ejpmr, 2020,7(7), 262-269

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

SUPPLIMENTATION OF GREEN TEA EXTRACT RESULTS IN CURING VARIOUS AILMENTS

Ardra K.*, Nasiya N.[1], Jerrin Jose K.[1], Dr. Shijikumar P. S.[2], Dr. Sirajudheen M. K.[3] and Sherin A.[4]

[1]Department of Pharmacology, Jamia Salafiya Pharmacy College, Pulikkal, Malappuram, India-673637.
[2]Department of Pharmaceutical Analysis, Jamia Salafiya Pharmacy College, Pulikkal, Malappuram, India-673637.
[3]Department of Pharmaceutics, Jamia Salafiya Pharmacy College, Pulikkal, Malappuram, India-673637.
[4]Department of Pharmaceutical chemistry, Jamia Salafiya Pharmacy College, Pulikkal, Malappuram, India- 673637.

***Corresponding Author: Ardra K.**

Department of Pharmacology, Jamia Salafiya Pharmacy College, Pulikkal, Malappuram, India-673637.

Article Received on 10/05/2020 **Article Revised on 30/05/2020** **Article Accepted on 20/06/2020**

ABSTRACT

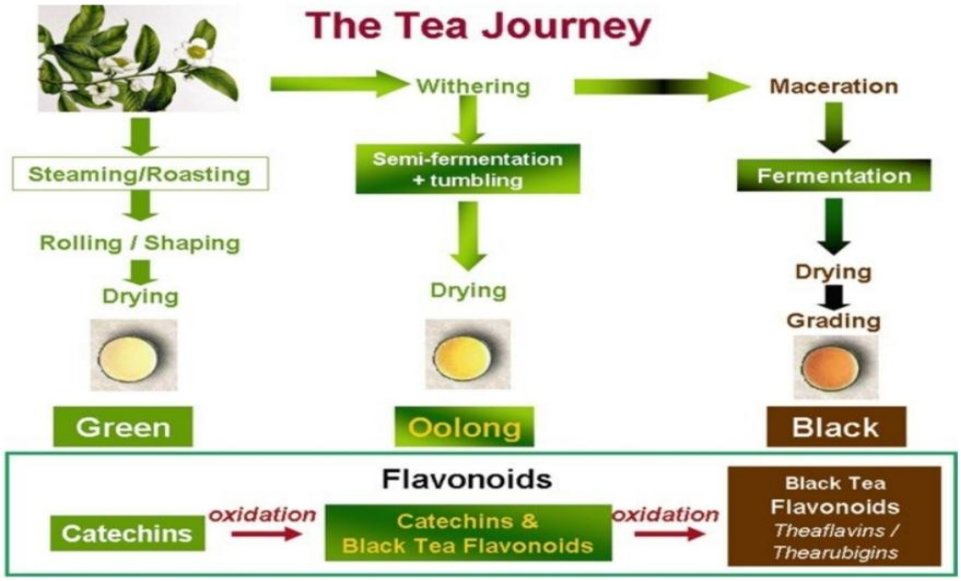
Green tea is a type of tea that is obtained from Camellia sinensis leaves and buds which have not undergone the same searing and oxidation process used to make teas. The health benefits of green tea for a variety of ailments including different types of cancer, heart diseases and liver diseases were reported. Many of these beneficial effects are related to it's polyphenols such as catechins, eespecially epigallocatechin-3-gallete content. There is good evidences from invitro studies that green tea catechin have role in protection against degenerative disorders. There are also human studies using green tea catechins to treat metabolic disorders like obesity, type 2 diabetes and cardiovascular risk factors. Generally studies show that green tea catechins could act as anti tumering agent and as immune modulator in immuno dysfunction. It has antiproliferative activity and hypolipidemic activity in hematoma cells and act as preventive agent in breast cancer. Long term consumption of tea catechin could be effective in suppression of fat diet induced obesity by modulation of lipid metabolism and also reduces so many risk factors. Further research that confirms to international standards should be done to monitor the Pharmacological as well as clinical effects of green tea and to elucidate it's mechanism of action.

KEYWORDS: Green tea extract, Polyphenols, Catechins, Health promotion.

INTRODUCTION

Tea is the most popular drinks consumed worldwide. Tea from the Camellia sinensis plant is consumed in different parts of the world as green, black or oolong tea.

