leaves due to differences in variety, origin, and growing conditions[10]. The preparation of fresh green tea cannot totally extract catechins from the leaves; therefore, the concentration found differs from the absolute values determined through the complete extraction of leaves[11]. Moreover, catechins are relatively unstable and could be quantitatively and qualitatively modified during the time frame of an experiment[12-13].

4. PLEIOTROPIC EFFECTS OF GT

4.1 Antioxidant activity of GT

Oxidative stress is defined as disturbance in the balance between the production of reactive oxygen species and antioxidant defense, may cause tissue injury[14]. GT possesses antioxidant and anti-

inflammatory properties. Anti-inflammatory effects may be a result of increased production of IL-10, an anti-inflammatory cytokine [4, 15]. EGCG is a chemical constituent of GT and is a powerful antioxidant, traps peroxy radicals and exhibits multifunctional properties as indicated by laboratory results[8]. Antioxidants are compounds that protect cells against the damaging effects of reactive oxygen species, such as singlet oxygen, superoxide, peroxyl radicals, hydroxyl radicals, and peroxynitrite. An imbalance between anti-oxidants and reactive oxygen species results in oxidative stress, leading to cellular damage, Catechins are hypothesized to help protect against these diseases by contributing, along with antioxidant vitamins and enzymes to the total antioxidant defense system[16]. A plenty of evidence recommend strong antioxidant potentials of tea flavanoids in suppressing the production of excess free radicals. Chief catechins present in GT have strong anti-oxidant potential.

4.2 Nephroprotective activity of GT

EGCG could inhibited various intracellular signal transduction pathways mediated by NF-κB, epidermal growth factor κB, epidermal growth factor κ receptor (EGFR), insulin-like growth factor-I (IGF-I) and mitogen-activated protein kinases (MAPKs)[1]. EGCG and GT extract enhance production of beneficial *nitric oxide* (NO), which in turn signals vessel walls to relax and dilate in response to blood flow[17-18]. Diabetes is generally accompanied by nephropathy due to microvascular dysfunction or impairment. In normal kidney tissue the production of thromboxane A_2 (TXA_2) and prostacyclin I_2 (PGI_2) is controlled, and the balance between them is important to maintain homeostasis *in vivo*. A modification of the PGI_2:TXA_2 ratio accelerates thrombogenesis in the renal tubules, increasing the risk of impaired function and atherosclerosis. The production of these compounds depends on the activity of phospholipase A_2 (which is higher in the case of kidney disorders) and the fatty acid composition. Streptozotocin increases the synthesis of TXA_2 and decreases that of PGI_2. Administration of GT catechins in rats pretreated with streptozotocin decreases the synthesis of TXA_2 and increases that of PGI_2 and so returns the ratio to that of untreated rats. Kidney function is improved by GT catechin supplementation as a result of its antithrombogenic action, which in turns controls the arachidonic acid cascade system[19]. Thus, GT catechins appear to reduce oxidative stress in the kidney[20].

4.3 Anti-atherosclerotic activity of GT

GT catechins affect lipid metabolism by different pathways and prevent the appearance of atherosclerotic plaque. GT extract intake decreases the absorption of triglycerides and cholesterol and these findings are in accordance with the fact that fat excretion increases[21-22]. Some studies report that GT catechins decrease plasma total cholesterol and blood triglyceride levels, but the effects differ among studies[23]. Cardiovascular effects include the antioxidant and anti-inflammatory effects, and consumption of green tea has been shown to inhibit atherosclerosis, reduce lipid levels overall, and improve the ratio of LDL to HDL[4, 15]. This difference could be due to the different animal models used. Moreover, regarding the GT catechin intake levels in these studies, plasma cholesterol apparently decreases only when GT intake is 0.5% of the diet. This suggests that the effect on plasma cholesterol occurs only at high doses. Nevertheless, GT ingestion decreases LDL cholesterol[24]. Concurrently, HDL cholesterol increases, showing that green tea polyphenols exert an antiatherosclerotic effect[25]. The results demonstrate that long-term consumption of tea catechins can be beneficial in suppressing of high-fat diet–induced obesity by modulating lipid metabolism. By this mechanism, green tea could possibly beneficial in reducing the risk of associated diseases, including diabetes and cardiovascular diseases etc.

