

Phcog Rev.:Plant Review

Green tea (*Camellia sinensis*): Chemistry, Traditional, Medicinal uses and its Pharmacological activities- a review

Vitthal V. Chopade*¹, Atul A. Phatak¹, Aman B. Upaganlawar² and Anil A. Tankar²

¹Modern College of Pharmacy, Sector No- 21, Yamuna Nagar, Nigdi Pune-411044, India.

²Institute of Pharmaceutical Education and Research, Borgaon (Meghe), Wardha 442 001, India.

*Author for Correspondence: vi_research@rediffmail.com

ABSTRACT

The Green tea is obtained from the tea plant *Camellia sinensis* (L.) Kuntze (Common names: Green tea extract, Chinese tea) which belongs to the family Theaceae. It is a widely used medicinal plant by the tribals 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. Following the various traditional claims on utility of this plant in curing number of diseases, considerable efforts have been made by researchers to verify its utility through scientific pharmacological screenings. In traditional Chinese and Indian medicine, practitioners used green tea as a stimulant, diuretic (to promote the excretion of urine), astringent (to control bleeding and help heal wounds), and to improve heart health. Other traditional uses of green tea include treating flatulence (gas), regulating body temperature and blood sugar, promoting digestion, and improving mental processes.

KEYWORDS: Green tea, *Camellia sinensis*, Chemistry, Traditional and pharmacological activities

INTRODUCTION

Archeological evidence suggests that people consumed tea leaves steeped in boiling water as many as 500,000 years ago. Botanical evidence indicates that India and China were among the first countries to cultivate tea. Today, hundreds of millions of people drink tea around the world, and studies are now suggesting that green tea (*Camellia sinensis*) in particular has many health benefits.

There are three main varieties of tea-green, black, and oolong. The difference between the teas is in their processing. Green tea is made from unfermented leaves and reportedly contains the highest concentration of powerful antioxidants called polyphenols. Antioxidants are substances that scavenge free radicals -- damaging compounds in the body that alter cells, tamper with DNA (genetic material), and even cause cell death. Free radicals occur naturally in the body, but environmental toxins (including ultraviolet rays from the sun, radiation, cigarette smoke, and air pollution) also give rise to these damaging particles. Scientists believe that free radicals contribute to the aging process as well as the development of a number of health problems including cancer and heart disease. Antioxidants such as polyphenols in green tea can neutralize free radicals and may reduce or even help prevent some of the damage they cause [1].

Green tea has been consumed throughout the ages in India, China, Japan, and Thailand. In traditional Chinese and Indian medicine, practitioners used green tea as a stimulant, diuretic (to promote the excretion of urine), astringent (to control bleeding and help heal wounds), and to improve heart health [2]. Other traditional uses of green tea include treating flatulence (gas), regulating body temperature and blood sugar, promoting digestion, and improving mental processes [3].

Plant Description

Green, tea derived from the leaves of the *Camellia sinensis* plant. Originally cultivated in East Asia, this plant grows as large as a shrub or tree. Today, *Camellia sinensis* grows throughout Asia and parts of the Middle East and Africa. People in Asian countries more commonly consume green and oolong tea while black tea is most popular in the United States. Green tea is prepared from unfermented leaves, the leaves of oolong tea are partially fermented, and black tea is fully fermented. [4]

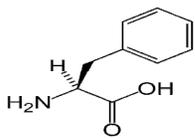
Chemical Constituents

The healthful properties of green tea are largely attributed to polyphenols, chemicals with potent antioxidant properties. In fact, the antioxidant effects of polyphenols appear to be greater than vitamin C. The polyphenols in green tea also give it a somewhat bitter flavor [5].

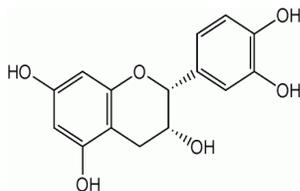
Polyphenols contained in teas are classified as catechins. Green tea contains six primary catechin compounds: catechin, gallate, epicatechin, epigallocatechin, epicatechin gallate, and apigallocatechin gallate (also known as EGCG) [6-9]. EGCG is the most studied polyphenol component in green tea and the most active [10].

