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# BENEFICIAL EFFICT OF GREEN TEA WITH SPECIAL REFERENCE TO NEUROPTATHY: REVIEW AND PILOT TRIAL

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## INTRODUCTION

*Green Tea* botanically known as Camellia sinensis is tea in its natural state that had not undergone fermentation.

Tea, a beverage produced by steeping processed top leaves and buds of the tea plant in freshly boiled water, originated in China 2700 BC, but its medicinal properties were know much before that. China was the first country to cultivate tea. In Japan the cultivation began about 200 AD. The use of tea later spread to the other Asian countries. Tea cultivation in India was suggested as early as 1778. The tea plants growing wild in Assam were discovered in 1823.

*Camellia sinensis* is a native of South East Asia and is cultivated in hilly regions in Assam and to the east and south of it. It also cultivated in the hilly districts of North and South India1. *Camellia sinensis* is a hardy, multi-stemmed, slow-growing evergreen shrub or a small tree 1-6 meters in hight, apparently indigenous to china and cultivated in India and Nepal

The main constituents, which give tea its distinctive character as a beverage, are caffeine, polyphenols and essential oil. The most important constiuent of both black and *GreenTea* is the purine base alkaloid, caffeine, which accounts for the stimulating effect of tea liquor.

The leaf contains carotene, riboflavin, and nicotinic, pantothenic and ascorbic acids. Of these, pantothenic acid and riboflavin content are appreciable. Ascorbic acid, present in the fresh leaf, is destroyed during manufacture of black tea. The presence of malic and oxalic acids has also been reported. The other constituents present are theophylline; theobromine, xanthine, hypoxanthine, adenine, gums, dextrins and inositol. Kaempferol and quercetin are present both in the fresh leaf and *GreenTea.* The young tea shoots contain upto 30 per cent of polyphenols. Strength and color are developed better in teas manufactured form terminal shoots in which the polyphenol content may be as high as 35%. The flavanols identified include (+) and (-) catechin, (+) and (-) gallocatechin, (-) catechin gallate, (-)-gallocatechin gallate, (-) epiafzelechin, (-) epicatechin and its gallate. Among the flavonols, kaempferol, its-3-glucoside,-3-rhamnodiglucoside 3-rhamnoglucoside, and 3- rutinoside, quercetin and its -3-rhamnodiglucoside,myricentin, its 3-glucoside, 3- rhamnoglucoside and -3-glactoside, isoquercitrin, quercimeritrin and rutin are the important compounds of this group. The above glycosides are present both in *GreenTea* and black tea though their content is low in the latter. The flavonols content was 15-20 per cent less in black tea than in *Green Tea* . The flavonols and their glycosides are the main constituents

responsible for the yellow colour in black tea. Saponaretin, vitexin, isovitexin, theiferin A and B and several other flavone glycosides of the C-glucosylflavone skeleton have also been reported in Green Tea. Which produce the greenish yellow color in it. The presence of leucocyanidin, leucodelphinidin, chlorogenic, neo-chlorogenic, p-coumarylquinic, gallic, ellagic acids, theogallin and 5,7-dihydroxycoumarin is also reported in the leaf.

**MEDICINAL USES:**

The is a stimulating beverage, which relieves muscular and mental fatigue and can be taken during fever, its stimulating action is attributed to the pruine base alkaloid, caffeine (1,3,7-trimethylxanthine). Caffeine has a diuretic effect on the kidneys and stimulates gastric secretion. Hence, tea is though to aid digestion and relieve post-prandial distress.

Tea polyphenols may inhibit the absorption of dietary cholesterol and prevent the degradation of catecholamines. There is indication the successive administration of tea could stimulate the degradation of triglycerides in the adipose tissue, thereby reducing weight [2.3.]

*Green Tea* polyphenols have been found to normalize thyroid hyperfunction, which induces thyrotoxicosis. This has been attributed to flavanols, especially gallocatechins. Flavanols, especially gallocatechins, flavonol glycosides exhibit a similar action. Tea has been used extensively to combat plague, in Japan. Polyphenols aid the synthesis of folic acid by the intestinal microflora. *Green tea* infusion shows anti-bacterial activity against a number of bacteria and is an effective cure against dysentery. Without milk and sugar, the tea liquor is beneficial in diarrhea but with milk and sugar it acts as a laxative. Tea infusion shows anti-viral activity in several species of entero-viruses in cell culture[4-6]

*Green Tea* inhibits the growth of cancer tumors. Tea affords protection against the development of leukemia after exposure to radiation in mice. Tea flavanols probably eliminate 90 Sr from the body before it reaches the bone marrow and causes radiation damage. Flavanol gallates afford significant radioprotection, *Green tea* ploy phenols exhibit anti-tumour activity on induced skin cancer by teleocidin. Epigallocatechin gallate (EGCG) from *Green Tea* changes the properties of the receptor on the surface of mouse cells and blocks the action of tumor promoter and thus prevents the formation of tumor cells.

Epigallocatechin gallate may also prevent the growth of tumors in humans especially cancers of oesophagus, stomach and intestines. The epidemiological data have shown that the death rate from cancer of all sites and stomach cancer in the Midwest areas of Shizuoka (Japan) where *GreenTea* is the staple beverage as much lower than the national average, in both sexes. A low death rate due to stomach cancer was observed in habitual tea drinkers and a high death rate in people who do not consume tea. *Green tea* extracts inhibit the growth of muse sarcoma 180 at a dose of 400 mg/kg/day on oral administration. *Green tea* polyphenols may play a role in the prevention of cancer formation by the following probable mechanisms:

(1) inhibition of ultimate carcinogen formation

(2) modulation of the metabolism of initiating agent.

