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Review Article

Phytochemical, Pharmacological and Beneficial Effects of Green Tea

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ABSTRACT

Green tea is obtained from the plant *Camellia sinensis* by minimal oxidation during processing is "natural secret for a healthier life". Tea is one of the most widely consumed beverages in the world, second only to water, and its medicinal properties have been widely explored. The tea plant, *Camellia sinensis*, is a member of *Theaceae* family, green tea is produced from its leaves. It is an evergreen shrub or tree. The main constituent present in green tea is Epigallocatechin-3-gallate. This component is responsible for all the biological activities that it shows like anticancer, antioxidant, antidiabetic, antiobesity, antihypertensive, antistroke, use in skin disorder etc. The present review complies the existing literature related to botanical description, morphology, climate and soil, phyto-chemical constituents, biochemical properties, biological activity of *Camellia sinensis.*

Keywords: Antioxidant, *Camellia sinensis*, antiobesity, phyto-chemical

INTRODUCTION

The modern era faces a number of growing ailments and diseases that are a serious concern to normal sustenance of an individual scenario. These include cancer, diabetes, hypertension, bacterial and fungal infections, dental caries, skin diseases like acne and many more. Control and cure of these diseases require a source that can overcome these health concerns and that has minimal potential to cause adverse effects. Catechin present in green tea is the solution for all problems.[1] This situation and need has brought *Camellia sinensis* (*C. sinensis*) into picture which is a potent antioxidant and antihypertensive agent existing in nature. Antioxidants are substances that may protect the cells against the effects of free radicals. Free radicals are molecules produced when your body breaks down food, or by environmental exposures like tobacco smoke and radiation. Free radicals can damage cells, and may play a role in heart disease, cancer and other diseases. Another study shows that green tea is also helpful in reducing stroke, myocardial infarction and coronary heart diseases.[2] The literature survey reveals that green tea polyphenols are more potent antioxidants than vitamin C, vitamin E, rosemary extract, and even curcumin in some systems. Curcumin, a potent antioxidant and chemopreventive agent, has recently been found to be capable of inducing apoptosis in human hepatoma and leukemia cells by way of an elusive mechanism, but green tea is proved to be more effective than curcumin.[3]

Green tea lowers blood pressure and helps prevent hypertension. Tea increases body's production of nitric oxide, which dilates arteries and thereby reduces blood pressure. Among persons consuming tea regularly for at least one year, the risk of developing high blood pressure was 46% lower among those who drank half cup to two and a half cups per day and 65% less among those consuming more than two and a half cups per day.[4] Tea contains catechins, a type of antioxidant. In a freshly picked tea leaf, catechins can compose up to 30% of the dry weight. Catechins are highest in concentration in white and green teas, while black tea has substantially fewer due to its oxidative preparation.[5]

Morphology: *C. sinensis*, a member of theaceae family is an evergreen tree or shrub that attains a height of 10 - 15 m in the wild and 0.6-1.5 m when cultivated. The leaves are light green, short stalked, coriaceous, alternate, lanceolate, serrate margin, glabrous or pubescent beneath, varying in length from 5 - 30 cm and about 4 cm width. [6] Mature leaves are bright green colored, smooth and leathery while young leaves are pubescent. Flowers are white fragrant, 2.5 - 4 cm in diameter, found in solitary or in clusters of two or four. Flowers bear numerous stamens with yellow anther and produce brownish red capsules. Fruit is a flattened, smooth, rounded trigonous three celled capsule, seed solitary in each, size of a small nut.[7, 8]

Climate and Soil: Tea is cultivated on well drained soil preferably with pH 4.5-5.0, but in practice it may range from 3 to 6.5. Tea is basically a rain fed crop which grows in humid climate of temperate, tropical and sub tropical regions.[9] The soil is maintained at pH of 4.5-5.0 by regular liming. Weeds growth can also be controlled by chemical methods. Fertilizers like N, P, K are added through broadcasting methods in field to reduce soil erosion. No tillage cultivation system helps in reducing erosion.[10, 11]

Chemical Constituents: Tea leaves contain many compounds, such as polysaccharides, volatile oils, vitamins, minerals, purines, alkaloids (caffeine) and polyphenols (catechins and flavonoids). Although all three tea types have antibacterial and free radical capturing (anti