Among all of these, however, the most significant human health effects from green tea consumption were observed.[1] Depending on the degree of oxidation, tea can be divided into three types, ie green tea (not oxidized). Oolong tea (partially oxidized) and black tea (oxidized).



The tea manufacturing process is intended to prevent or enable tea polyphenols to be oxidized by naturally occurring polyphenol oxidase in the tea leaves. Green tea is prepared by inactivating polyphenol oxidase in the fresh leaves either by burning or by steaming. This process prevents the enzymatic oxidation of catechins.[2,3]

The chemical composition of green tea is complex: proteins (15-20% dry weight), the enzymes of which make up an important part; Amino acids (1-4% dry weight) such as theanine or 5-N-ethylglutamine, glutamic acid, tryptophan, glycine, serine, aspartic acid, valine, thyrosine, leucine, arginine, and lysine; Carbohydrates (5-7% dry weight) such as cellulose, pectins, sucrose, glucose and fructose; Minerals and trace elements (5% dry weight) such as magnesium, calcium, chromium, manganese, iron, zinc, copper, molybdenum, selenium, phosphorus, strontium, cobalt, sodium, nickel, potassium, fluorine and aluminum; and trace amounts of lipids (linoleic acid and a-linolenic acid), sterols (stigmasterol), vitamins (B, C, E), xanthic bases (caffeine, theophylline), pigments (chlorophyll, carotenoids) and volatile compounds (aldehydes, alcohols), esters, Lactones, hydrocarbons). Due to the great importance of the mineral content in tea, many studies have determined the content of tea leaves and their infusions.[4] Fresh leaves contain an average of 3-4% of the alkaloids known as methylxanthines like caffeine, theobromine and theophylline. Phenolic acids such as gallic acids and characteristic amino acids such as theanine are also present.[5]

Green tea contains polyphenols, which include flavanols, flavanediols, flavonoids and phenolic acids. These compounds can make up up to 30% of the dry weight. Most green tea polyphenols (GTPs) are flavonols, commonly known as catechins. Products made from green tea are mainly extracts from green tea in liquid or powder form, the proportion of polyphenols (45-90%) and caffeine content (0.4-10%) varies. The main flavonoids of green tea are various catechins, which are found in larger amounts in green tea than in black or oolong tea [6]. The main catechins of green tea are (-) - epicatechin (EC), (-) - epicatechin -3-gallate (EKG), (-) - epigallocatechin (EGC) and (-) - epigallocatechin-3-gallate (EGCG).[2,3]

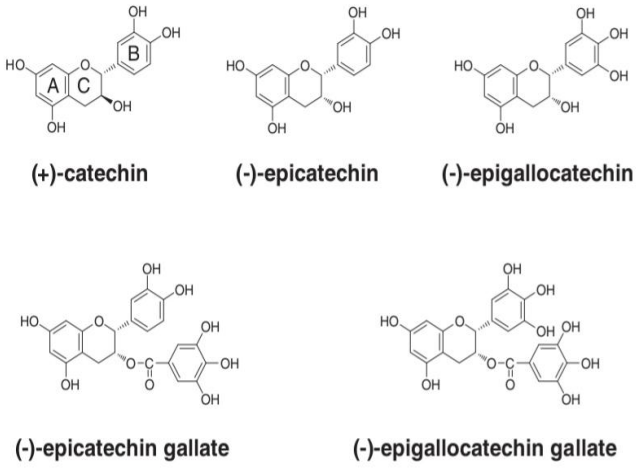


Fig. 1: Chemical structure of catechins. (!)-Epicatechin, (!)-epigallocatechin, (!)-epicatechin gallate and EGCG are major green tea catechins.