Green tea also contains alkaloids including caffeine [11], theobromine [12], and theophylline. These alkaloids provide green tea's stimulant effects. Tea leaves contain many compounds, such as polysaccharides, volatile oils, vitamins, minerals, purines, alkaloids e.g. caffeine and polyphenols e.g. catechins, flavonoids. Although all three tea types have antibacterial and free radical capturing (antioxidising) activities, the efficacy decreases substantially the darker the variety of tea. This is due to lower contents of anti-oxidising polyphenols remaining in the leaves. The polyphenols found in tea are more commonly known as flavanols or catechins and comprise 30-40 percent of the extractable solids of dried

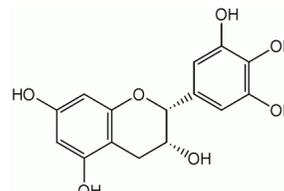
Active components present in Green tea



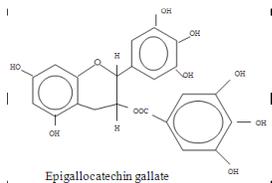
Phenylalanine



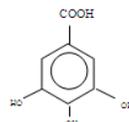
Epicatechin (EC)



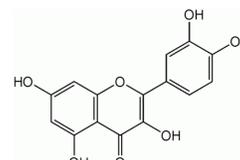
Epigallocatechin (EGC)



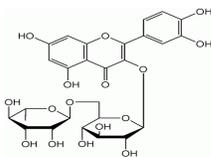
Epigallocatechin gallate



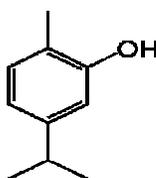
Quercetin



Rutin



Carvacrol



Geraniol

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 [13-20].

Pharmacological activities of green tea

Green tea has been extensively studied in people, animals, and laboratory experiments. Results from these studies suggest that green tea may be useful for the following health conditions.

Atherosclerosis

Population-based studies indicate that the antioxidant properties of green tea may help prevent atherosclerosis, particularly coronary artery disease. (Population-based studies means studies that follow large groups of people over time and/or studies that are comparing groups of people living in different cultures or with different dietary habits, etc.) In May 2006, however, the U.S. Food and Drug Administration (FDA) rejected a petition from teamakers to allow tea labels to claim that green tea reduces the risk of heart disease. The FDA concluded that there is no credible evidence to support qualified health claims for green tea or green tea extract reducing the risk of heart disease [21-25].

High cholesterol

Research shows that green tea lowers total cholesterol and raises HDL ("good") cholesterol in both animals and people.

One population-based study found that men who drink green tea are more likely to have lower total cholesterol than those who do not drink green tea. Results from one animal study suggest that polyphenols in green tea may block the intestinal absorption of cholesterol and promote its excretion from the body. In another small study of male smokers, researchers found that green tea significantly reduced blood levels of harmful LDL cholesterol [26-28].

Cancer

Several population-based studies have shown that green tea helps protect against cancer. For example, cancer rates tend to be low in countries such as Japan where people regularly consume green tea. However, it is not possible to determine from these population-based studies whether green tea actually prevents cancer in people. Emerging studies suggest that the polyphenols in green tea may play an important role in the prevention of cancer. Researchers also believe that polyphenols help kill cancerous cells and stop their progression [29-35].

Bladder cancer. Only a few studies have examined the relationship between bladder cancer and green tea consumption. In one study that compared people with and without bladder cancer, researchers found that women who drank black tea and powdered green tea were less likely to develop bladder cancer [36-41].

Breast cancer.