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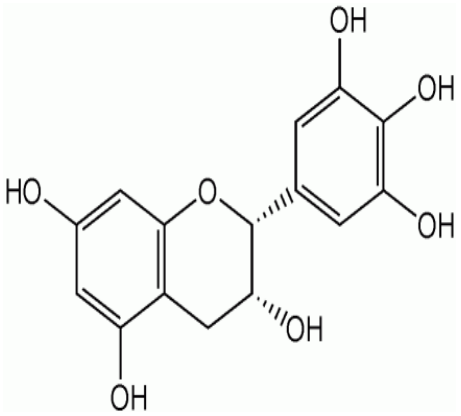
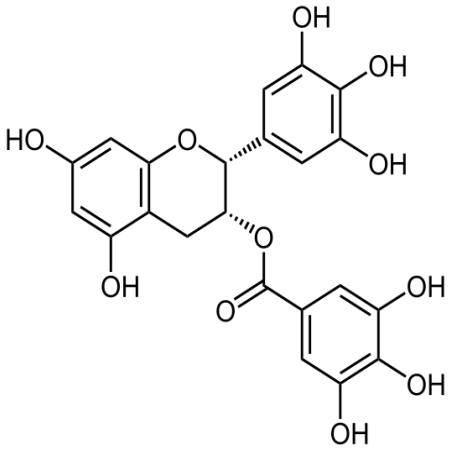


Epigallocatechin



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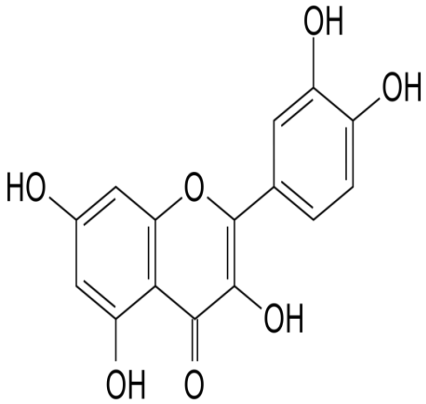
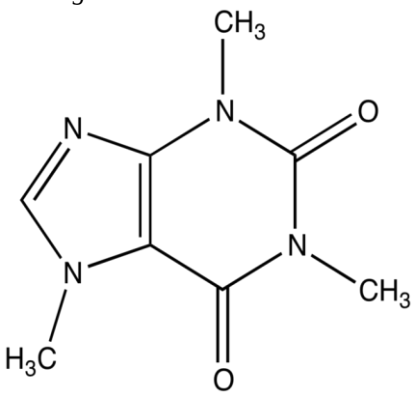


Quercetin



Caffeine

Fig: 1 Chemical constituent of Green Tea

oxidising) activities, the efficacy decreases substantially the darker the variety of tea is. This is due to lower contents of anti-oxidising polyphenols remaining in the leaves.[12]

Flavonoids (polyphenols): Green tea polyphenols consist of both simple and complex p olyphenols. The large majority of polyphenols in green tea are flavonoid monomers called catechins and flavonols. The flavonols including kaempferol, quercitin, myricitin and their glycosides have only been recognized recently as significant components in tea, although their presence as trace constituents has always been acknowledged. They have proven medicinal properties which include antioxidant, anti-inflammatory, anti-allergic, antibacterial and antiviral effects. They also have the ability to strengthen veins and decrease their permeability. It is widely believed that the anti oxidising effects of both black and green varieties are reduced when taken with milk. This is thought to be due to the effective binding of flavonoids by proteins.[12] However, a recent *ex vivo* study concluded that flavonols are absorbed from tea and their bioavailability is not affected by milk.[13]

Tea tannins-called catechins (polyphenols): Catechins are members of a more general class of flavonoid, the flavan-3-ols (also referred to as flavanols). The tea catechins, a term commonly used to refer to both catechins and gallocatechins make up as much as 30% wt/wt of dissolved solids. A large percentage of the catechins present in tea exist as gallic acid esters. They appear to be the most potent therapeutic plant-derived chemicals, aside from their antiseptic and antioxidant properties, they are able to form complexes with other molecules, thereby detoxifying the system.[14] Major catechins include gallocatechin, epicatechin (EC), epigallocatechin (EGC), epicatechin gallate (EGC) and epigallocatechin gallate (EGCG). Catechins make up approximately one-quarter of fresh dried green tea leaves, of which EGCG comprises 60 %.[12]