(3) Direct interaction of the electrophilic ultimate carcinogenic metabolite.

(4) Scavenging of free radicals

(5) inhibition of ornithine decarboxylase activity

(6) inhibition of convalent bonding of carcinogen to DNA.

Black tea is not likely to inhibit tumors as it contains only tiny amounts of EGCG. Consumption of 5g of tea every day can reduce the synthesis of nitrosamine, which is a major carcinogen. Vitamin C and polyphenols, especially catechins, block synthesis of endogenous nitrosamines. High selenium content in teas has also been correlated with low incidence of cancer in Japan. Green tea is best in preventing the synthesis of the carcinogen, followed by black and jasmine teas. Oolong tea also reduces and lung neoplasia induced by urethane in animals [8,9]

**Pharmacological Activities of *Green Tea***

*Green tea* extract has been report to be more effective in preventing tooth decay than fluoride compounds. An extract of Japanese *Green Tea* inhibited the growth of Streptococcus mutans (S.mutans) Clarke, the cariogenic bacterium responsible for causing dental caries. The main anti-bacterial substances are the polyphenolic compounds, especially (+)-gallocatechin, (-)-epigallocatechin and (-)-epigallocatechin gallate. Gallocatechin was the most active component and its minimum inhibitory concentration against the bacterium was 250 µg\ml. The *Green Tea* extract strongly inhibits the formation of dextran and levan from sucrose by the cariogenic bacteria. This also supports the role of polyphenols in inhibiting the growth of S. mutans and preventing the cause of caries [10-12].

**Hepatoprotective:**

The extract of *Green Tea* shows anti-hepatotoxic effects. The antioxidant polyphenoilc extract, consisting predominantly of epigallocatechin gallate, protects against early alcohol induced liver injury in rates. TNF aplha protein levels were increased in liver by alcohol, a product or lipid peroxidation and an indication of oxidative strees. *Green tea* extract completely blocked this effect[13].

**Antioxidant mechanism:**

The free radical scavenging activity of *Green Tea* leaf extract was evaluated with a chemical test involving dephenylpicrylhyrazy1 radical (DPPH). The hot aqueous *GreenTea* leaf extract demonstrated antiradical activity comparable with rutin and vitamin E used as a standard[14.]

**Neurotransmission:**

The effect of hot water extract of *Green Tea* on skeletal muscle and its neurotransmission was studies employing innervated and denervated rat diaphragm, *Green tea* extract showed facilitatory effect at lower concentrations an a paralytic effect at higher concentrations on skeletomotor junction. The extract may have acted through Ca 2= channels at the skeletomotor junction. The crude polyphenol content of *Green Tea* extract was the active constituent found responsible for its effect on neuromuscular junction [15.]

**Cancer cells:**

The inhibitory potencies of *Green Tea* polyphenols against human lung cancer cell

line A 549 was compared with genistein as a control. Treatment of A 546 cells with Epigallocatechin gallate (EGCG), (-) – epicatechin gallate (ECG) and genistein significantly inhibited the expression levels of hn RNP B1 mRNA and the elevated levels of hn RNP B1 protein, both of which are constitutively elevated in cancer cells. Also the active constituents inhibited the promoter activity of hn RNP A2/B1 gene expression, with IC 50 values 29 microM for EGCG and 66 microM for genistein, suggesting the interaction EGCG or genistein with the transcriptional complex[16.]

**LDL- cholesterol:**

The administration of *Green Tea* Polyphenol effectively inhibted LDL oxidation and elevated serum antioxidative activity to the same extent when compared to probucol, in cholesterol fed rats. It also increased the levels of high-density lipoprotein cholesterol leading to dose –dependant improvement of the atherogenic index [17.]

**Antiviral:**

Epigallocatechin-3 gallate (ECGC) strongly inhibited the replication of both virus LAI/IIBor Bal HIV strains as determined by reverse transcriptase and p24asays on the cell supernatants[18.]

**CLINICAL STUDY**

A pilot clinical study was conducted using *Green Tea* in patients identified with diabetic neuropathy or patients with long-standing diabetes for more then 5-8 years. Twenty patients were included in this study. A majority of the patients complained of intermittent pain and tingling numbness in the feet. These patients were continuing with conventional antidiabetic drugs and revealed controlled fasting and postprandial blood sugar. *Green Tea* was added as a part of the daily management. The dose was 1 tea bag twice daily for 3 months. All the patients were evaluated every 2 weeks for 3 months for evaluation of symptomatic relief. The following symptoms, if positive, were evaluated for determination of the efficacy. The symptoms were numbness, tingling, decreased sensation to a body part, loss of sensation to a body part or area, diarrhea, constipation, loss of bladder control, impotence, facial drooping , drooping eyelid, drooping mouth, vision changes, dizziness, weakness, difficulty in swallowing, speech impairment and muscle contractions, the primary efficacy measure was daily pain severity as measured on the Likert scale. Scale. Secondary measures include sleep interference scores, the short-Form McGill pain Questionnaire scores, Patient Global Impression of Change and Clinical Global Impression of Change, the Short From-36 Quality of Life Questionnaire scores, and the Profile of Mood States results.

A significant number of patients taking Green Tea expressed positive compliance. All the patients tolerated *GreenTea* without any side-effects. More than 70% of the patients who were in glycemic control showed relief of pain and tingling numbness in the feet. There were no disturbances in the quality of sleep. The addition of *GreenTea* produced a feeling of wellbeing and freshness in all the patients.

Thus, *Green Tea* was found to be effective in relief of tingling numbness of diabetic neuropathy without producing any side effects. This efficacy of *Green Tea* can be confirmed in the larger controlled clinical trials.

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