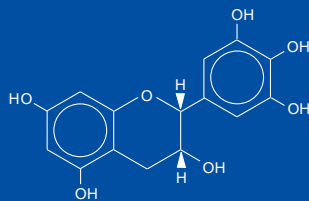
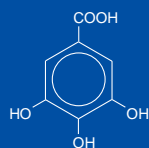


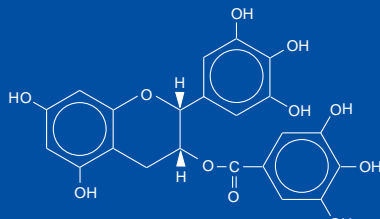
Epicatechin



Epigallocatechin (EGC)



Gallic Acid



Epigallocatechin gallate (EGCG)

Monograph

Green Tea

Description and Constituents

Tea is one of the most widely consumed beverages in the world today, second only to water, and its medicinal properties have been widely explored. The tea

plant, *Camellia sinensis*, is a member of the Theaceae family, and black, oolong, and green tea are produced from its leaves. It is an evergreen shrub or tree and can grow to heights of 30 feet, but is usually pruned to 2-5 feet for cultivation. The leaves are dark green, alternate and oval, with serrated edges, and the blossoms are white, fragrant, and appear in clusters or singly. Unlike black and oolong tea, green tea production does not involve oxidation of young tea leaves. Green tea is produced from steaming fresh leaves at high temperatures, thereby inactivating the oxidizing enzymes and leaving the polyphenol content intact. The polyphenols found in tea are more commonly known as flavanols or catechins and comprise 30-40 percent of the extractable solids of dried green tea leaves. The main catechins in green tea are epicatechin, epicatechin-3-gallate, epigallocatechin, and epigallocatechin-3-gallate (EGCG), with the latter being the highest in concentration. Green tea polyphenols have demonstrated significant antioxidant, anticarcinogenic, anti-inflammatory, thermogenic, probiotic, and antimicrobial properties in numerous human, animal, and *in vitro* studies.^{1,2}

Mechanisms of Action

The anticarcinogenic properties of green tea polyphenols, mainly EGCG, are likely a result of inhibition of biochemical markers of tumor initiation and promotion, induction of apoptosis, and inhibition of cell replication rates, thus retarding the growth and development of neoplasms.^{3,4} Their antioxidant potential is directly related to the combination of aromatic rings and hydroxyl groups that make up their structure, and is a result of binding and neutralization of free radicals by the hydroxyl groups. In addition, green tea polyphenols stimulate the activity of hepatic detoxification enzymes, thereby promoting detoxification of xenobiotic compounds, and are also capable of chelating metal ions, such as iron, that can generate radical oxygen species.^{5,6}

Green tea polyphenols inhibit the production of arachidonic acid metabolites such as pro-inflammatory prostaglandins and leukotrienes, resulting in a decreased inflammatory response. Human and animal studies have demonstrated EGCG's ability to block inflammatory responses to ultraviolet A and B radiation as well as significantly inhibiting the neutrophil migration that occurs during the inflammatory process.⁷⁻⁹

Research on green tea's thermogenic properties indicates a synergistic interaction between its caffeine content and catechin polyphenols may result in prolonged stimulation of thermogenesis. Studies

have also shown green tea extracts are capable of reducing fat digestion by inhibiting digestive enzymes.^{10,11} Although the exact mechanism is unknown, green tea catechins have been shown to significantly raise levels of Lactobacilli and Bifidobacteria while decreasing levels of numerous potential pathogens.¹² Studies have also demonstrated green tea's antibacterial properties against a variety of gram-positive and gram-negative species.¹³

Clinical Indications

Cancer Prevention/Inhibition

Several studies have demonstrated green tea polyphenols' preventative and inhibitory effects against tumor formation and growth. While the studies are not conclusive, green tea polyphenols, particularly EGCG, may be effective in preventing cancer of the prostate, breast, esophagus, stomach, pancreas, and colon.¹⁴ There is also some evidence that green tea polyphenols may be chemopreventative or inhibitory toward lung, skin, and liver cancer,¹⁵⁻¹⁷ bladder and ovarian tumors,^{18,19} leukemia,²⁰ and oral leukoplakia.²¹