Simple Polyphenols: Gallic acid and its quinic acid ester commonly referred as theogallin have been identified in tea[15, 16] and have been detected by HPLC[17]. Cinnamic acid derivatives of quinic acid, the coumaryl and caffeoyl-quinic acids (including chlorogenic acid or 5-caffeoylquinic acid) have also been identified in tea[15]

Vitamin C: A recent study by[18] showed that black, green and oolong tea are all extremely good sources of vitamin C. They found that 1 or 2 cups a day provide the equivalent of three glasses of orange juice or two capsules (200 mg) of vitamin C.[13] Thearubigins are a heterogeneous group of phenolic pigments with relative molecular mass of 700-40000 Da.[19]

Biological Activities of Green Tea-

Anti fungal activity: Antifungal activity of green tea leaves sampled 3 different harvest time (May, July and September against a number of fungi (*Candida albicans, Candida glabrata, Candida kruseii, Candida parapsilosis* and *Candida dubliensis*) has been investigated. In addition, the catechin-based flavonoids in green tea leaves such as epigallocatechin-3-gallate (EGCG), epicatechin-3-gallate

(ECG), epigallocatechin (EGC) and epicatechin (EC) were determined. All methanol extract of green tea samples showed a broad-spectrum antifungal activity against all *Candida* species in broth microdilution bioassays. However maximum activity of methanol extract (>17 mm inhibition zone) was observed against *Candida albicans* at 3rd harvest time.[20]

Anti-inflammatory activity and skin protection: Topical treatment or oral consumption of green tea polyphenols inhibits chemical carcinogen- or ultraviolet radiation-induced skin tumorigenesis in different animal models. Studies have shown that green tea extract also possesses anti-inflammatory activity. These anti-inflammatory and anti-carcinogenic properties of green tea are due to their polyphenolic constituents present therein. The major and most chemopreventive constituent in green tea responsible for these biochemical or pharmacological effects is (-)-epigallocatechin-3-gallate (EGCG). Treatment of green tea polyphenols to skin has been shown to modulate the biochemical pathways involved in inflammatory responses, cell proliferation and responses of chemical tumor promoters as well as ultraviolet (UV) light-induced inflammatory markers of skin inflammation. Topical treatment with EGCG on mouse skin also results in prevention of UVB-induced immune suppression, and oxidative stress.

The protective effects of green tea treatment on human skin either topically or consumed orally against UV light-induced inflammatory or carcinogenic responses are not well understood. Based on documented extensive beneficial effects of green tea on mouse skin models and very little in human skin, many pharmaceutical and cosmetic companies are supplementing their skin care products with green tea extracts. Therefore, the focus of this communication is to review and analyze the photoprotective effects of green tea polyphenols to skin**.**[21]

Antiviral activity: Polyphenolic compound catechins (−)-epigallocatechin gallate (EGCG), (−)-epicatechin gallate (ECG) and (−)-epigallocatechin (EGC)) from green tea were evaluated for their ability to inhibit influenza virus replication in cell culture and for potentially direct virucidal effect. Among the test compounds, the EGCG and ECG were found to be potent inhibitors of influenza virus replication in MDCK cell culture (*Madin-Darby canine kidney cell line)* and this effect was observed in all influenza virus subtypes tested, including A/H_1N_1, A/H_3N_2 and B virus.[22,23]

Antidiabetic activity: An aqueous solution of green tea polyphenols (GTP) was found to inhibit lipid peroxidation (LP), scavenge hydroxyl and superoxide radicals *in vitro*. Administration of GTP (500 mg/kg b.wt.) to normal rats increased glucose tolerance significantly (P<0.005) at 60 min. GTP was also found to reduce serum glucose level in alloxan diabetic rats significantly at a dose level of 100 mg/kg b.wt. Continued daily administration (15 days) of the extract 50, 100 mg/kg b.wt. produced 29 and 44% reduction in the elevated serum glucose level produced by alloxan administration. Elevated hepatic and renal enzymes produced by alloxan were found to be reduced (P<0.001) by GTP. The serum LP levels which was increased by alloxan and was reduced by significantly (P<0.001) by the administration of 100 mg/kg b.wt. of GTP. Decreased liver glycogen, after alloxan administration showed a significant (P<0.001) increase after GTP treatment.

