

Camellia Sinensis (Green Tea): A Review

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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. Green Tea is one of the most ancient and popular therapeutic beverages consumed around the world. 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”.

Key words: *Camellia sinensis* • Green Tea • Theaceae • Medicinal properties

INTRODUCTION

Since ancient times, plants have been an exemplary source of medicine. Ayurveda and other Indian literature mention the use of plants in treatment of various human ailments. India has about 45,000 plant species and among them, several thousands have been claimed to possess medicinal properties. Traditional system of medicine is found to have utilities as many accounts. Due to population rise adequate supply of drug and high cost of treatment in side effect along with drug resistance has been encountered in synthetic drugs, which has lead to an elevated emphasis for the use of plants to treat human diseases. The affordability of herbals has also drawn the attraction towards their use. India is one of the oldest civilizations which is known for rich repository of medicinal plants. *Camellia sinensis* is the species of plant whose leaves and leaf buds are used to produce Chinese tea. It is of the genus *Camellia*, a genus of flowering plants in the family Theaceae. White tea, green tea, oolong and black tea are all harvested from this species, but are processed differently to attain different levels of oxidation. Kukicha (twig tea) is also harvested from *Camellia sinensis*, but uses twigs and stems rather than leaves. Common names include tea plant, tea tree and tea shrub.

General Information: The Green tea is obtained from the tea plant *Camellia sinensis* belongs to the family Theaceae. 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 anti-oxidants. In addition, its content of certain minerals and vitamins increases the antioxidant potential of this type of tea. Presently, it is cultivated in at least 30 countries around the world. Tea beverage is an infusion of the dried leaves of *Camellia sinensis*. It is a widely used medicinal plant by the trials throughout India, China and popular in various indigenous system of medicine like Ayurveda, Unani and Homoeopathy Green tea has been consumed throughout the ages in India, China, Japan and Thailand.

Scientific Classification:

Kingdom : Plantae
Order : Ericales
Family : Theaceae
Genus : *Camellia*
Species : *C. sinensis*
Binomial name : *Camellia sinensis* (L.) Kuntze

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Common Names:

India : Chha
 China : Cha
 Russia : Chai
 Africa : Ite
 Italy : Te
 England : Tea plant
 United State : Tea

Description: Chinese *Camellia sinensis* is native to mainland China, South and Southeast Asia, but it is today cultivated across the world in tropical and subtropical regions. It is an evergreen shrub or small tree that is usually trimmed to below two metres (six feet) when cultivated for its leaves. It has a strong taproot. The flowers are yellow-white, 2.5-4 cm in diameter, with 7 to 8 petals. The seeds of *Camellia sinensis* and *Camellia oleifera* can be pressed to yield tea oil, a sweetish seasoning and cooking oil that should not be confused with tea tree oil, an essential oil that is used for medical and cosmetic purposes and originates from the leaves of a different plant. The leaves are 4-15 cm long and 2-5 cm broad. The young, light green leaves are preferably harvested for tea production; they have short white hairs on the underside. Older leaves are deeper green. Different leaf ages produce differing tea qualities, since their chemical compositions are different. Usually, the tip (bud) and the first two to three leaves are harvested for processing. This hand picking is repeated every one to two weeks.



Leaves



Fruits

Figure 1: *Camellia sinensis*

Chemical Constituents: Tea is reported to contain nearly 4000 bioactive compounds of which one third is contributed by polyphenols [1]. Other compounds are alkaloids (caffeine, theophylline and theobromine), amino acids, carbohydrates, proteins, chlorophyll, volatile organic compounds (chemicals that readily produce vapors and contribute to the odor of tea), fluoride, aluminum, minerals and trace elements [2]. Polyphenols found in tea are mostly flavonoids [3]. The polyphenols, a large group of plant chemicals that includes the catechins, are thought to be responsible for the health benefits that have traditionally been attributed to tea, especially green tea [4]. Major catechins are (-)-epicatechin gallate (ECG), (-)-epicatechin (EC), (-)-epigallocatechin (EGC) and (-)-epigallocatechin gallate (EGCG) (Figure 2). The most active and abundant catechin in green tea is epigallocatechin-3-gallate (EGCG). Black tea contains much lower concentrations of these catechins than green tea [5]. Oolong tea contains a mixture of simple polyphenols, such as catechins and complex polyphenols [6]. Black, Green and Oolong tea are all extremely good sources of vitamin C.

