

A Brief Review on Green Tea

Nayan Dilip Deore¹, Rutuja S. Abhonkar²

^{1,2} Swami Vivekanand Sanstha's Institute of Pharmacy, Mungase, Malegaon

ABSTRACT:

Green Tea, which is produced from the leaves of the *Camellia sinensis* plant and belongs to the family Theaceae, is one of the most popular beverages worldwide. In This paper, the phytochemistry, Pharmacology, and toxicology of green tea are reviewed systematically and comprehensively. Key findings Green Tea has been demonstrated to be good for human health. Nowadays, multiple pharmacologically active components have been isolated and identified from green tea, including tea polyphenols, alkaloids, amino acids, polysaccharides, and volatile components. Recent studies have demonstrated that green tea shows versatile pharmacological activities, such as antioxidant, anticancer, hypoglycemic, antibacterial, antiviral and neuroprotective. Studies on the toxic effects of green tea extract and its main ingredients have also raised concerns including hepatotoxicity and DNA damage. Additionally, Green tea polyphenols induce autophagy, thereby revitalizing the overall health of the organism consuming it. Green tea was able to activate autophagy in HL-60 Xenographs by increasing the activity of P13 kinase and BECLIN-1. This manuscript describes the reported anti-photoaging, stress resistance, and neuroprotective and autophagy properties of one of the most widely known functional foods-green tea.

Keywords : Medicinal Plants, Green Tea, Pharmacology, Human Health, Antioxidant Activity, Green Tea, Unfermented tea, Medicinal Plants

INTRODUCTION:

According To legend, tea was discovered accidentally by either a man named Shien Non Shei or the Emperor Shen Nung. Either way, green tea soon became popular among wealthy Chinese nobles. (1) The First green tea was exported from India to Japan during the 17th century. (2) It is a popular beverage crop having medicinal, anti-oxidalive and anti-microbial properties. The tea plant has been cultivated in asia for thousands of years. The consumption of green tea has a history that spans back to over 5000 yrs. Traditionally, it was prescribed for a number of aliments while aslo being consumed for its refreshing qualities and the prevention of future health problems. This increase in popularity is in part due to the increasing awareness of green tea's many health benefits. Tea is an aromatic beverage commonly prepared by pouring hot or boiling water over cured leaves of the tea plant *Camellia sinensis*. (3)

HISTORY

"Tea" is the most widely distributed one. Green tea is widely popular in East Asia (particularly in China and Japan), whereas, black tea is the preferred tea in the West. The use of tea leaves probably first originated more than 3,000 years ago, in the southwest area of China and initially was used by people only for chewing and eating, in just the same way that coffee was first used. (4)

CULTIVATION OF GREEN TEA

Indigenous to East Asia, South East Asia and the Indian subcontinent (Table 4 & 5), *Camellia sinensis* is cultivated today in tropical and subtropical regions throughout the world. The tea plant thrives in sunny climates where the temperatures are hot and rain is regular and plentiful, with a growing season that stretches for at least eight months of the year. Generally there are three growing spurts within the growing season. The Spring shoots grow from the end of March to the beginning of May and this is the period when the plant is most bountiful. From early June to the start of July the second growing stage takes place and the season comes to an end with the final flux of growth occurring from mid July to October. *Camellia sinensis* is happiest in acidic conditions and grown in a range of soils. The perfect soil mix is "sandy loam" which consists of approximately 40% sand, 40% silt and 20% clay, allowing the water to drain well out the soil while still enabling it to trap all the essential nutrients the plant requires from the earth. (5)



Green Tea Leaves



Green Tea Flower



Cultivation of Green Tea

METHODS

The data were collected by searching PubMed, Google Scholar, Web of Science, and CNKI. The keywords used as search terms were green tea, phytochemical, chemical composition, EGCG, pharmacology, tea polyphenols, antioxidant, cancer, diabetes, antibacterial, antiviral, AD, PD, immune T cells, and toxicology. Various related article and websites were also included. For further research, the references of some selected articles were also searched. The inclusion criteria for this review were systematic reviews and experimental studies on green tea. However, studies on other types of tea such as yellow tea, dark tea, or other natural plants were conference reports, case reports, and short communications, were also excluded, No time limitation was considered in this review.