GTP treated group showed increased antioxidant potential as seen from improvements in superoxide dismutase and glutathione levels. However catalase, LP and glutathione peroxidase levels were unchanged. These results indicate that alterations in the glucose utilizing system and oxidation status in rats increased by alloxan were partially reversed by the administration of the glutamate pyruvate transaminase.[24]

Antiasthamatic activity: Aqueous fraction of green tea using specific *in-vitro* and *in-vivo* assays in an ovalbumin-induced asthmatic model. Mice sensitized to ovalbumin were orally administered an aqueous extract of *C. sinensis*. The lungs of these mice were then examined by haematoxylin and eosin staining and ELISA analysis to measure cytokine expression. The aqueous extract of *C. sinensis* exhibited potent anti-asthmatic activity by increasing the expression level of tumor necrosis factor-beta, interferon-gamma and decreasing the expression of anti-asthmatic cytokines in the lung. Together, these results indicate that the aqueous fraction of *C. sinensis* is effective in alleviating asthmatic symptoms by increasing the expression of Th1 cell specific anti-asthmatic biomarkers.[25]

Hepatoprotective activity: The present study was undertaken to examine the inhibitory effect of the green tea *(C. sinesis)* on cadmium chloride induced hepatoprotective activity in liver. In rats injected with cadmium chloride, the activities of serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), lactate dehydrogenase (LDH), γ-glutamyl transferase (GGT) was significantly ($p < 0.05$) increased when compared to those values in control rats. The rats administrated with green tea extract and cadmium chloride showed a significantly ($p < 0.05$) decreased levels of serum SGOT, SGPT, LDH and GGT.[26]

Antimicrobial activity: Extracts of leaves from the tea plant *C. sinensis* contain polyphenolic components with activity against a wide spectrum of microbes. Studies conducted over the last 20 years have shown that the green tea polyphenolic catechins, in particular (−)-epigallocatechin gallate (EGCG) and (−)-epicatechin gallate (ECG), can inhibit the growth of a wide range of gram-positive and gram-negative bacterial species with moderate potency. Evidence is emerging that these molecules may be useful in the control of common oral infections, such as dental caries and periodontal disease. Sub-inhibitory concentrations of EGCG and ECG can suppress the expression of bacterial virulence factors and can reverse the resistance of the opportunistic pathogen *Staphylococcus aureus* to β-lactam antibiotics. For example, relatively low concentrations of ECG can sensitize methicillin-resistant *S. aureus* (MRSA) clinical isolates to levels of oxacillin that can be readily achieved in clinical practice. Catechin gallates such as ECG intercalate into phopsholipid bilayers and it is likely that

they affect both virulence and antibiotic resistance by perturbing the function of key processes associated with the bacterial cytoplasmic membrane.[27]

Antioxidant activity: The antioxidant activity of the plant extracts and the standard was assessed on the basis of the radical scavenging effect of the stable 1, 1-diphenyl-2-picryl- hydrazyl (DPPH)-free radical activity by modified method.[28,29] The diluted working solutions of the test extracts were prepared in methanol. Ascorbic acid was used as standard in 1-100 µg/ml solution 0.002% of DPPH was prepared in methanol and 1 ml of this solution was mixed with 1 ml of sample solution and standard solution separately[30]. These solution mixtures were kept in dark for 30 min and optical density was measured at 517 nm using Cecil-Elect Spectrophotometer. Methanol (1 ml) with DPPH solution (0.002%, 1 ml) was used as blank. The IC_{50} values of green tea was 6.7 ± 0.1 The results indicate that the antioxidant activity of the crude extract of green tea is higher than that of ascorbic acid .The antioxidant activity showed that the percentage inhibition of 10 µg/ml of green tea (*C. sinensis* Linn.) extract was 69.4%, which is comparable with the standard antioxidant activity of ascorbic acid (55.8%).[31, 32]