Medicinal Properties and Pharmacology

Anti-Aging Activity: According to the free radical theory of aging, [7] increased free radical generation and oxidative stress are the basis for phenotypic changes that lead to age-associated functional deterioration and neurodegeneration. Several age associated diseases such as cancer, Parkinson's disease, Alzheimer's disease, cardiovascular diseases and diabetes have their etiologies linked to changes in oxidant/anti-oxidant balances and free radical damage [8, 9]. However, Kitani *et al.* [10] report that green tea as the sole source of liquid did not significantly increase life span in mice, compared to controls. However, green tea did protect against ethanol-induced oxidative stress in aged mice and prevented serum lipids and protein from oxidative damage, produced by ethanol and enhanced by aging [11].

Neurodegenerative Diseases

Anti Alzheimer 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 [12]. In addition, EGCG regulates

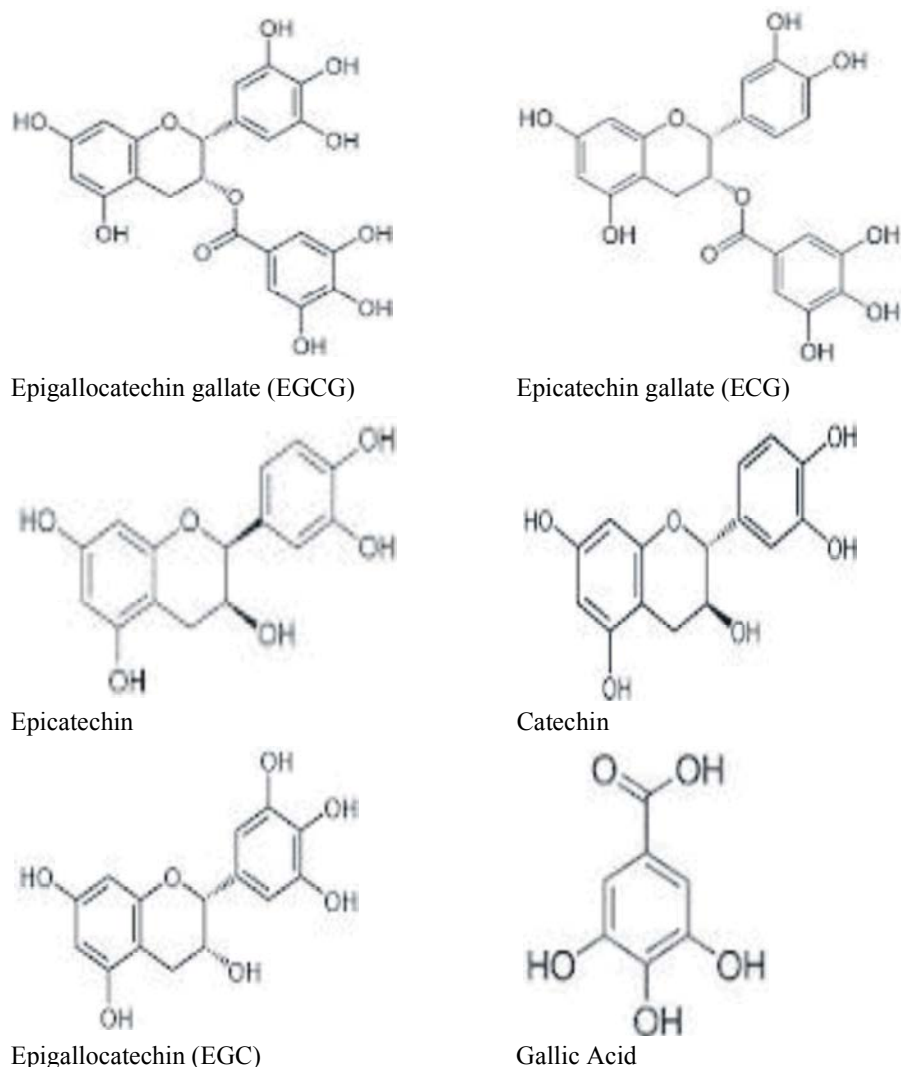


Fig. 2: Basic structures of different green tea polyphenols

the processing of APP, through PKC activation, to the nonamyloidogenic soluble APP (sAPP), thus preventing the formation of the neurotoxic beta-amyloid [13]. EGCG and other green tea catechins have also been shown to inhibit the beta secretase enzyme (BACE1) that is responsible for processing sAPP to beta-amyloid, thus having a potentially synergistic inhibitory effect on the production of beta-amyloid [14].

Antiparkinson Activity: Various studies have shown that green tea and EGCG significantly prevent these pathologies in animal models [15]. 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 [16]. EGCG

prevented the accumulation of iron and alpha-synuclein in MPTP-treated mice [17]. 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 green tea consumption do show a 5- to 10-fold lower incidences of the disease in Asian populations, [18, 19] although several other studies show a protective effect of iron chelators and antioxidants in general [20-22].

Antistroke Activity: A population based prospective cohort study of 40,530 Japanese aged 40-79 years with no previous history of cardiovascular disease was carried out over 11 years [23]. Reduced risk from cardiovascular disease and especially from stroke, was found to be