Studies in animals and test tubes suggest that polyphenols in green tea inhibit the growth of breast cancer cells. In one study of 472 women with various stages of breast cancer, researchers found that women who consumed the most green

tea experienced the least spread of cancer (particularly premenopausal women in the early stages of breast cancer). They also found that women with early stages of the disease who drank at least 5 cups of tea every day before being diagnosed with cancer were less likely to suffer recurrences of the disease after completion of treatment. However, women with late stages of breast cancer experienced little or no improvement from drinking green tea. In terms of breast cancer prevention, the studies are inconclusive. In one very large study from Japan, researchers found that drinking green tea was not associated with a reduced risk of breast cancer [41-44].

Ovarian cancer.

In a study conducted on ovarian cancer patients in China, researchers found that women who drank at least one cup of green tea per day survived longer with the disease than those who didn't drink green tea. In fact, those who drank the most tea, lived the longest [45-47].

Colorectal cancer.

Studies on the effects of green tea on colon or rectal cancer have produced conflicting results. Some studies show decreased risk in those who drink the tea, while others show increased risk. Further research is needed before researchers can recommend green tea for the prevention of colorectal cancer [48-49].

Esophageal cancer.

Studies in laboratory animals have found that green tea polyphenols inhibit the growth of esophageal cancer cells. However, studies in people have produced conflicting findings. For example, one large-scale population-based study found that green tea offered significant protection against the development of esophageal cancer (particularly among women). Another population-based study revealed just the opposite -- green tea consumption was associated with an increased risk of esophageal cancer. In fact, the stronger and hotter the tea, the greater the risk. Given these conflicting results, further research is needed before scientists can recommend green tea for the prevention of esophageal cancer [50-51].

Lung cancer.

While green tea polyphenols have been shown to inhibit the growth of human lung cancer cells in test tubes, few studies have investigated the link between green tea consumption and lung cancer in people and even these studies have been conflicting. One population-based study found that Okinawan tea (similar to green tea but partially fermented) was associated with decreased lung cancer risk, particularly among women. A second study revealed that green tea and black tea significantly increased the risk of lung cancer. As with colon and esophageal cancers, further studies are needed before researchers can draw any conclusions about green tea and lung cancer [52-53].

Pancreatic cancer.

In one large-scale study researchers compared green tea drinkers with non-drinkers and found that those who drank the most tea were significantly less likely to develop pancreatic cancer. This was particularly true for women -- those who drank the most green tea were half as likely to

develop pancreatic cancer as those who drank less tea. Men who drank the most tea were 37% less likely to develop pancreatic cancer. However, it is not clear from this population-based study whether green tea is solely responsible for reducing pancreatic cancer risk. Further studies in animals and people are needed before researchers can recommend green tea for the prevention of pancreatic cancer [54-55].

Prostate cancer.

Laboratory studies have found that green tea extracts prevent the growth of prostate cancer cells in test tubes. In a large study conducted in Southeast China researchers found that the risk of prostate cancer declined with increasing frequency, duration and quantity of green tea consumption. However, both green and black tea extracts also stimulated genes that cause cells to be less sensitive to chemotherapy drugs. Given this potential interaction, people should not drink black and green tea (as well as extracts of these teas) while receiving chemotherapy [56-58].

Skin cancer.

The main polyphenol in green tea is epigallocatechin gallate (EGCG). Scientific studies suggest that EGCG and green tea polyphenols have anti-inflammatory and anti-cancer properties that may help prevent the onset and growth of skin tumors [59-61].

Stomach cancer.

Laboratory studies have found that green tea polyphenols inhibit the growth of stomach cancer cells in test tubes, but studies in people have been less conclusive. In two studies that compared green tea drinkers with non-drinkers, researchers found that people who drank tea were about half as likely to develop stomach cancer and gastritis (inflammation of the stomach) as those who did not drink green tea. However, a study including more than 26,000 men and women in Japan found no association between green tea consumption and stomach cancer risk. Some studies even suggest that green tea may increase the risk of stomach cancer [62].

Inflammatory Bowel Disease (IBD)

Green tea may help reduce inflammation associated with Crohn's disease and ulcerative colitis, the two types of IBD. If green tea proves to be helpful for preventing colon cancer, this would be an added benefit for those with IBD because they are at risk for colon cancer [63-64].