Catechins are polyphenol compounds with a diphenylpropane structure. The chemical structure consists of a polyphenol ring (A) that is condensed with a six-membered oxygen that contains a heterocyl ring (C) that bears another polyphenol ring (B) at position 2. Catechins are characterized by several hydroxyl groups on the A and B rings. EC is an epimer that contains two hydroxyl groups at the 3 'and 4' positions of the B ring and one hydroxyl group at the 3 'position of the C ring (Figure 1). The only structural difference between EGC and EC is that EGC has an additional hydroxyl group at the 5 'position of the B ring. EKG and EGCG are ester derivatives of ECh and EGC, respectively, by esterification at the 3-hydroxyl position of the C ring with a gallate unit.[7,8] In the production of black tea, freshly harvested leaves are naturally semi-dried before the withered leaves are rolled and crushed so that the polyphenol oxidase can catalyze the oxidation, which leads to the conversion of catechins into theaflavins and thearubigines.[9]

A typical tea drink made in a ratio of 1 g tea leaves to 100 ml boiling water in a 3 minute infusion usually contains 250-350 mg dry matter, which consists of 30-42% catechins and 3-6%% caffeine.[10] In green tea, catechins consist of 80% to 90% of total flavonoids, with EGCG being the most common catechin (48–55%), followed by EGC (9–12%), EKG (9–12%) and EK (5) - 7%).[11] The catechin content of green tea is influenced by various factors such as drying conditions, degree of fermentation, preparation of the infusion and decaffeination. The catechin content of black tea is only 20–30%, while theaflavine and thearubigine account for about 10 and 50–60% of the total flavonoids.[10] The bioavailability of green tea catechins in humans is an important variable for evaluating their biological activity in the target tissue. In humans, the catechin concentration in plasma was significantly increased 2 to 4 hours after consuming green tea.[12] However, the bioavailability of catechins is relatively low, with reports that plasma catechin concentrations (EGCG and EGC) only make up 0.2% to 2% of the amount ingested in healthy people.[13] The total catechin levels in plasma after taking a large single dose of green tea are between 0.6 and 1.8 μM.[14] A study comparing the pharmacokinetics of pure EGC, EKG and EGCG in healthy volunteers showed that the average peak plasma concentrations after taking 1.5 mM EGC, EKG and EGCG as a single bonus were 5.0 μM, 3.1 μM and 1, 3 μM were[15], indicating that the bioavailability differs significantly between catechins and that EGCG may be less bioavailable in humans than other green tea catechins. Evidence suggests that absorbed catechins are subject to extensive biotransformations, like methylation, glucuronidation, sulfation, and ring-cleavage metabolism.[7] More than 80% of the most important tea catechins occur as conjugates in plasma and urine. However, these conjugates still contain intact catechol and gallate units and can scavenge superoxide with the same potency as their parent compounds[8], suggesting that the antioxidant capacity of some catechin metabolites is similar to that of their parent compounds.[12] Even because of their low bioavailability, absorbed catechins can still be sufficient to have beneficial effects on cardiovascular parameters in vivo.[16]

Health benefits of green tea includes prevention of cancer, cardiovascular diseases, anti inflammatory, anti arthritic, anti angiogenic, anti viral,anti bacterial, anti oxidative, neuroprotective and cholesterol lowering effects.

Antioxidants are substances which significantly causes the distribution of free radicals- the reactive oxygen species leads to degenerative diseases. Secondary metabolites of shikimic acid pathway and phenylalanine propanoid metabolism such as phenols, tannins, flavonoids, challenges etc.... are the major plant antioxidants. Tea catechins are important antioxidants. Different studies revealed that catechin exert the antioxidant activity by scavenging ROS, chelating redox

transition-metal ions, inhibiting sensitive transcription factors and inducing antioxidant enzymes.

The second common type of infection found in any organ system and most common nosocomial infection is urinary tract infection. UTI results from the infection of Escherichia coli. Most of studies were accomplished on targeting the action of EGCG. But one study found that EG is responsible for the antimicrobial activity. It will bind to the ATP binding site of bacterial gyrase B subunit and inhibits the gyrase activity.

The effect of oral health are related to both teeth and gums. Bacteria Streptococcus mutants are the causative agent of dental caries. Green tea hasdurect antimicrobial effect on this bacteria, because it inhibit the attachment of the bacteria to oral surface. Green tea also have effects against gram negative and gram positive bacteria,some fungi,variety of virus and also act as a source of fluoride.

Rheumatoid arthritis is a chronic and complex autoimmune disease characterized by leukocyte infiltration and inflammation in the synovial membrane of joints. EGCG is an immunomodulatory polyphenol which have cartilage preserving and chondroprotective action. The disease modifying effects of green tea extract on various types of arthritis are studied on several aspects.