associated with increased consumption of green tea particularly in women. One study found an inverse relationship between the habit of drinking over 5 cups of green tea daily with having a history of stroke [24]. A follow up study showed those who drank less green tea were at least twice as likely to die of stroke or cerebral hemorrhage [24]. A recent meta analysis of current literature found people consuming 3 or more cups of green or black tea had 21% less chance of suffering a stroke [25]. EGCG has been shown to afford protection against neuronal damage after ischemia in gerbils, when administered systemically at 50 mg/kg immediately after excitotoxic ischemic insult [26]. At this dose, EGCG was also found to exhibit a significant antioxidant effect in rats and protected against neurological deficit and infarction due to the focal ischemia, when administered 24 h after a transient cerebral occlusion [27].

Cardiovascular Diseases: The protective effect of green tea in cardiovascular diseases is also thought to stem from its antioxidant activity. Indeed, oral intake of green tea extract by human volunteers increased resistance of plasma LDL to oxidation *in vivo*, an effect that may lower the risk of arterogenesis [28]. Green tea extract also attenuated blood pressure increases in spontaneously hypertensive rats, an effect attributed to its antioxidant properties [29]. Coronary artery disease is associated with increased oxidative stress and dysfunction of the endothelium (cells lining the heart, blood and lymphatic vessels and various other cavities). Some antioxidants are known to reverse endothelial dysfunction [30]. Thus numerous studies have aimed at determining whether or not the antioxidant polyphenols (flavonoids and catechins) present in tea, can perform the same function. Although results tended to be equivocal, several findings were quite common. Various case studies show that tea does not decrease blood pressure, nor plasma lipids (cholesterol) *ex vivo* [31] and while tea catechins do inhibit the peroxidation of LDL (low density lipoprotein) cholesterol *in vitro*, the effect *ex vivo* is small [31, 32] cholesterol lowering has been documented in mice and green tea consumption has been shown to reduce the development of aortic atherosclerosis (hardening, thickening and elasticity-loss of arteries) in rabbits, it is more difficult to show in humans and results are inconsistent. While most epidemiological studies support the suggested role of tea in decreasing the risk of coronary artery disease, there is much debate as to the mechanisms of benefit. However, the potential benefits of tea consumption are worthy of confirmation by more human trials.