Antiobesity activity: Green tea catechins (GTC) are polyphenolic compounds present in the unfermented dried leaves of the plant, *C. sinensis*. Results from a number of randomized, controlled intervention trials have shown that consumption of GTC (270 mg to 1200 mg/day) may reduce body weight and fat. There are several proposed mechanisms whereby GTC may influence body weight and composition. The predominating hypothesis is that GTC influences sympathetic nervous system (SNS) activity, increasing energy expenditure and promoting the oxidation of fat. Caffeine, naturally present in green tea, also influences SNS activity, and may act synergistically with GTC to increase energy expenditure and fat oxidation. Other potential mechanisms include modifications in appetite, up-regulation of enzymes involved in hepatic fat oxidation, and decreased nutrient absorption. This article reviews the evidence for each of these purported mechanisms, with particular reference to studies in humans.[33]

Anticancer activity: Increasing observational evidence suggests that epigallocatechin gallate the major polyphenolic component of green tea is instrumental in suppressing the growth of cancer cells in various tumour models.[34,35] Prostate cancer is the most recently diagnosed malignancy and second leading cause of cancer related deaths, but this cancer can also be cured by green tea.[35,36] Tea polyphenols are known to exhibit cytotoxicity toward various tumour cell lines as well as growth inhibition that is accompanied by cell cycle arrest.[30] Therefore, methods that promise to enhance the suppressive potential of green tea have the highest clinical relevance. Human cervical cancer cells, HeLa, the first continuous cancer cell line, represent a mainstay model in cancer research. Green tea inhibited their growth, whereas their exposure to moderate levels of laser light resulted in an opposite effect. Both effects are individually documented in the literature. HeLa cells were supplemented with green tea, irradiated with moderately intense laser light (670 nm) for 1 min, and incubated for 52 h. An extraordinary inhibition of HeLa cells by a combination of green tea and red light. An inhibition of 1,460%, compared with non-irradiated samples. Our result receives clinical relevance from a recent study in which epigallocatechin gallate suppressed the growth of melanoma *in-vivo*.[37] It has also been proved that daily oral EGCG in polyphenon E preparation was tolerated by chronic lymphatic leukaemia patient in Phase 1 trial.[38, 39]

Effects of fluoride: In general, the level of fluoride in tea is inversely related to the EGCG contents. The more natural EGCG in the tea leaves, the less fluoride. According to Andreas Schuld of the Canadian 'Parents of Fluoride Poisoned Children' tea is very high in fluoride content much higher than the Maximum Contaminant Level (MCL) set for fluoride in drinking water. Decaffeinated teas have an even higher fluoride content as compared to their caffeinated counterparts. According to him, fluoride could possibly reduce the anti-cancer properties of tea or even cause cancer, as fluoride is considered a cancer promoter. For instance, he mentions a 1998 study which found positive correlation between colon cancer and tea intake. The high fluoride content could also cause neurological and renal damage, especially in the presence of aluminium. Additionally, the high fluoride content could cause osteoporosis, arthritis and other bone disorders.[40]

Anti spasmodic activity: Hot water extract and tannin fraction of the dried entire plant were active on the rabbit and rat intestines vs. pilocarpine-induced spasms and barium induced contractions.[41]

Anticataract activity: Tea, administered in culture to enucleated rat lens, reduced the incidence of selenite cataract *in-vivo.* The rat lenses were randomly divided into normal, control and treated groups and incubated for 24 hours at 37ºC. Oxidative stress was induced by sodium selenite in the culture medium of the two groups (except the normal group). The medium of the treated group was additionally supplemented with tea extract. After incubation, lenses were subjected to glutathione and malondialdehyde estimation. Enzyme activity of superoxide dismutase, catalase, and glutathione peroxidase were also measured indifferent sets of the experiment. *In-vivo* cataract was induced in 9-day-old rat pups of both control and treated groups by a single subcutaneous injection of sodium selenite. The treated pups were injected with tea extract intraperitonally prior to selenite challenge and continued for 2 consecutive days thereafter. Cataract incidence was evaluated on 16 postnatal days by slit lamp examination. There was positive modulation of biochemical parameters in the organ culture study. The results indicated that tea act primarily by preserving the antioxidant defence system.[42]