4.4 Anticancer activity of GT

Many epidemiological, case-control, and cohort studies have been conducted to investigate the effects of tea consumption on human cancer incidence, and this topic has been reviewed by several authors (26). The anti-carcinogenic effects of GT have been seen in many types of cancer, and the mechanisms may include inhibiting angiogenesis and cell growth, and inducing apoptosis in cancer cells[4, 15, 27]. In a Japanese cohort study, a negative association was found between green tea consumption and total cancer incidence, especially among females drinking more than 10 cups per day[28]. The effect of tea on stomach cancer has been the most extensively studied. The five case-control studies showed a protective effect of tea on the risk of stomach cancer[29-32]. Several studies have been done on tea drinking and colorectal cancer, with inconclusive or no evidence of an association. A recent study indicated a positive association between increased GT consumption and colon cancer risk. However, the results with GT showed a protective effect[33-34]. A large study of pancreatic, colon, and rectal cancers indicated decreased incidents of these cancers with consumption of tea[35]. EGCG and other tea polyphenols inhibit growth of human lung cancer cells with a G_2/M phase arrest of the cell cycle[36]. There is also some evidence that green tea polyphenols have a chemopreventive effect against cancers in smokers[37]. The frequency of sister-chromatid exchange in lung cells was lower in smokers who consumed GT. In a seven-year follow-up study of patients with breast cancer, it was found that increased consumption of GT was associated with decreased numbers of axillary lymph node metastases especially among premenopausal patients with stage I and II breast cancers and it controls the esophageal cancer[38-39]. The anti-carcinogenic activities of tea polyphenols are generally believed to be related to their antioxidant properties. GT increases glucuronyl transferase activity, which may facilitate the detoxification pathway of certain carcinogens and inhibit the tumor promotion-related enzymes, such as lipoxygenase and cyclooxygenase, ornithine, decarboxylase protein kinase C and 5α steroid reductase isoenzymes[40-45]. In cell lines, EGCG and other tea catechins have been shown to inhibit cell growth and transformation. Some of these activities are believed to be attributable to the inhibition of MAP-kinases and AP-1 activities[46-48]. The involvement of the tumor necrosis factor α pathway in the inhibition process has been suggested. EGCG has also been shown to inhibit angiogenesis by inhibiting the growth of endothelial cells whereas green tea reduced significantly vascular endothelial growth factor- induced corneal neovascularisation[49].

4.5 Anti-Alzeimer activity of GT

Although there is no epidemiological evidence in human studies of the benefit of green tea for Alzheimer's disease, several studies in animal and cell culture models suggest that EGCG from green tea may affect several potential targets associated with Alzheimer's disease progression. EGCG protects against beta-amyloid induced neurotoxicity in cultured hippocampal neurons, an effect attributed to its antioxidant properties[50]. In addition, EGCG regulates the processing of Amyloid precursor protein (APP), through PKC activation, to the nonamyloidogenic soluble APP, thus preventing the formation of the neurotoxic beta-amyloid[51]. EGCG and other GT catechins have also been shown to inhibit the beta secretase enzyme that is responsible for processing APP to beta-amyloid, thus having a potentially synergistic inhibitory effect on the production of beta-amyloid[52].

4.6 Antiparkinsonian activity of GT

Various studies have shown that GT and EGCG significantly prevent the neurodegenerative pathologies in animal models[53]. EGCG administered orally in doses as low as 25 mg/kg, prevented loss of dopaminergic neurons in the substantia nigra and preserved striatal levels of dopamine[54]. EGCG prevented the accumulation of iron and alpha-synuclein in MPTP (1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine) treated mice[55]. These effects have been attributed to the antioxidant activity and iron-chelating properties of EGCG, respectively. Epidemiological studies on the prevalence of Parkinson's disease and GT consumption do show a 5-10 fold lower incidences of the disease in Asian populations[56].

4.7 Antidiabetic activity of GT

Green tea has an antidiabetic effect. It lowered glucose levels in the bloodstreams of diabetic mice without affecting insulin levels[57]. Consumption of GT has anti-diabetic effects[58]. Long-term administration of green tea extract to normal rats increased insulin sensitivity. When administered to fructose-fed rats, GT extract was also found to prevent development of insulin resistance, oxidative stress, hyperglycemia and other metabolic defects[59, 60]. The investigators showed that EGCG mimics insulin, increases tyrosine phosphorylation of the insulin receptor and the insulin receptor substrate, and reduces gene expression of the gluconeogenic enzyme phosphoenolpyruvate carboxy-kinase[61]. Recently, GT and

GT extracts were demonstrated to modify glucose metabolism beneficially in experimental models of type II diabetes mellitus. In addition, EGCG ameliorates cytokine induced b-cell damage in vitro and prevents the decrease of islet mass induced by treatment with multiple low doses of streptozotocin in vivo[62-63].

5. CONCLUSION

Laboratory studies showed the health effects of GT in many diseases like cancer, nephrotoxicity, hepatotoxicity, diabetes, neurodegenerative diseases. As the human clinical evidence is still limited, future research needs to define the actual magnitude of health benefits, establishes the safe range of tea consumption associated with these benefits, and elucidates the mechanisms of action. Development of more specific and sensitive methods with more representative models along with the development of good predictive biomarkers will give a better understanding of how green tea interacts with endogenous systems and other exogenous factors. The research interest based on tea components may provide an approach to decrease the incidence of and mortality from various diseases. Overall tea is an affordable beverage of natural origin as compared to modern beverages such as soft drinks.

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