Anticancer Activity: Green tea has a reputed role in cancer prevention as tea catechins have been shown to inhibit tumour cell proliferation as well as promote the destruction of leukaemia cells [33]. Laboratory studies on cultures of tumour cells and mice given carcinogenic chemicals, showed green tea's potential to inhibit cancer cell growth. Stomach cancer is the second most common form of cancer worldwide. Thus much research has gone into searching for cures and treatments thereof. One such study, conducted in China, [34] aimed at investigating the effect of green tea consumption on chronic gastritis and the risk of stomach cancer. Their sample included 133 stomach cancer cases, 166 chronic gastritis cases and 433 healthy controls. Results showed an inverse association between green tea drinking and both diseases. Furthermore, dose-response relationships were observed, with years of green tea consumption being more effective in combating both stomach cancer and chronic gastritis. A study using 8552 residents, representative of Japan's population, tested whether or not Green tea was an effective anti-carcinogenic.[35] Results showed a decreased relative risk of cancer incidence for those consuming over ten cups, compared with those consuming below three cups of green tea per day. The risks decreased by 57 % for women, 54 % for men and 59 % for both sexes. In addition, increased consumption was associated with a significant delay in the onset of cancer. Green tea and black tea polyphenols inhibit cell growth and induce apoptosis of human cervical cancer cells [36]. Green tea consumption helps protect against colorectal cancer as suggested by a four year study of 69,710 women aged 40-70 years. Studies in animal models have demonstrated that green tea and EGCG can inhibit carcinogenesis at all stages, viz. initiation, promotion and progression [37]. This multifaceted inhibition of the tumorigenic process is attributed to a combination of antioxidative, antiproliferative and pro-apoptotic effects [38]. Green tea and EGCG have also been shown to inhibit the process of angiogenesis, tumor metastasis and invasion in animal models [39-41]. The relevance of the various mechanisms of antiproliferative, anti-angiogenic and anti-invasive activities of green tea and catechins, to the prevention of carcinogenesis in humans, represents a monumental challenge, yet to be addressed [42].

Antidiabetic Activity: Green tea has an antidiabetic effect. It lowered glucose levels in the bloodstreams of diabetic mice without affecting insulin levels [43]. Long-term administration of green tea extract to normal rats increased insulin sensitivity [44]. When administered to fructose-fed

rats, green tea extract was also found to prevent development of insulin resistance, hyperglycemia and other metabolic defects [45].

Anticaries Activity: Green tea extract is effective in preventing dental caries because of its dual effect, that is, its flavor compounds are antibacterial while polyphenols possess a antiplaque activity. A synergistic effect of 128-folds to 256-folds was observed when combined with sesquiterpene hydrocarbons (delta cadinene and caryophyllene) and indole [46]. Tea leaves are rich in fluoride, which is known to enhance dental health and prevents dental caries. However, the possible dental health benefits of tea are not limited to fluoride, but involve other tea components [47]. Dental caries are induced by oral microflora. Several green tea polyphenols have preventative effects on dental caries [48, 49]. Among the catechins, GC and EGC are most active, inhibiting the growth of 10 strains of cariogenic bacteria [48]. ECG, GCG and EGCG strongly inhibit GTase and inhibit adherence of the bacteria to dental surfaces [49-51]. In humans, a double-blind study showed that rinsing the mouth after meals with 0.05 to 0.5% green tea polyphenols for 3 days inhibits dental plaque formation by 30 to 43% [52].

Obesity and Weight Loss: Green tea extract standardised to 8.35% caffeine and 24.7% catechins has been shown to stimulate brown adipose tissue *in vivo*, with thermogenesis greater than the effect the caffeine content accounts for long term ingestion of tea catechins stopped the accumulation of body fat in mice with high fat diet induced obesity, [53] possibly due to the activation of hepatic lipid metabolism [54]. This effect was also found in non obese rats [55]. An open study found that an 80% ethanol extract of green tea standardised to 25% catechins reduced weight in moderately obese by 4.6% and waist circumference by 4.5% after 3 months use. However a double blind placebo controlled parallel trial of 46 women showed no difference between the placebo and green tea groups over 87 days in either weight loss or metabolic parameters. Several studies have suggested that oral consumption of green tea may protect against obesity-related disorders such as atherosclerosis, diabetes and hypertension. Interestingly, [56] showed that purified EGCG (50-100 mg/kg), but not other green tea catechins, significantly reduced or prevented an increase in body weight in lean and obese Zucker rats, an effect that appeared to be reversible and associated with a reduction in food intake.