Diabetes

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. People with type 1 diabetes produce little or no insulin, a hormone that converts glucose (sugar), starches, and other foods into energy needed for daily life. Green tea may help regulate glucose in the body [65].

Liver disease

Population-based studies have shown that men who drink more than 10 cups of green tea per day are less likely to develop disorders of the liver. Green tea also seems to protect the liver from the damaging effects of toxic

substances such as alcohol. Animal studies have shown that green tea helps protect against the development of liver tumors in mice.

Results from several animal and human studies suggest that one of the polyphenols present in green tea, known as catechin, may help treat viral hepatitis (inflammation of the liver from a virus). In these studies, catechin was isolated from green tea and used in very high concentrations. It is not clear whether green tea (which contains a lower concentration of catechins) confers these same benefits to people with hepatitis [66].

Weight loss

Studies suggest that green tea extract may boost metabolism and help burn fat. One study confirmed that the combination of green tea and caffeine improved weight loss and maintenance in overweight and moderately obese individuals. However, a second study found that weight maintenance following weight loss was not affected by green tea. Some researchers speculate that substances in green tea known as polyphenols, specifically the catechins, are responsible for the herb's fat-burning effect [67-68].

Interactions of Green tea [69].

If you are currently being treated with any of the following medications, you should not drink green tea or take green tea extract without first talking to your doctor:

Adenosine. Green tea may inhibit the actions of adenosine, a medication administered in a hospital setting for an irregular (and usually unstable) heart rhythm.

Antibiotics, beta-lactam. Green tea may increase the effectiveness of beta-lactam antibiotics by reducing bacterial resistance to treatment [70].

Aspirin . Green tea and aspirin should not be mixed because they both prevent platelets from clotting. Using the two together may increase your risk of bleeding.

Benzodiazepines. Caffeine (including caffeine from green tea) has been shown to reduce the sedative effects of benzodiazepines (medications commonly used to treat anxiety, such as diazepam and lorazepam).

Beta-blockers, propranolol and metoprolol. Caffeine (including caffeine from green tea) may increase blood pressure in people taking propranolol and metoprolol (medications used to treat high blood pressure and heart disease).

Blood Thinning Medications . People who take warfarin, a blood thinning medication, should not drink green tea. Since green tea contains vitamin K, it can make warfarin ineffective. (See also the aspirin listing, above.)

Chemotherapy. The combination of green tea and chemotherapy medications, specifically doxorubicin and tamoxifen, increased the effectiveness of these medications in laboratory tests. However, these results have not yet been demonstrated in studies on people. On the other hand, there have been reports of both green and black tea extracts stimulating a gene in prostate cancer cells that may cause them to be less sensitive to chemotherapy drugs. Given this potential interaction, people should not drink black and green tea (as well as extracts of these teas) while receiving chemotherapy for prostate cancer in particular.

Clozapine. The anti-psychotic effects of the medication clozapine may be reduced if taken less than 40 minutes after drinking green tea.

Ephedrine. When taken together with ephedrine, green tea may cause agitation, tremors, insomnia, and weight loss.

Lithium. Green tea has been shown to reduce blood levels of lithium (a medication used to treat manic/depression).

Monoamine oxidase inhibitors (MAOIs) . Green tea may cause a severe increase in blood pressure (called a "hypertensive crisis") when taken together with MAOIs used to treat depression. Examples of MAOIs include phenelzine and tranylcypromine.

Oral contraceptives. Oral contraceptives can prolong the amount of time caffeine stays in the body and may increase its stimulating effects.

Phenylpropanolamine. A combination of caffeine (including caffeine from green tea) and phenylpropanolamine (an ingredient used in many over-the-counter and prescription cough and cold medications and weight loss products) can cause mania and a severe increase in blood pressure. The FDA issued a public health advisory in November 2000 to warn people of the risk of bleeding in the brain from use of this medication and has strongly urged all manufacturers of this drug to remove it from the market.