Antioxidant Applications

Many chronic disease states and inflammatory conditions are a result of oxidative stress and subsequent generation of free radicals. Some of these include heart disease (resulting from LDL oxidation), renal disease and failure, several types of cancer, skin exposure damage caused by ultraviolet (A and B) rays, as well as diseases associated with aging. Green tea polyphenols are potent free radical scavengers due to the hydroxyl groups in their chemical structure. The hydroxyl groups can form complexes with free radicals and neutralize them, preventing the progression of the disease process.²²

Obesity/Weight Control

Recent studies on green tea's thermogenic properties have demonstrated a synergistic interaction between caffeine and catechin polyphenols that appears to prolong sympathetic stimulation of thermogenesis. A human study of green tea extract containing 90 mg EGCG taken three times daily concluded that men taking the extract burned 266 more calories per day than did those in the placebo group and that green tea extract's thermogenic effects may play a role in controlling obesity.²³ Green tea polyphenols have also been shown to markedly inhibit digestive lipases *in vitro*, resulting in decreased lipolysis of triglycerides, which may translate to reduced fat digestion in humans.^{10,11}

Intestinal Dysbiosis and Infection

A small study in Japan demonstrated a special green tea catechin preparation (30.5% EGCG) was able to positively affect intestinal dysbiosis in nursing home patients by raising levels of Lactobacilli and Bifidobacteria while lowering levels of Enterobacteriaceae, Bacteroidaceae, and eubacteria. Levels of pathogenic bacterial metabolites were also decreased.¹² An *in vitro* study also demonstrated green tea's antimicrobial activity against a variety of gram-positive and gram-negative pathogenic bacteria that cause cystitis, pyelonephritis, diarrhea, dental caries,²⁴ pneumonia, and skin infections.¹³

Other Applications

Sickle cell anemia is characterized by a population of "dense cells" that may trigger vaso-occlusion and the painful sickle cell "crisis." One study demonstrated that 0.13 mg/mL green tea extract was capable of inhibiting dense-cell formation by 50 percent.²⁵

Another potential therapeutic application of green tea is the treatment of psoriasis. The combination therapy of psoralens and ultraviolet A radiation is highly effective but has unfortunately been shown to substantially increase the risk for developing squamous cell carcinoma and melanoma. An *in vitro* study using human and mouse skin demonstrated that pre- and post-treatment with green tea extract inhibited DNA damage induced by the psoralen/ultraviolet A radiation exposure.⁸

Dosage and Toxicity

Green tea is generally considered a safe, non-toxic beverage and consumption is usually without side-effects. The average cup of green tea, however, contains from 10-50 mg of caffeine and over-consumption may cause irritability, insomnia, nervousness, and tachycardia. Because studies on its possible teratogenic effect are inconclusive, caffeine consumption is contraindicated during pregnancy. Lactating women should also limit caffeine intake to avoid sleep disorders in infants.²⁶

The dosage for green tea beverage varies, depending on the clinical situation and desired therapeutic effect. The phenolic content of green tea infusion is between 50-100 mg polyphenols per cup, depending on species, harvesting variables, and brewing methods,²⁷ with typical dosages ranging from 3 to 10 cups per day. Cancer preventative effects are usually associated with dosages in the higher end of the range.²⁸ Green tea extracts standardized to 80-percent total polyphenols are dosed at an average of 500-1500 mg per day.