Skin Disorders: Using different animal models, 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 [57].

CONCLUSIONS

Human studies suggest that green tea may contribute to a reduction in the risk of cardiovascular disease and some forms of cancer, as well as to the promotion of oral health and other physiological functions such as antihypertensive effect, body weight control, antibacterial and antiviral activity, bone mineral density increase, antifibrotic properties and neuroprotective power. Increasing interest in its health benefits has led to the inclusion of green tea in the group of beverages with functional properties. Other traditional uses of green tea include treating flatulence (gas), regulating body temperature and blood sugar, promoting digestion and improving mental processes. As an herbal remedy, green tea is often recommended to ease stomach discomfort, vomiting and to stop diarrhea. The antibacterial action of tea is useful in treating infections and wounds. 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 compared to modern beverages such as soft drinks.

REFERENCES

1. Tariq, M., A. Naveed and K. Barkat Ali, 2010. The morphology, characteristics and medicinal properties of '*Camellia sinensis*' tea. J. Med. Plants Res., 4(19): 2028-33.
2. Cabrera, C., R. Gimenez and M.C. Lopez, 2003. Determination of tea components with antioxidant activity. J. Agric. Food Chem., 51(15): 4427-35.

3. Sumpio, B.E., A.C. Cordova, D.W. Berke-Schlessel, F. Qin and Q.H. Chen, 2006. Green tea, the Asian Paradox and cardiovascular disease. *J. Am. Coll. Surg.*, 202: 813-20.
4. Cabrera, C., R. Artacho and R. Gimenez, 2006. Beneficial effects of green tea-a review. *J. Am. Coll. Nutr.*, 25(2): 79-99.
5. Wu, A.H. and M.C. Yu, 2006. Tea, hormone-related cancers and endogenous hormone levels. *Mol. Nutr. Food Res.*, 50(2): 160-69.
6. Mukhtar, H. and N. Ahmad, 2000. Tea polyphenols: Prevention of cancer and optimizing health. *Am. J. Clin. Nutr.*, 71(6 Suppl): 1698S-1702S.
7. Harman, D., 1994. Free-radical theory of aging. Increasing the functional life span. *Annals of the New York Academy of Sci.*, 717: 1-15.
8. Polidori, M.C., 2003. Antioxidant micronutrients in the prevention of age-related diseases. *J. Postgraduate Medicine*, 49(3): 229-35.
9. Junqueira, V.B., S.B. Barros, S.S. Chan, L. Rodrigues, L. Giavarotti, R.L. Abud and G.P. Deucher, 2004. Aging and oxidative stress. *Molecular Aspects of Medicine*, 25(1-2): 5-16.
10. Kitani, K., T. Yokozawa and T. Osawa, 2004. Interventions in aging and age-associated pathologies by means of nutritional approaches. *Annals of the New York Academy of Sci.*, 1019: 424-26.
11. Luczaj, W., E. Waszkiewicz, E. Skrzydlewska and W. Roszkowska-Jakimiec, 2004. Green tea protection against age-dependent ethanol-induced oxidative stress. *J. Toxicology and Environmental Health*, 67(7): 595-606.