PHYTOCHEMISTRY

Tea is rich in healthcare ingredients and pharmacologically active ingredients. From 500 chemical components have been reported that more than 500 chemical components have been isolated from tea, including more than 400 organic compounds and more than 40 inorganic compounds (6)

Tea Polyphenols

Tea Polyphenols is a general term for polyphenols in tea. There are about 30 kinds of compounds, mainly composed of catechins, flavonoids, anthocyanis, and phenolic acids. (7)

Catechins

The Catechins in tea mainly include catechin (C), epicatechin (FC), epigallocatechin (EGC), epicatechin gallate (ECG), and epigallocatechin Gallate (EGCG). (8)

PHARMACOLOGY:

Antioxidant Effects:

As early as 1997, it was reported that green tea extract and its three main components, including tea polyphenols, theanine, and caffeine, have the ability to effectively inhibit copper-catalyzed low-density lipoprotein (LDL) lipid peroxidation. Moreover, Yokozawa T et al. found that the antioxidant activity of green tea extract was in dose-dependent manner, and the antioxidant activity of green tea extract was in a dose-dependent manner, and the antioxidant activity of the three components was tea polyphenols>theanine>caffeine. Finally, they came to the conclusion that chelated metal ion copper is considered to be one of the possible mechanisms of green tea against peroxidation. (9)

Anticancer Effects

Inhibiting the proliferation of tumor cells. Studies have found that EGCG could inhibit the growth of androgen-sensitive human prostate cancer cells (PCA) in a dose-dependent manner, and this effect may be mediated by G₀/G₁ phase cell cycle arrest caused by WAF1/p21. (10)

Anti Diabetic Effects

Improving glucose metabolism. Sundaram et al. (2013) revealed that green tea extract (75mg/kg, i.g., for 30 days) had significant hypoglycemic effects on streptozotocin-induced diabetic rats. Moreover, its ability to lower blood sugar was comparable to the oral hypoglycemic drug metformin. The mechanism of this action was related to the increase of glycogen content in the liver and the change of the activity of key enzymes in glucose metabolism. (11)