Green tea extract ingestion with or without caffeine promote weight loss. The anti obesity effects of GTE consumption may be attributed to elevated fat oxidation and total energy expenditure. There are so many investigations are going on the effect of GTE intake on up regulating fat metabolism at rest and during exercise in humans.

In developed and developing countries, one of the leading causes of death is lung cancer due to smoking tobacco products. Elimination of tobacco exposure is the major strategy to care or prevent lung cancer. There are some evidences from in vitro, animal and human trials that the possibilities of reduction in risk of lung cancer among smokers who consumed green tea.

Influenza virus prevalent worldwide during endemic or epidemic seasons. The recommended preventive measures includes pharmaceutical measures and non pharmaceutical measures. Some invitro studies have revealed that catechins show viral infectivity and proliferation by blocking it's absorption, hemagglutinatiom, viral assembly or maturation cleavage. In adults, Green tea consumption enhances systemic immunity and prevents cold and flu symptoms.

Malathion phoshorodithioate is an organophosphate pesticide used to control pest and to eliminate disease inducing arthropods. Malathion acts by inhibiting acetyl cholinesterase activity which leads to dysfunction of several organ system. Green tea is a potent neuroprotective in degenerative disease. At present the studies are going on to determine the amelioration property of green tea on hepatotoxicity during malathion induced oxidative stress in Male rat.

In past, studies were published on analysis of association between green tea consumption and cognitive functioning in humans. Studies reveal that green tea extract enhances the cognition as neuronal effects.

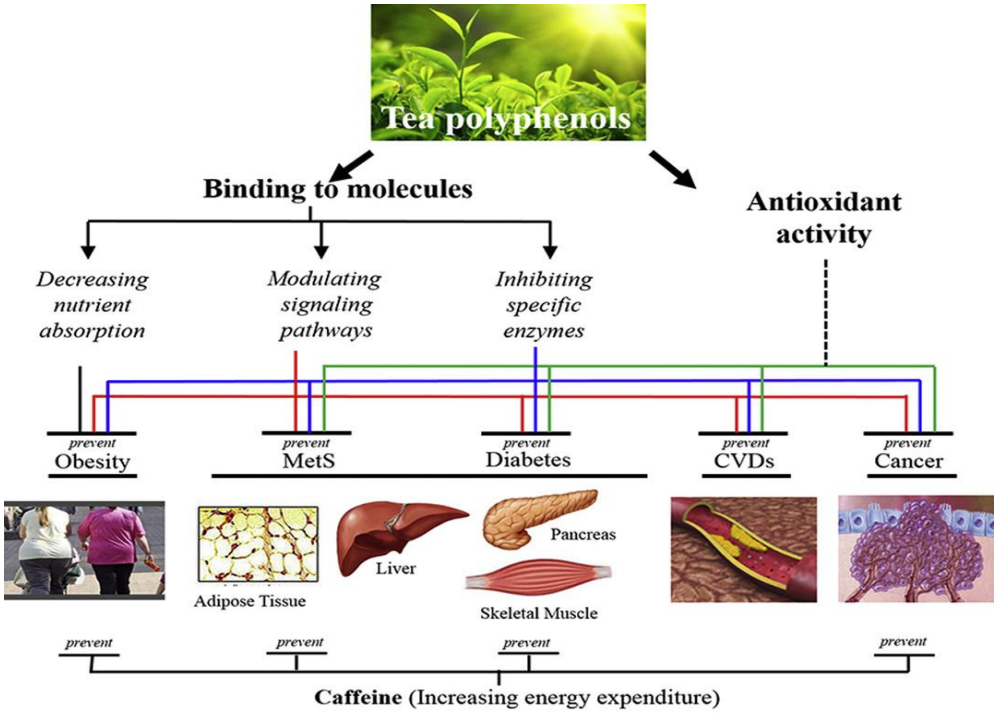
Diabetesmellitus and dyslipidemia are the two disease states with risk factors of atherosclerosis. Green tea catechins have properties to improve glycemic and lipid profiles in patients. The mechanism of action of catechin on glucose and lipid is still unclear. So the study is to investigate the effects of decaffeinated GTE on anthropometric measurements, glycemic and lipid profile as well as hormonal levels by a randomized, double blinded and placebo controlled clinical studies.