12. Choi, Y.T., C.H. Jung, S.R. Lee, J.H. Bae, W.K. Baek, M.H. Suh, J. Park, C.W. Park and S.I. Suh, 2001. The green tea polyphenol (-)-Epigallocatechin gallate attenuates beta-amyloid-induced neurotoxicity in cultured hippocampal neurons. *Life Sci.*, 70(5): 603-14.
13. Levites, Y., T. Amit, S. Mandel and M.B. Youdim, 2003. Neuroprotection and neurorescue against A beta toxicity and PKC-dependent release of nonamyloidogenic soluble precursor protein by green tea polyphenol (-)-epigallocatechin-3-gallate. *FASEB J.*, 17(8): 952-54.
14. Jeon, S.Y., K. Bae, Y.H. Seong and K.S. Song, 2003. Green tea catechins as a BACE1 (beta-secretase) inhibitor. *Bioorganic Medicinal Chemistry Letters*, 13(22): 3905-08.
15. Levites, Y., O. Weinreb, G. Maor, M.B. Youdim and S. Mandel, 2001. Green tea polyphenol (-)-epigallocatechin-3-gallate prevents N-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced dopaminergic neurodegeneration. *J. Neurochemistry*, 78(5): 1073-82.
16. Choi, J.Y., C.S. Park, D.J. Kim, M.H. Cho, B.K. Jin, J.E. Pie and W.G. Chung, 2002. Prevention of nitric oxide-mediated 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced Parkinson's disease in mice by tea phenolic epigallocatechin 3-gallate. *Neurotoxicol.*, 23(3): 367-74.
17. Mandel, S., G. Maor and M.B. Youdim, 2004a. Iron and alpha-synuclein in the substantia nigra of MPTP-treated mice: effect of neuroprotective drugs Rapomorphine and green tea polyphenol (-)-epigallocatechin-3-gallate. *J. Molecular Neuroscience*, 24(3): 401-16.
18. Zhang, Z.X. and G.C. Roman, 1993. Worldwide occurrence of Parkinson's disease: an updated review. *Neuroepidemiol.*, 12(4): 195-208.
19. Pan, T., J. Jankovic and W. Le, 2003. Potential therapeutic properties of green tea polyphenols in Parkinson's disease. *Drugs Aging*, 20(10): 711-21.
20. Youdim, M.B., M. Gassen, A. Gross, S. Mandel and E. Grunblatt, 2000. Iron chelating, antioxidant and cytoprotective properties of dopamine receptor agonist; apomorphine. *J. Neural Transmission Supplementum*, 58: 83-96.
21. Sanz, E., M. Romera, L. Bellik, J. Marco and M. Unzeta, 2004. Indolalkylamines derivatives as antioxidant and neuroprotective agents in an experimental model of Parkinson's disease. *Medical Science Monitor*, 10(12): BR477-BR484.
22. Zheng, H., L.M. Weiner, O. Bar-Am, S. Epsztejn, Z.I. Cabantchik, A. Warshawsky, M.B. Youdim and M. Fridkin, 2005. Design, synthesis and evaluation of novel bifunctional iron-chelators as potential agents for neuroprotection in Alzheimer's, Parkinson's and other neurodegenerative diseases. *Bioorganic Medicinal Chemistry*, 13(3): 773-83.
23. Kuriyama, S., T. Shimazu, K. Ohmori, N. Kikuchi, N. Nakaya and Y. Nishino, 2006. Green tea consumption and mortality due to cardiovascular disease, cancer and all causes in Japan: The Ohsaki Study. *JAMA*, 296(10): 1255-65.
24. Sato, Y., H. Nakatsuka, T. Watanabe, S. Hisamichi, H. Shimizu and S. Fujisaku, 1989. Possible contribution of green tea drinking habits to the prevention of stroke. *Tohoku J. Exp. Med.*, 157(4): 337-43.