References

1. Alschuler L. Green Tea: Healing tonic. *Am J Natur Med* 1998;5:28-31.
2. Graham HN. Green tea composition, consumption, and polyphenol chemistry. *Prev Med* 1992;21:334-350.
3. Nihal A, Hasan M. Green tea polyphenols and cancer: biological mechanisms and practical implications. *Nutr Rev* 1999;57:78-83.
4. Ahmad N, Feyes DK, Nieminen AL, et al. Green tea constituent epigallocatechin-3-gallate and induction of apoptosis and cell cycle arrest in human carcinoma cells. *J Natl Cancer Inst* 1997;89:1881-1886.
5. Serafini M, Ghiselli A, Ferro-Luzzi A. In vivo antioxidant effect of green and black tea in man. *Eur J Clin Nutr* 1996;50:28-32.
6. Erba D, Riso P, Colombo A, Testolin G. Supplementation of Jurkat T cells with green tea extract decreases oxidative damage due to iron treatment. *J Nutr* 1999;129:2130-2134.
7. Katiyar SK, Matsui MS, Elmets CA, Mukhtar H. Polyphenolic antioxidant (-)epigallocatechin-3-gallate from green tea reduces UVB-induced inflammatory responses and infiltration of leukocytes in human skin. *Photochem Photobiol* 1999;69:148-153.
8. Zhao JF, Zhang YJ, Jin XH, et al. Green tea protects against psoralen plus ultraviolet A-induced photochemical damage to skin. *J Invest Dermatol* 1999;113:1070-1075.
9. Hofbauer R, Frass M, Gmeiner B, et al. The green tea extract epigallocatechin gallate is able to reduce neutrophil transmigration through monolayers of endothelial cells. *Wien Klin Wochenschr* 1999;111:276-282.
10. Dulloo AG, Seydoux J, Girardier L, et al. Green tea and thermogenesis: interactions between catechin-polyphenols, caffeine, and sympathetic activity. *Int J Obes Relat Metab Disord* 2000;24:252-258.
11. Juhel C, Armand M, Pafumi Y, et al. Green tea extract (AR25) inhibits lipolysis of triglycerides in gastric and duodenal medium in vitro. *J Nutr Biochem* 2000;11:45-51.
12. Goto K, Kanaya S, Nishikawa T, et al. Green tea catechins improve gut flora. *Ann Long-Term Care* 1998;6:1-7.
13. Chou CC, Lin LL, Chung KT. Antimicrobial activity of tea as affected by the degree of fermentation and manufacturing season. *Int J Food Microbiol* 1999;48:125-130.
14. Katiyar SK, Mukhtar H. Tea antioxidants in cancer chemoprevention. *J Cell Biochem* 1997;27:S59-S67.

15. Lee IP, Kim YH, Kang MH, et al. Chemopreventative effect of green tea (*Camellia sinensis*) against cigarette smoke-induced mutations (SCE) in humans. *J Cell Biochem* 1997;27:S68-S75.
16. Picard D. The biochemistry of green tea polyphenols and their potential application in human skin cancer. *Altern Med Rev* 1996;1:31-42.
17. Hirose M, Hoshiya T, Akagi K, et al. Effects of green tea catechins in a rat multi-organ carcinogenesis model. *Carcinogenesis* 1993;14:1549-1553.
18. Sato D. Inhibition of urinary bladder tumors induced by N-butyl-N-(4-hydroxybutyl)-nitrosamine in rats by green tea. *Int J Urol* 1999;6:93-99.
19. Sugiyama T, Sadzuka Y. Enhancing effects of green tea components on the antitumor activity of adriamycin against M5076 ovarian sarcoma. *Cancer Lett* 1998;133:19-26.
20. Otsuka T, Ogo T, Eto T, et al. Growth inhibition of leukemic cells by (-)-epigallocatechin gallate, the main constituent of green tea. *Life Sci* 1998;63:1387-1403.
21. Khafif A, Schantz SP, al-Rawi M, et al. Green tea regulates cell cycle progression in oral leukoplakia. *Head Neck* 1998;20:528-534.
22. Ichihashi M, Ahmed NU, Budiyanto A, et al. Preventive effect of antioxidant on ultraviolet-induced skin cancer in mice. *J Dermatol Sci* 2000;23:S45-S50.
23. Dulloo AG, Duret C, Rohrer D, et al. Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am J Clin Nutrition* 1999;70:1040-1045.
24. You S. Study on feasibility of Chinese green tea polyphenols (CTP) for preventing dental caries. *Chung Hua Kou Hsueh Tsa Chih* 1993;28:197-199.
25. Ohnishi ST, Ohnishi T, Ogunmola GB. Sick cell anemia: a potential nutritional approach for a molecular disease. *Nutrition* 2000;16:330-338.
26. DerMarderosian A. *The Review of Natural Products*. St. Louis, MO: Facts and Comparisons, Wolters Kluwer Co. 1999.
27. Yamamoto T, Juneja LR, Djoing-Chu C, Kim M. *Chemistry and Applications of Green Tea*. Boca Raton, FL: CRC Press, 1997: 51-52,
28. Imai K, Suga K, Nakachi K. Cancer-preventative effects of drinking tea among a Japanese population. *Prev Med* 1997;26:769-775.