Although green tea has several positive health effects, the effects of green tea and its components up to a certain dose can be beneficial, but higher doses can have some unknown adverse effects. In addition, the effects of green tea catechins may not be the same for everyone. The EGCG of green tea extract is cytotoxic and higher consumption of green tea can cause acute cytotoxicity in the important metabolic organ in the body, liver.[17,18] Another study found that higher green tea intake could cause oxidative DNA damage to the pancreas and hamster liver. Yun et al.[19] clarified that EGCG acts in vivo in pancreatic B cells as a pro-oxidant rather than an antioxidant. Therefore, high intake of green tea can be harmful to diabetic animals to control hyperglycemia. At a high dose (5% of the food for 13 weeks) green tea extract induced an enlargement of the thyroid (goiter) in normal rats.[20] This high level treatment changed the plasma concentrations of thyroid hormones. However, drinking a very high amount of green tea through food is unlikely to cause these adverse effects in humans.

The deleterious effects of overconsumption of tea (black or green) can be attributed to three main factors: (1) its caffeine content, (2) the presence of aluminum and (3) the effects of tea polyphenols on the bioavailability of iron. Green tea should not be taken by patients suffering from heart disease or major cardiovascular problems. Pregnant and breastfeeding women should not drink more than one or two cups a day as caffeine can increase the heart rhythm. Because of the diuretic effects of caffeine, it is also important to control the simultaneous consumption of green tea and some drugs.[21] Some studies have shown that tea plants are able to accumulate a lot of aluminum. This aspect is important for patients with kidney failure, since aluminum can accumulate in the body, which leads to neurological diseases. It is therefore necessary to control food intake with high amounts of this metal. Green tea catechins can also have an affinity for iron, and green tea infusions can

significantly reduce the bioavailability of iron from food.[22]

DISCUSSION



Green tea effect on metal ions

Tea catechins can affect iron absorption, particularly in groups at risk of iron deficiency[23], but their effects on other ions are poorly understood. Green tea ingestion over a long period does not affect the apparent absorption of copper, whereas it decreases that of zinc and increases that of manganese. However, catechin intake does not affect the plasma concentration of these ions.[24]

Effect of green tea on fat oxidation

Some, but not all, studies have shown that chronic intake of green tea extract (GTE) with and without caffeine promotes weight loss.[15] It is outside the scope of this review to discuss evidence of GTE intake when losing weight [for a full review, see.[25] However, it is believed that the anti-obesity effects of GTE intake are due to increased fat oxidation and total energy consumption (EE). In addition, animal and in vitro findings have suggested a number of proposed mechanisms by which GTE alters fat metabolism such as GTE and catechol-O-methyltransferase inhibition.

Effects on antioxidant markers and oxidative stress

In vivo studies showed that green tea catechins increase the total antioxidative activity of the plasma.[26,27] The uptake of green tea extracts also increases the activity of the superoxide dismutase in the serum and the expression of the catalase in the aorta; These enzymes are involved in cellular protection against reactive oxygen species.[27,28] This effect is combined with a direct effect on oxygen species through a decrease in the nitrogen oxide plasma concentration.[29] Malondialdehyde, a marker for oxidative stress, also decreases after taking green tea. These results suggest that catechins may have a direct (antioxidant) or indirect (increase in activity or expression) effect.

Effect on lipid Profile

Green tea catechins influence fat metabolism through various mechanisms and prevent the occurrence of atherosclerotic plaque in various models of hyperlipidemia.[30,31] In addition, catechins influence micellular solubility, luminal lipid hydrolysis and intestinal lipid absorption.[32] In addition, catechins can up-regulate LDL receptor expression in the liver and thus modulate the biosynthesis, excretion and intracellular processing of lipids.[33,34] While it is unclear how catechins modulate the hepatic LDL receptor in vivo, one study suggests that this may be due to a decrease in liver cholesterol levels[39] as LDL receptor synthesis increases in response to decreased intracellular cholesterol levels is[35]., Tea catechins have been shown to lower blood cholesterol and prevent cholesterol accumulation in various tissues, including the liver and heart, in hypercholesterolemia rats.[36,37] In an in vitro study it was shown that EC, EGC, EKG or EGCG suppressed the intracellular lipid accumulation at 5 μM.[38]