25. Arab, L., W. Liu and D. Elashoff, 2008. Green and black tea consumption and risk of stroke. A meta-analysis. *Stroke*, 40(5): 1786-92.
26. Lee, H., J.H. Bae and S.R. Lee, 2004. Protective effect of green tea polyphenol EGCG against neuronal damage and brain edema after unilateral Cerebral ischemia in gerbils. *J. Neuroscience Res.*, 77(6): 892-900.
27. Choi, Y.B., Y.I. Kim, K.S. Lee, B.S. Kim and D.J. Kim, 2004. Protective effect of epigallocatechin gallate on brain damage after transient middle cerebral artery occlusion in rats. *Brain Res.*, 1019(1-2): 47-54.
28. Miura, Y., T. Chiba, S. Miura, I.I. Tomita, K. Umegaki, M. Ikeda and T. Tomita, 2000. Green tea polyphenols (flavan 3-ols) prevent oxidative modification of low density lipoproteins: an ex vivo study in humans. *J. Nutritional Biochemistry*, 11(4): 216-22.
29. Negishi, H., J.W. Xu, K. Ikeda, M. Njelekela, Y. Nara and Y. Yamori, 2004. Black and green tea polyphenols attenuate blood pressure increases in stroke-prone spontaneously hypertensive rats. *J. Nutrition*, 134(1): 38-42.
30. Duffy, S.J., J.F.J. Keaney, M. Holbrook, N. Gokce, P.L. Swerdloff, B. Frei and J.A. Vita, 2001. Short-and long-term black tea consumption reverses endothelial dysfunction in patients with coronary artery disease. *Circulation*, 104(2): 151-6.
31. Riemersma, R.A., C.A. Rice-Evans, R.M. Tyrell, M.N. Clifford and M.E. Lean, 2001. Tea flavonoids and cardiovascular health. *QJM*, 94(5): 277-82.
32. Samman, S., B. Sandstrom, M.B. Toft, K. Bukhave, M. Jensen, S.S. Sorensen and M. Hansen, 2001. Green tea extract added to foods reduces nonheme-iron absorption. *Am. J. Clin. Nutr.*, 73(3): 607-12.
33. Smith, D.M. and Q.P. Dou, 2001. Green tea polyphenol epigallocatechin inhibits DNA replication and consequently induces leukemia cell apoptosis. *Int. J. Mol. Med.*, 27(6): 645-52.
34. Setiawan, V.W., Z.F. Zhang, G.P. Yu, Q.Y. Lu, Y.L. Li, M.L. Lu, M.R. Wang, C.H. Guo, S.Z. Yu, R.C. Kurtz and C.C. Hsieh, 2001. Protective effect of green tea on the risks of chronic gastritis and stomach cancer. *Int. J. Cancer*, 92(4): 600-604.
35. Nakachi, K., S. Matsuyama, S. Miyake, M. Suganuma and K. Imai, 2000. Preventive effects of drinking green tea on cancer and cardiovascular disease: epidemiological evidence for multiple targeting prevention. *Biofactors*, 134(1-4): 49-54.
36. Singh, M., S. Tyagi, K. Bhui, S. Prasad and Y. Shukla, 2009. Regulation of cell growth through cell cycle arrest and apoptosis in HPV 16 positive human cervical cancer cells by tea polyphenols. *Invest New Drug*. <http://www.ncbi.nlm.nih.gov/pubmed/19271153>
37. Chung, F.L., J. Schwartz, CR. Herzog and Y.M. Yang, 2003. Tea and cancer prevention: studies in animals and humans. *J. Nutrition*, 133(10): 3268S-3274S.
38. Gouni-Berthold, I. and A. Sachinidis, 2004. Molecular mechanisms explaining the preventive effects of catechins on the development of proliferative diseases. *Current Pharmaceutical Design*, 10(11): 1261-71.
39. Fassina, G., R. Vene, M. Morini, S. Minghelli, R. Benelli, D.M. Noonan and A. Albini, 2004. Mechanisms of inhibition of tumor angiogenesis and vascular tumor growth by epigallocatechin-3-gallate. *Clinical Cancer Res.*, 10(14): 4865-73.
40. Jung, Y.D. and LM. Ellis, 2001. Inhibition of tumour invasion and angiogenesis by epigallo catechin gallate (EGCG), a major component of green tea. *International J. Experimental Pathol.*, 82(6): 309-16.
41. Garbisa, S., L. Sartor, S. Biggin, B. Salvato, R. Benelli and A. Albini, 2001. Tumor gelatinases and invasion inhibited by the green tea flavanol epigallocatechin-3-gallate. *Cancer*, 91(4): 822-32.
42. Yang, C.S., 1999. Tea and health. *Nutrition*, 15(11-12): 946-49.
43. Tsuneki, H., M. Ishizuka, M. Terasaw, J. Wu, T. Sasaoka and I. Kimura, 2004. Effect of green tea on blood glucose levels and serum proteomic patterns in diabetic (db/db) mice and on glucose metabolism in healthy humans. *BMC Pharm.*, 4: 18.
44. Wu, L.Y., C.C. Juan, L.T. Ho, Y.P. Hsu and L.S. Hwang, 2004a. Effect of green tea supplementation on insulin sensitivity in Sprague-Dawley rats. *J. Agricultural and Food Chemistry*, 52(3): 643-48.
45. Wu, L.Y., C.C. Juan, L.S. Hwang, Y.P. Hsu, P.H. Ho and L.T. Ho, 2004b. Green tea supplementation ameliorates insulin resistance and increases glucose transporter IV content in a fructose-fed rat model. *European J. Nutrition*, 43(2): 116-24.
46. Duke, J.A., 2000. *Handbook of Medicinal Herbs*. 2nd ed. Florida: CRC Press, pp: 353-54.
47. Onisi, M., N. Shimura, C. Nakamura and M. Sato, 1981b. A field test on the caries preventive effect of tea drinking. *Koku Eisei Gakkai Zasshi*, 31: 13-17.