CONCLUSION

Green tea extract helps decrease hormone activity and is an effective treatment for acne. Green tea leaf is anti bacterial, helps lower cholesterol, reduces inflammation, and lowers blood pressure. It also helps to prevent some forms of cancer including colon, pancreatic, and stomach cancer. Green tea extract stimulates the immune system, and also helps defend against dental plaque. Green tea extract also protects against liver damage. Some new research suggests green tea may help prevent liver transplant failure in patients.

Tea is a great immune enhancer that helps to boost our body's immune system and ward off germs and disease. Each type of tea has particular health components. Tea contains a variety of bioflavonoids that act as antioxidants? The antioxidants in tea have been shown more effective than vitamins C or E in protecting cells from damage by toxic compounds.

Scientific studies are finding that tea is rich in flavonoids- a plant substance that functions as an antioxidant to neutralize free radicals that can damage cells and lead to diseases such as heart disease and cancer. Researchers of a study published in the *Archives of Internal Medicine* (1995) reported that the flavonoids in tea may make blood cells less prone to clots that can cause heart attacks or strokes.

A number of epidemiological studies have suggested that green tea maybe protective against certain types of cancer, including lung ovarian, breast, prostate, stomach cancer and its precancerous condition, gastritis, the possible protective action of green tea is unclear, although a number of in vitro and animal studies are attempting to explain this. In addition to its potential anti-carcinogenic and antioxidant effects, other studies have shown green tea to have anti-inflammatory, antithrombotic, cholesterol lowering, antiviral and antibacterial properties.