Effects on the Immune System

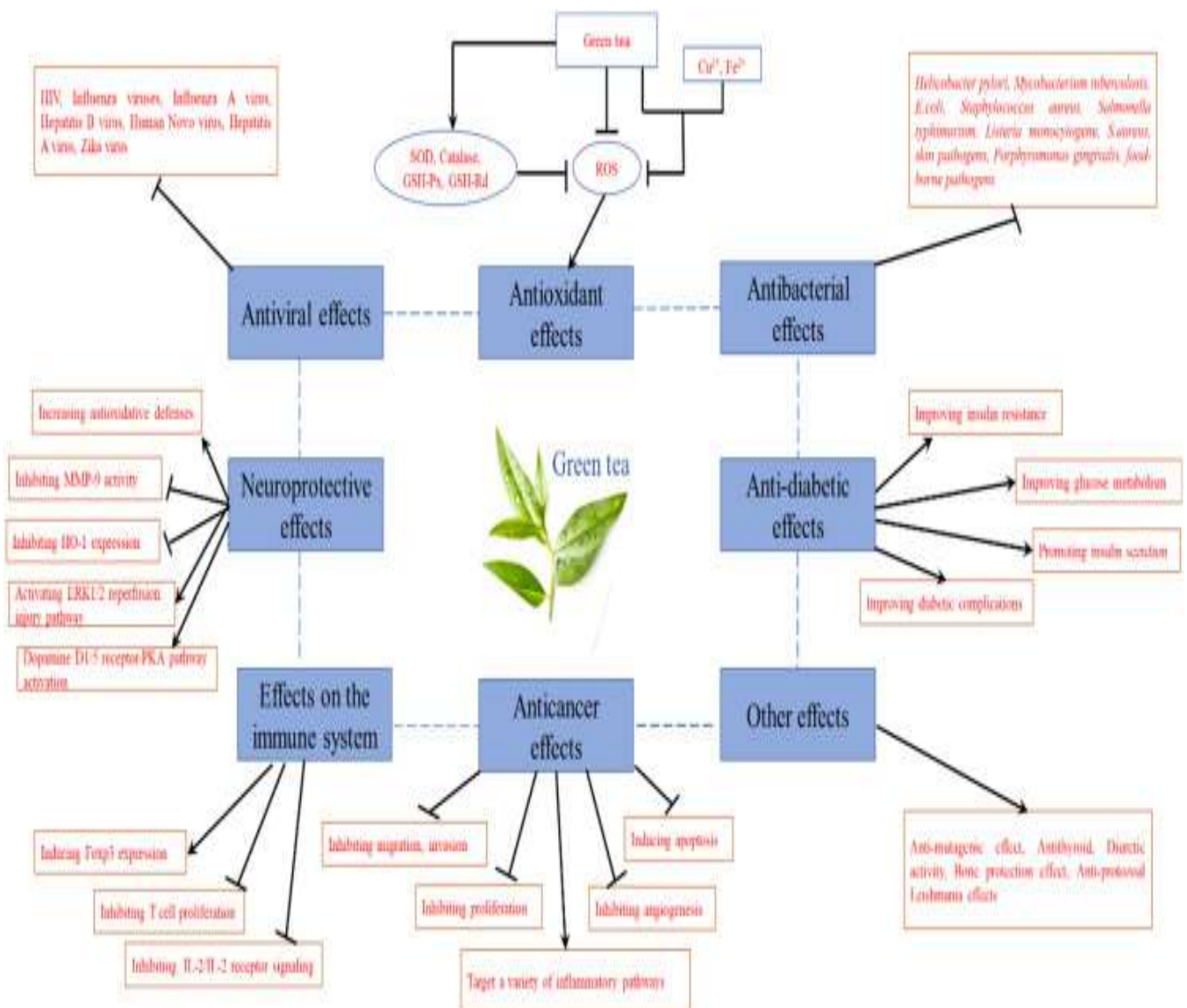
To date, there has been the little pharmacological study of green tea on the immune system. EGCG (2.5μM 10μM) could inhibit the proliferation of spleen T cells in C57BL mice in a dose-dependent manner. This mechanism may be related to the inhibition of IL-2/IL-2 receptor signaling. (12) In 2014, Balaji J et al. found that green tea water extract can significantly reduce the mortality of mice with anaphylactic shock induced by compound C48/80. This finding provided experimental support for green tea in the treatment of asthma and allergic rhinitis. (13)

Other Pharmacological Effects

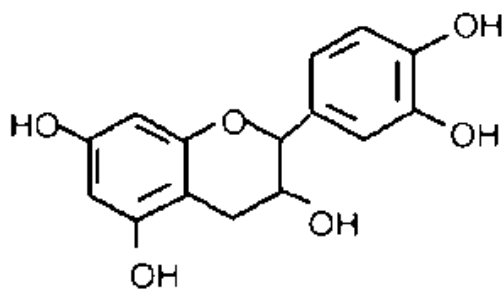
Apart from these, in in vivo experiments, it was observed that thyroid peroxidase and 50-deiodinase I activities were reduced in male albino rats after treatment with high doses of green tea and catechins. These results indicated that catechins in green tea extract may play an antithyroid role. (14) An in vivo experiment in rats demonstrated that green tea polyphenols have beneficial effects on the bone mineral density of cancellous and cortical bone compartment ovariectomized rats. (15) Tea is the most consumed drink in the world after water. Green tea is a 'non-fermented' tea, and contains more catechins than black tea or oolong tea. Catechins are in vitro and in vivo strong antioxidants. In addition, its content of certain minerals and vitamins increases the antioxidant potential of this type of tea. (16)