Hepatoprotective effects

It is known that galactosamine causes liver damage in rats, the pathophysiology of which is similar to that of viral hepatitis and drug-induced hepatitis in humans. Rat

green tea has been shown to suppress galactosamine-induced hepatic damage and one of the active components has been identified as glycosidic flavonoids. In a study, intraperitoneal injection of galactose amine amine (500 mg / kg) induced liver damage with necrosis in rats and oral administration of green tea, which is rich in catechins, inhibited the effects of galactosamine. Green tea restored the values of several biomarkers to nearly control values in rats treated with Galactos amine.[40] These biomarkers included serum transaminase activities, serum concentrations of tumor necrosis factor (TNF) and interleukin 1-O as well as the hepatic mRNA expression of these inflammatory cytokines. The serum concentration in rats treated with green tea was approximately 55% of the rats untreated after galactosamine injection. Since apoptosis of liver cells is involved in galactosamine-induced liver damage and TNF- and induces apoptosis,[41] the modulation of TNF- appears to be a key effect of EGCG.

Effect in lung cancer among smokers

Carcinogens contained in cigarette smoke are activated by phase I enzymes in the body, which leads to the formation of DNA adducts. If DNA adducts escape the cellular repair mechanisms, this can lead to incorrect coding and ultimately to a stable mutation. Blocking a step on the way would reduce the incidence of lung cancer in smokers.[42] The evidence suggests that catechins in green tea, particularly EGCG, can prevent the formation of a mutated cell. In both animal and in vitro studies, green tea has been found to increase the activity of phase II enzymes.[43] Phase II enzymes convert carcinogens into non-toxic molecules for subsequent excretion. The amount of carcinogens that can be further activated and DNA adducts are thus reduced.

Anti diabetic effect

Increased gluconeogenesis is a major source of increased liver glucose production, and the ability of insulin to regulate the transcription of the rate-controlling gluconeogenic enzymes phosphoenolpyruvate carboxykinase (PEPCK) and glucose-6-phosphatase (G6Pase) can contribute to this problem.Recent results suggest that EGCG down-regulates gene expression of these gluconeogenic enzymes by reducing gene and protein expression of hepatocyte core factor (HNF) 4, an important transcription factor for PEPCK and G6Pase (Fig. 5). Insulin is known to decrease HNF4 protein expression, and therefore EGCG has an insulin-like property in this sense. EGCG also reduced the intestinal expression of these gluconeogenic enzymes in conjunction with the downregulation of HNF4 and HNF1.[44,45]

Effect on influenza infection

In vitro studies have mentioned that green tea catechins inhibit viral infectivity and proliferation by blocking adsorption, hemagglutination, virus assembly or cleavage.[46] However, among the non-pharmaceutical, preventive measures against influenza infections, only a few clinical studies have investigated the antiviral preventive effects of green tea catechins. A recent study reported that eating a particular formulation of tea extracts improves systemic immunity (gd-T cell function) and prevents cold and flu symptoms from occurring in healthy adults.[47]

Antibacterial effects

Many of the direct antibacterial effects of tea catechins result from the catechins binding to the bacterial lipid bilayer cell membrane, which then causes membrane damage. Damage to the bacterial cell membrane inhibits the ability of the bacteria to bind to host cells and inhibits the ability of the bacteria to bind to one another to form biofilms that are important for pathogenesis.[48] Damage to the bacterial membrane also means that the bacteria are unable to remove toxins.[49] Researchers have found that green tea components (especially EGCG) inhibit specific reductases (FabG, FabI) in bacterial type II fatty acid synthesis. It has also been found that the inhibition of fatty acid synthesis by green tea inhibits the bacterial production of toxic metabolites.[50] Green tea catechins inhibit protein tyrosine phosphatase and cysteine proteinases in certain anaerobic oral bacteria. Researchers have also found that green tea catechins have the ability to interfere with, and thereby inhibit, DNA replication by interacting with DNA gyrase.[51]

Antiplatelet activity of green tea

Catechins inhibit intracellular calcium mobilization by activating Ca2 + -ATPase and inhibiting inositol-1,4,5-triphosphate formation in human platelets, which leads to inhibition of fibrinogen-GPIIb / IIIa binding. Data from a recent study showed that EGCG also inhibits phospholipase Cγ2 phosphorylation, but increases prostaglandin D2 production. ECG and EGCG can reduce platelet activation factor (PAF) production by inhibiting acetyl-CoA: LysoPAF acetyltransferase, thereby reducing platelet stickiness and the likelihood of platelet aggregation.[52]