REFERENCES

1. A. G. Dulloo, C. Duret and D. Rohrer. 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 Nutr.* **70**:1040-1045 (1999).
2. E. Ernst. The Desktop Guide to Complementary and Alternative Medicine: An Evidence-Based Approach. *Mosby, Edinburgh.* **4**: 119-121 (2001).
3. M. Blumenthal. The Complete German Commission E Monographs. Therapeutic Guide to Herbal Medicines, (Integrative Medicine Communications Boston 1998) pp 132.
4. M. Alic. Green tea for remission maintenance in Crohn's disease. *Am J Gastroenterol.* **94** (6):1710 (1999).
5. W. J. Craig. Health-promoting properties of common herbs. *Am J Clin Nutr.* **70**: 491-499 (1999).
6. J. Gruenwald, T. Brendler and C. Jaenicke. *PDR for Herbal Medicines*, (Medical Economics Company, Montvale, 2000) pp 369-372.
7. D.J. McKenna, K. Hughes and K. Jones. Green tea monograph. *Alt Ther.* **6**(3):61-84. (2000)
8. J. E. Robbers and V.E. Tyler. *Tyler's Herbs of Choice*, (The Haworth Herbal Press, New York, 1999) pp 249-250.
9. Y. Sadzuka, T. Sugiyama and S. Hirota. Modulation of cancer chemotherapy by green tea. *Clin Cancer Research.* **4**(1):153 – 156 (1998)
10. K. Nakachi, K. Suemasu, K. Suga, T. Takeo, K. Imai and Y. Higashi. Influence of drinking green tea on breast cancer malignancy among Japanese patients. *Journal of Cancer Research.* **89**(3): 254-261(1998).
11. C. Windridge. *The Fountain of Health. An A-Z of Traditional Chinese Medicine.* (Mainstream Publishing London, England 1994) pp 259.
12. N. Harold and P. D. Graham. Green tea composition, consumption and polyphenol chemistry. *Prev Med.* **21**:334-50 (1992).
13. L. Zhong. A population-based case-control study of lung cancer and green tea consumption among women living in Shanghai, China. *Epidemiology.* **12**(6): 695-700 (2001)
14. N. Ahmad, D. K. Feyes and A. L. Nieminen. Green tea constituent epigallocatechin-3-gallate and induction of apoptosis and cell cycle arrest in human carcinoma cells. *Journal of Cancer Research.* **89**:1881-1886 (1997).
15. S. K. Katiyar, M. S. Matsui, C. A. Elmetts and H. Mukhtar. Polyphenolic antioxidant (-)-epigallocatechin-3-gallate from green tea reduces UVB-induced inflammatory responses and infiltration of leukocytes in human skin. *PhotochemPhotobiol.* **69**:148-153 (1999).
16. R. Hofbauer, M. Frass and B. Gmeiner. The green tea extract epigallocatechin gallate is able to reduce neutrophil transmigration through monolayers of endothelial cells. *Wien Klin Wochenschr.* **111**: 276-282 (1999).
17. D. M. Smith and Q. P. Dou. Green tea polyphenol epigallocatechin inhibits DNA replication and consequently induces leukemia cell apoptosis. *Int. J. Mol. Med.* **7**(6): 645-652 (2001).
18. A.G. Dulloo, J. Seydoux and L. Girardier. Green tea and thermogenesis: interactions between catechin-polyphenols, caffeine, and sympathetic activity. *Int J. Obes Relat Metab Disord.* **24**: 252-258 (2000).
19. S. Samman, B. Sandstrom, M. B. Toff, K. Bukhave, M. Jensen, S. S. Sorensen and M. Hansen. Green tea extract added to foods reduces nonheme-iron absorption. *Am. J. Clin. Nutr.* **73**(3): 607-612 (2001).
20. L. Alschuler. Green Tea: Healing tonic. *Am J Natur Med.* **5**: 28-31 (1998).
21. J. M. Geleijnse L. J. Launer, A. Hofman H. A. Pols and J. C. M. Witteman. Tea flavonoids may protect against atherosclerosis: the Rotterdam study. *Arch Intern Med.* **159**:2170-2174 (1999).
22. S. Kono, K. Shintchi, N. Ikeda, F. Yanai and K. Imanishi. Green tea consumption and serum lipid profiles: a cross-sectional study in northern Kyushu, Japan. *Prev Med.* **21**(4):526-531 (1992).
23. W. Lee, W. K. Min, S. Chun, Y. W. Lee, H. Park, H. Lee, Y. K. Lee and J. E. Son. Long-term effects of green tea ingestion on atherosclerotic biological markers in smokers. *Clin Biochem.* **38**(1): 84-87 (2005).
24. Y. Miura, T. Chiba and I. Tomita. Tea catechins prevent the development of atherosclerosis in apolipoprotein E-deficient mice. *Am. J. Clin. Nutr.* **131**(1):27-32 (2001).
25. S. Sazuki, H. Kodama and K. Yoshimasu. Relation between green tea consumption and the severity of coronary atherosclerosis among Japanese men and women. *Ann. Epidemiol.* **10**: 401-408 (2000).
26. K. H. Van Het Hof, H. S. De Boer, S. A. Wiseman Lien, J. A. Weststrate and L. B. Tijburg. Consumption of green or black tea does not increase resistance of low-density lipoprotein to oxidation in humans. *Am J Clin Nutr.* **66**(5):1125-1132 (1997).
27. T. T. Koo and M. W. Yang. Hypocholesterolemic effects of Chinese tea. *Pharmacol Res.* **35**(6):505-512 (1997).
28. T. T. C. Yang and M. W. L. Koo. Chinese green tea lowers cholesterol level through an increase in fecal lipid excretion. *Life Sciences.* **66**(5): 411-423 (1999).
29. M. D. Brown. Green tea (*Camellia sinensis*) extract and its possible role in the prevention of cancer. *Alt Med Rev.* **4**(5): 360-370 (1999).
30. J. L. Bushman. Green tea and cancer in humans: a review of the literature. *Nutr Cancer* **31**(3):151-159 (1998).
31. E. Ernst and B. R. Cassileth. How useful are unconventional cancer treatments *Eur J Cancer.* **35**(11):1608-1613. (1999).
32. H. Fujiki, M. Sukanuma and S. Okabe. Cancer inhibition by green tea. *Mutation Research.* 307-310 (1998).