Health benefits

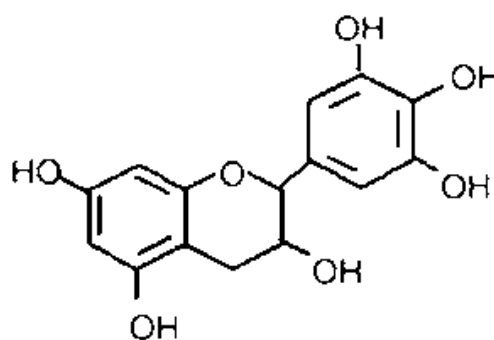
The major and most chemo-preventive constituent in green tea responsible for these biochemical or pharmacological effects is (-) -epigallocatechin-3 gallate. Understanding the molecular mechanisms of these effects of green tea is a subject of investigation in many laboratories. (17) Green, oolong and black teas all come from the leaves of the *Camellia sinensis* plant. What sets green tea apart is the way it is processed. Green tea leaves are steamed, which prevents the EGCG compound from being oxidized. In contrast, black and oolong tea are made from fermented leaves, which results in the EGCG being converted into other compounds that are not nearly as effective in preventing and fighting various diseases. In general, green tea has been found to be superior to black tea in terms of antioxidant activity, owing to the higher content of EGCG. (18)



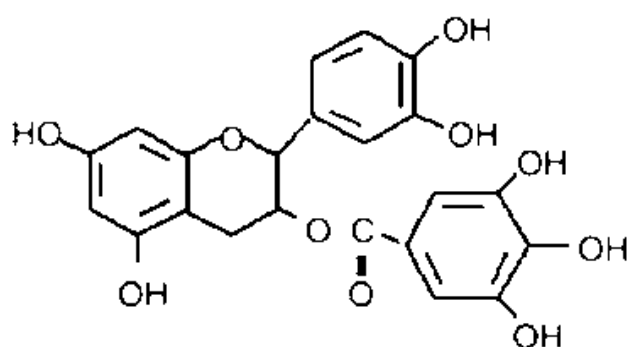
Pharmacological Effect of Green Tea



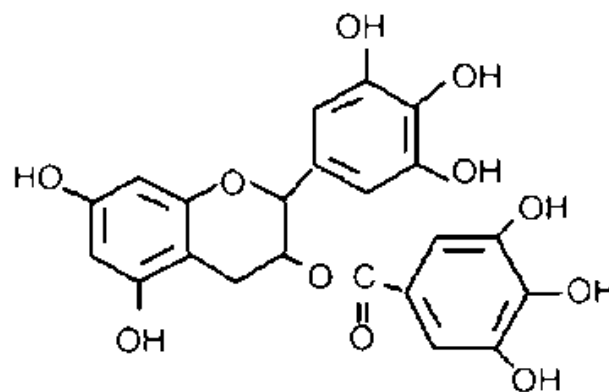
(-)-Epicatechin (EC)



(-) Epigallocatechin (EGC)



(-)-Epicatechin-3-gallate (ECG)



(-)-Epigallocatechin-3-gallate (EGCG)

Major Polyphenols in Green Tea

Green tea for skin treatment

Research using pooled human keratinocytes (skin cells) to study the normal growth of the skin cells alone and comparing it to the growth of the cells when exposed to EGCG revealed that EGCG reactivated dying skin cells. Cells that migrate toward the surface of the skin normally live about 28 days and, by day 20, they sit on the epidermis getting ready to die and slough off. Current research seems to show that EGCG reactivates epidermis cells.

Anti-fungal activity

These results indicate that EGCG enhances the anti-fungal effect of amphotericin B or fluconazole against anti-mycotic-susceptible and resistant *C. albicans*. Combined treatment with catechin allows the use of lower doses of anti-mycotics and induces multiple anti-fungal effects. It is hoped that this may help to avoid the side effects of anti-mycotics.

Anti-viral effects EGCG and ECG were found to be potent inhibitors of influenza virus replication in cell culture. This effect was observed in all influenza virus sub-types tested, including A/H₁N₁, A/H₃N₂ and B virus. Quantitative analysis revealed that, at high concentration, EGCG and ECG also suppressed viral RNA synthesis in cells. (19)

Cholesterol reduction

population-based and clinical studies indicate that the antioxidant properties of green tea may help prevent atherosclerosis, particularly coronary artery disease. According to Japanese research, green tea reduces the levels of LDL cholesterol, thereby reducing the risk of coronary heart disease. Studies have found that

regular consumption of tea protects against heart disease, with one study documenting that the risk was 36% lower for tea drinkers. (20)