CONCLUSION

Modern scientific techniques have laid the foundation for the health benefits of green tea, which have been recognized since ancient times. Because clinical evidence for humans is still limited, future research needs to define the actual level of health benefits, determine the safe range of tea consumption associated with these benefits, and elucidate the mechanisms of action. Developing more specific and sensitive methods with more representative models, as well as developing good predictive biomarkers, will provide a better understanding of how green tea interacts with endogenous systems and other exogenous factors. The final conclusions on the protective effects of green tea have to be drawn from well-designed epidemiological observational and intervention studies. The development of biomarkers for the consumption of green tea as well as

molecular markers for its biological effects will facilitate future research in this area.

REFERENCES

1. Cabrera C, Artacho R, Giménez R: Beneficial effects of green tea: a review.J Am Coll Nutr, 2006; 25: 79-99.
2. McKay DL, Blumberg JB: The role of tea in human health: An update. J Am Coll Nutr, 2002; 21: 1-13.
3. Kavanagh KT, Hafer LJ, Kim DW, Mann KK, Sherr DH, Rogers AE, Sonenshein GE: Green tea extracts decrease carcinogen-induced mammary tumor burden in rats and rate of breast cancer cell proliferation in culture. J Cell Biochem, 2001; 82: 387-398.
4. Belitz DH, Grosch W: Quı'mica de los Alimentos Zaragoza: Acribia, 1997.
5. Graham HN: Green tea composition, consumption, and polyphenol chemistry. Prev Med, 1992; 21: 334-350.
6. Vinson JA: Black and green tea and heart disease: a review. Biofactors, 2000; 13: 127-132.
7. Khan N, Mukhtar H. Life Sci., 2007; 81: 519. [PubMed: 17655876]
8. Rice-Evans CA, Miller NJ, Paganga G. Free Radic Biol Med, 1996; 20: 933. [PubMed: 8743980]
9. Crespy V, Williamson G. J Nutr, 2004; 134: 3431S. [PubMed: 15570050] ences
10. Balentine DA, Wiseman SA, Bouwens LC. Crit Rev Food Sci Nutr, 1997; 37: 693. [PubMed: 9447270]
11. Shahidi F. Nahrung, 2000; 44: 158. [PubMed: 10907235]
12. Higdon JV, Frei B. Crit Rev Food Sci Nutr, 2003; 43: 89. [PubMed: 12587987]
13. Nakagawa K, Okuda S, Miyazawa T. Biosci Biotechnol Biochem, 1997; 61: 1981. [PubMed: 9438978]
14. Riemersma RA, Rice-Evans CA, Tyrrell RM, Clifford MN, Lean ME. QJM, 2001; 94: 277. [PubMed: 11353103]
15. Van Amelsvoort JM, Van Hof KH, Mathot JN, Mulder TP, Wiersma A, Tijburg LB. Xenobiotica, 2001; 31: 891. [PubMed: 11780763]
16. Erdman JW Jr, Balentine D, Arab L, Beecher G, Dwyer JT, Folts J, Harnly J, Hollman P, Keen CL, Mazza G, Messina M, Scalbert A, Vita J, Williamson G, Burrowes J. J Nutr, 2007; 137: 718S. [PubMed: 1731196]
17. Schmidt M, Schmitz HJ, Baumgart A, Guedon D, Netsch MI, Kreuter MH, Schmidlin CB, Schrenk D: Toxicity of green tea extracts and their constituents in rat hepatocytes in primary culture. Food Chem Toxicol, 2005; 43: 307-314.
18. Takabayashi F, Tahara S, Kanerko T, Harada N: Effect of green tea catechins on oxidative DNA damage of hamster pancreas and liver induced by N nitrosobis (2-oxopropyl) amine and/or oxidized soybean oil. Biofactors, 2004; 21: 335-337.
19. Yun SY, Kim SP, Song DK: Effects of (-)-epigallocatechin-3-gallate on pancreatic beta-cell damage in streptozotocin-induced diabetic rats. Eur J Pharmacol, 2006; 541: 115-121.