48. Sakanaka, S., M. Kim, M. Taniguchi and T. Yamamoto, 1989. Antibacterial substances 88 LIAO S, KAO YH AND HIIPAKKA RA in Japanese green tea extract against *Streptococcus mutans*, a cariogenic bacterium. *Agric. Biol. Chem.*, 53: 2307-11.
49. Sakanaka, S., T. Sate, M. Kim and T. Yamamoto, 1990. Inhibitory effects of green tea polyphenols on glucan synthesis and cellular adherence of cariogenic streptococci. *Agric. Biol. Chem.*, 54: 2925-29.
50. Sakanaka, S., N. Shimura, M. Aizawa, M. Kim and T. Yamamoto, 1992. Preventive effect of green tea polyphenols against dental caries in conventional rats. *Biosci. Biotechnol. Biochem.*, 56: 592-94.
51. Otake, S., M. Makimura, T. Kuroki, Y. Nishihara and M. Hirasawa, 1991. Anticaries effects of polyphenolic compounds from Japanese Green tea. *Caries Res.*, 25: 438-43.
52. Sakanaka, S., 1997. Green tea polyphenols for prevention of dental caries. In "Chemical Applications of Green Tea" (T. Yamamoto, L.R. Juneja, D.C. Chu and M. Kim, Eds.), CRC Press, Boca Raton, FL, pp: 87-101.
53. Dulloo, A., J. Seydoux, L. Girardier, P. Chantre and J. Vandermander, 2000. Green tea and thermogenesis: interactions between catechin-polyphenols, caffeine and sympathetic activity. *Int. J. Obesity*, 2(252-8): 56.
54. Tokimitsu, I., 2004. Effects of tea catechins on lipid metabolism and body fat accumulation. *Biofac.*, 22(1-4): 141-3.
55. Ito, Y., T. Ichikawa, Y. Morohoshi, T. Nakamura, Y. Saegusa and K. Ishihara, 2008. Effect of tea catechins on body fat accumulation In rats fed a normal diet. *Biomed Res.*, 291: 27-32.
56. Kao, Y.H., R.A. Hiipakka and S. Liao, 2000. Modulation of obesity by a green tea catechin. *American J. Clinical Nutrition*, 72(5): 1232-34.
57. Katiyar, S.K. and C.A. Elmets, 2001. Green tea polyphenolic antioxidants and skin photoprotection (Review). *Int. J. Oncol.*, 18(6): 1307-13.