Other benefits

There is also epidemiological evidence that drinking green tea (but not black tea or oolong tea) may help prevent diabetes (30), although it is worth noting that this is evidence of an association and that future studies are needed to confirm the effect. Green tea has been used traditionally to control blood sugar in the body. Animal studies suggest that green tea may help prevent the development of type 1 diabetes and slow the progression once it has developed. (21)

Protective effect of green tea

Twenty Chinese women were volunteers in analyzing the effect of varying concentrations of green tea extract (2-5%) in protecting skin from UV induced photoaging through topical application. (93) Along with the levels of erythema, the thickness of stratum corneum and epidermis, as well as the level of matrix metalloproteases, were measured by using microscopic and immunohistochemical analysis. On Day 1, a 3% topical application showed less erythema, whereas 5% showed damage along with the vehicle control and control with no topical application, which also showed post inflammatory hyperpigmentation. The sample using a 3% topical application showed mild pigmentation, whereas the other samples (2 and 4%) showed moderate pigmentation. Between 2 and 3% of topical applications showed a controlled level of thickening of the stratum corneum and epidermis when compared to other samples. A significant reduction of matrix metalloproteases was observed in applications ranging from 2 to 4%. Overall, this study suggests that an optimum concentration of green tea extract (3%) can protect the skin from UV radiation-induced damage (22). Additionally, EGCG suppressed AB-induced cytotoxicity by reducing ROS-mediated NF- κ B activation and mitogen-activated protein kinase (MAPK) signaling, including C-Jun N-terminal kinase (JNK) and p38 signaling (23)

Interestingly, higher concentrations of EGCG, for example, 100 μ M in macrophage cell lines, can inhibit autophagy leading to apoptosis. (24) Atrazine is a widely used herbicide which also has neurotoxic effects and can induce cell death in deoaminergic neurons, which could be overcome by autophagy. Green tea polyphenols, along with isoflavones, resveratrol, quercetin, and curcumin, were observed to activate autophagy in SH-SY5Y cells, which was suppressed by atrazine (25).

Effect on obesity

African black extract has been shown to suppress the elevation of blood glucose during food intake and reduce the body weight in KK-A(y)/TaJcl diabetic mice. (26) The increases and prolonged sympathetic stimulation of thermogenesis by the interaction between polyphenols and caffeine could be of value in assisting the management of obesity. (27) Tea components possess antioxidant, antimutagenic, and anticarcinogenic effects and could protect humans against the risk of cancer by environmental agents (28).

Adverse effects of green tea

This high-level treatment modified the plasma concentrations of the thyroid hormones. However, drinking even a very high dietary amount of green tea would be unlikely to cause these adverse effects in humans. Harmful effects of tea overconsumption (black or green) are due to three main factors: (1) its caffeine content, (2) the presence of aluminum, and (3) the effects of tea polyphenols on iron bioavailability. Green tea should not be taken by patients suffering from heart conditions or major cardiovascular problems. Pregnant and breast-feeding women should drink no more than one or two cups

per day, because caffeine can cause an increase in heart rhythm. It is also important to control the concomitant consumption of green tea and some drugs, due to caffeine's diuretic effects. (29) The effects of green tea and its constituents may be beneficial up to a certain dose yet higher doses may cause some unknown adverse effects. Moreover, the effects of green tea catechins may not be similar in all individuals. EGCG of green tea extract is cytotoxic, and higher consumption of green tea can exert acute cytotoxicity in liver cells, a major metabolic organ in the body. (30) Some studies revealed the capacity of tea plants to accumulate high levels of aluminum. This aspect is important for patients with renal failure because aluminum can be accumulated by the body, resulting in neurological diseases; it is therefore necessary to control the intake of food with high amounts of this metal. (31)

CONCLUSION:

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. In 2006, the FDA approved "Veregen ointment", a green tea extract external preparation, for clinical use and it has already appeared on the market in the United States. However, the research on the pharmacological activity of green tea is still in the laboratory research stage. Preclinical studies of green tea and its polyphenolic components have demonstrated antimutagenic and anticarcinogenic activity, and inhibition of growth of tumor cell lines and animal tumor models, including cancer. The development of biomarkers for green tea consumption, as well as molecular markers for its biological effects, will facilitate future research in this area.

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