33. H. Fujiki, M. Sukanuma and S. Okabe. Mechanistic findings of green tea as cancer preventive for humans. *Proc Soc Exp Biol Med.* **220**(4): 225 – 228 (1999)
34. S. K. Katiyar and H. Mukhtar. Tea antioxidants in cancer chemoprevention. *J. Cell Biochem Suppl.* **27**: 59-67 (1997).
35. H. Mukhtar and N. Ahmad. Green tea in chemoprevention of cancer. *Toxicol Sci.* **52**(2): 111-117 (1999).
36. T. Sano and M. Sasako. Green tea and gastric cancer. *British Journal of Medicinal Chem.* **344**(9): 675-676 (2001).
37. M. Sukanuma, S. Okabe and N. Sueoka. Green tea and cancer chemoprevention. *Mutat Res.* **16**: 339-344 (1999).
38. M. J. Wargovich, C. Woods, D. M. Hollis, M. E. Zander. Cancer prevention and health. *Journal of Nature.* **131**(11): 303-306 (2001).
39. T. Yamane, H. Nakatani and N. Kikuoka. Inhibitory effects and toxicity of green tea polyphenols for gastrointestinal carcinogenesis. *Cancer Causes Control.* **77**(8 Suppl):1662-1667 (1996).
40. G. P. Yu, C. C. Hsieh, L. Y. Wang, S. Z. Yu, X. L. Li and T. H. Jin. Green-tea consumption and risk of stomach cancer: a population-based case-control study in Shanghai, China. *Cancer Causes Control.* **6**(6): 532-538 (1995).
41. Y. Ohno, K. Aoki, K. Obata and A. S. Morrison. Case-control study of urinary bladder cancer in metropolitan Nagoya. *Natl Cancer Inst Monogr.* **69**:229-234. (1985)
42. K. Imai, K. Suga and K. Nagachi. Cancer-preventive effects of drinking green tea among a Japanese population. *Prev Med.* **26**(6):769-775 (1997).
43. M. Inoue, K. Tajima and M. Mizutani. Regular consumption of green tea and the risk of breast cancer recurrence: follow-up study from the Hospital-based Epidemiologic Research Program at Aichi Cancer Center (HERPACC), Japan. *Cancer Lett.* **167**(2):175-182. (2001)
44. K. Nakachi, K. Suemasu, K. Suga, T. Takeo, K. Imai and Y. Higashi. Influence of drinking green tea on breast cancer malignancy among Japanese patients. *J Cancer Res.* **89**(3): 254-261 (1998).
45. M. Zhang, A. H. Lee, C. W. Binns and X. Xie. Green tea consumption enhances survival of epithelial ovarian cancer. *Int J Cancer.* **112**(3): 465-469 (2004).
46. J. R. Taylor and V. M. Wilt. Probable antagonism of warfarin by green tea. *Ann. Pharmacother.* **33**(4): 426 – 428 (1999).
47. T. Sugiyama and Y. Sadzuka. Enhancing effects of green tea components on the antitumor activity of adriamycin against M5076 ovarian sarcoma. *Cancer Lett.* **133**(1): 19 – 26 (1998).
48. B. T. Ji, W. H. Chow and A. W. Hsing. Green tea consumption and the risk of pancreatic and colorectal cancers. *Int J Cancer.* **70**:255-258 (1997).
49. U. Thatte, S. Bagadey and S. Dahanukar. Modulation of programmed cell death by medicinal plants. [Review]. *Cell Mol Biol.* **46**(1):199-214. (2000).
50. Y. Gao, J. K. McLaughlin and W. J. Blot. Reduced risk of esophageal cancer associated with green tea consumption. *J Natl Cancer Inst.* **86**(11): 855-8 (1994).
51. J. Hu, O. Nyren, A. Wolk and R. Bergstrom. Risk factors for oesophageal cancer in northeast China. *Int J Cancer.* **57**(1): 38-46 (1994).
52. Y. Ohno, K. Wakai and K. Genka. Tea consumption and lung cancer risk: a case-control study in Okinawa. *J Cancer Res.* **86**(11):1027-1034 (1995).
53. T. Sugiyama and Y. Sadzuka. Enhancing effects of green tea components on the antitumor activity of adriamycin against M5076 ovarian sarcoma. *Cancer Lett* **133**(1): 19 – 26 (1998).
54. B. D. Lyn-Cook, T. Rogers, Y. Yan, E. B. Blann, F. F. Kadlubar and G. J. Hammons. Chemopreventive effects of tea extracts and various components on human pancreatic and prostate tumor cells in vitro. *Journal of Nature.* **35**(1): 80-86 (1999).
55. J. H. Shim, M. G. Kang, Y. H. Kim, C. Roberts and I. P. Lee. Chemopreventive effect of green tea (*Camellia sinensis*) among cigarette smoke. *Cancer-Epidemiol-Biomarkers-Prev.* **4**(4): 387-91 (1995).
56. L. Jian, L. P. Xie, A. H. Lee and C. W. Binns. Protective effect of green tea against prostate cancer: a case-control study in southeast China. *Int J Cancer.* **108**(1): 130-135 (2004).
57. E. Kaegi. Unconventional Therapies for cancer: 2. Green tea. [Review]. The Task Force on Alternative Therapies of the Canadian Breast Cancer Research Initiative. *CMAJ.* **158**(8):1033-1035 (1998).
58. K. Wakai, Y. Ohno, K. Obata and K. Aoki. Prognostic significance of selected lifestyle factors in urinary bladder cancer. *J Cancer Res.* **84**(12): 1223-1229 (1993).
59. S. K. Katiyar, N. Ahmad and H. Mukhtar. Green tea and skin. *Arch Dermatol* **136**(8): 989-994 (2000).
60. Y. Kuroda and Y. Hara. Antimutagenic and anticarcinogenic activity of tea polyphenols. [Review]. *Mutat Res.* **436**(1): 69-97 (1999).
61. D. Picard. Biochemistry of green tea polyphenols and their potential application in human skin cancer. *Altern Med Rev.* **1**(1): 31-42 (1996).
62. F. Borrelli, R. Capasso, A. Russo and E. Ernst. Systematic review: green tea and gastrointestinal cancer risk. *Aliment Pharmacol Ther.* **19**(5): 497-510 (2004).
63. V. W. Setiawan, Z. F. Zhang and G. P. Yu. Protective effect of green tea on the risks of chronic gastritis and stomach cancer. *Int J Cancer.* **92**(4): 600-604 (2001).