Skin disorder: Using different animal model, many laboratories have shown that green tea extract, taken orally or applied to the skin, inhibits skin tumour formation induced by chemical carcinogens or ultra-violet radiation (UVB). The extracts also possess anti-inflammatory activity that similarly to the anticancer forming activity, is

owed to the polyphenolic constituents present therein. The polyphenol mainly responsible for the prevention of cancer formation is epigallocatechin-3-gallate (EGCG). When applied to mouse skin, EGCG prevents UVB-induced oxidative stress and suppression of the immune system. Mouse skin models have illustrated extensive beneficial effects of green tea extracts and although only a few human skin studies have been conducted, many cosmetic and pharmaceutical companies are supplementing their skin care products with green tea extracts.[21]

Neurodegenerative Diseases-

Antialzheimer Activity: 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[43].

Antiparkinson activity: Various studies have shown that green tea and EGCG significantly prevent these pathologies in animal models[44]. 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[45]. Epidemiological studies on the prevalence of Parkinson's disease and green tea consumption do show 5- to 10-fold lower incidences of the disease in Asian populations[46, 47].

Biochemical Properties-

The biochemical properties of green tea extracts can be generally divided into four aspects-antioxidant, anticarcinogen, anti-inflammatory, and anti-radiation. Green tea extracts exhibit stronger antioxidant protection for human body than vitamin C and vitamin E. Scavenging effect of lipid free-radicals (one antioxidant property) of polyphenols in green tea extracts can be clearly observed in experiments. The ability of GTP in green tea extracts to eliminate lipid-derived free radicals is noticeably stronger (almost 50 times) than that of *Ginkgo biloba* extracts. Further investigations indicate that the boosting level of superoxide dismutase (SOD) and glutathione dismutase (GSHPx) may account for the inhibitory effect of GTC against lipid oxidation (rancidification). It should be mentioned that from the antioxidant perspective, green tea extracts are, generally speaking, more effective than black tea extracts due to the better preservation of catechins.[48]

Moreover, the anticarcinogenic property make the green tea extracts a hotspot in recent scientific researches. In many experiments, green tea extracts show inhibitory effects on cancer cells. *In vitro* assays, catechin and caffeine, which are main components in green tea extracts, block the cell cycle of cancer cells (cytotoxicity) and induce programmed cell death ; *in vivo*, green tea extracts also inhibits prostatic carcinoma transplanted in nude mice.[1]

In addition, green tea extracts also contain a wide-range of anti-inflammatory characteristics, so it may be helpful in treating chronic inflammatory states. The bactericidal activity against *S. mutans* is conspicuous in Japanese green tea extracts, and the maltose level in mouth is consistently lower after drinking tea. Therefore, green tea extracts may be effective in oral hygiene maintenance. Green tea extracts show anti-radiation properties on white rats in radioactive isotope experiments. The tea flavanols comprise of 20-30% of dry weight of fresh tea leaf tissue.[49]

CONCLUSION

Tea is the most popular drink after water. Increasing interest in its health benefits has led to the inclusion of green tea in the group of beverages with functional properties .Nowadays, green tea is considered one of the most promising dietary agents for the prevention and treatment of many diseases. The literature available suggests that aqueous extract of the green tea which mainly consists of catechins (EGCG, EGC, ECG and EC) possess antioxidant, antimutagenic, antidiabetic, anti-inflammatory, antibacterial and antiviral, and above all, cancer-preventive properties. Epidemiological studies suggest that consumption of green tea may have a protective effect against the development of several cancers. The tea also contains polyphenols which helps in decreasing the risk factor of specific type of cancers by inducing phase I and phase II metabolic enzymes that increase the formation and excretion of detoxified metabolites of carcinogens. Moreover the studies also reveal that regular green tea consumption has beneficial effects and it shows a significant rate of protection against the development of some oral diseases and against solar radiations. It also contributes to body weight control and to the rise of bone density as well as being able to stimulate the immune system. Most modern medicines used to treat cancer have serious side effects, high costs, and other associated risks. Green tea, on the other hand, is safe and widely available as a beverage and a nutritional supplement. Furthermore, growing scientific evidence suggests that green tea is effective in preventing many diseases associated with aging, including prostate and other cancers. Overall tea is an affordable beverage of natural origin compared to modern beverages such as soft drinks. It is yet promising area of research for future human studies.

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