64. Y. Tsubono, Y. Nishino and S. Komatsu. Green tea and the risk of gastric cancer in Japan. *Engl J Med*, **344(9)**: 632-636 (2001).
65. S. Luper. A review of plants used in the treatment of liver disease: part two. *Alt Med Rev*. **4(3)**: 178-188 (1999).
66. M. Luo, K. Kannar, M. L. Wahlqvist and R. C. O'Brien. Inhibition of LDL oxidation by green tea extract. *Lancet*. 360-361 (1997).
67. E. M. Kovacs, M. P. Lejeune, I. Nijs and M. S. Westerterp-Plantenga. Effects of green tea on weight maintenance after body-weight loss. *Journal of Nature*, **91(3)**: 431-437 (2004).
68. M. S. Westerterp-Plantenga, M. P. Lejeune and E. M. Kovacs. Body weight and weight maintenance in relation to habitual caffeine intake and green tea. *Obes Res*. **13(7)**:1195-1204 (2005)
69. F. Brinker. *Herb Contraindications and Drug Interactions*. 2nd edn. (Sandy, OR: Eclectic Medical Publications 1998) pp 126-129.
70. S. Shiota, M. Shimizu, T. Mizushima and H. Ito. Marked reduction in the minimum inhibitory concentration (MIC) of β -lactams in methicillin-resistant *Staphylococcus aureus* produced by epicatechin gallate, an ingredient of green tea (*Camellia sinensis*). *Biol. Pharm. Bull.* **22(12)**:1388-1390 (1999).