20. Sakamoto Y, Mikuriya H, Tayama K, Takahashi H, Nagasawa A, Yano N, Yuzawa K, Ogata A, Aoki N: Goitrogenic effects of green tea extract catechins by dietary administration in rats. Arch Toxicol, 2001; 75: 591-596.
21. Bruneton J: Pharmacognosie. Phytochimie. Plantes Me'dicinales Paris: Technique Documentation-Lavoisier, 2001.
22. Hamdaoui MH, Chabchob S, Heidhili A: Iron bioavailability and weight gains to iron-deficient rats fed a commonly consumed Tunisian meal "bean seeds ragout" with or without beef and with green or black tea decoction. J Trace Elem Med Biol, 2003; 17: 159-164.
23. Mandel S, Weinreb O, Amit T, Youdim MB: Cell signaling pathways in the neuroprotective actions of the green tea polyphenol(-)-epigallocatechin-3-gallate: implications for neurodegenerative diseases. J Neurochem, 2004; 88: 1555-1569.
24. Xiang YZ, Shang HC, Gao XM, Zhang BL: A comparison of the ancient use of ginseng in traditional Chinese medicine with modern pharmacological experiments and clinical trials. Phytother Res., 2008; 22(7): 851-858.
25. Rumpler W, Seale J, Clevidence B, Judd J, Wiley E, Yamamoto S, Komatsu T, Sawaki T, Ishikura Y, Hosoda K. Oolong tea increases metabolic rate and fat oxidation in men. J Nutr., 2001; 131: 2848–52.
26. Yokozawa T, Nakagawa T, Kitani K: Antioxidative activity of green tea polyphenol in cholesterol-fed rats. J Agric Food Chem, 2002; 50: 3549-3552.
27. Skrzydlewska E, Ostrowska J, Farbiszewski R, Michalak K: Protective effect of green tea against lipid peroxidation in the rat liver, blood serum and the brain. Phytomedicine, 2002; 9: 232-238.
28. Negishi H, Xu JW, Ikeda K, Njelekela M, Nara Y, Yamori Y: Black and green tea polyphenols attenuate blood pressure increases in stroke-prone spontaneously hypertensive rats. J Nutr, 2004; 134: 38-42.
29. Yokozawa T, Nakagawa T, Lee KI, Cho EJ, Terasawa K, Takeuchi S: Effects of green tea tannin on cisplatin-induced nephropathy in LLC-PK1 cells and rats. J Pharm Pharmacol, 1999; 51: 1325-1331.
30. Miura Y, Chiba T, Tomita I, Koizumi H, Miura S, Umegaki K, Hara Y, Ikeda M, Tomita T. J Nutr, 2001; 131: 27. [PubMed: 11208934]
31. Dhalla NS, Temsah RM, Netticadan T. J Hypertens, 2000; 18: 655. [PubMed: 10872549]
32. Koo SI, Noh SK. J Nutr Biochem, 2007; 18: 179. [PubMed: 17296491]
33. Stangl V, Lorenz M, Stangl K. Mol Nutr Food Res., 2006; 50: 218. [PubMed: 16404706]
34. Bursill CA, Roach PD. Lipids, 2007; 42: 621. [PubMed: 17582541]
35. Brown MS, Goldstein JL. Science, 1986; 232: 34. [PubMed: 3513311]

36. Babu PVA, Sabitha KE, Shyamaladevi CS. Clin Exp Pharmacol Physiol, 2006; 33: 1184. [PubMed: 17184499]
37. Yang TT, Koo MW. Pharmacol Res., 1997; 35: 505. [PubMed: 9356199]
38. Furuyashiki T, Nagayasu H, Aoki Y, Bessho H, Hashimoto T, Kanazawa K, Ashida H. Biosci Biotechnol Biochem, 2004; 68: 2353. [PubMed: 15564676]
39. Bursill CA, Roach PD. Lipids, 2007; 42: 621. [PubMed: 17582541]
40. American Heart Association. Heart and Stroke Statistical Update, 2000. 2001.
41. Okabe, S., Ochiai, Y., Aida, M., Park, K., Kim, S.J., Nomura, T., Suganuma, M. and Fujiki, H. (1999) Mechanistic aspects of green tea as a cancer preventive: effect of components on human stomach cancer cell lines. Jpn. J. Cancer Res., 90: 733-739.
42. Hecht SS. Tobacco smoke carcinogens and lung cancer. J Natl Cancer Inst., 1999; 91: 1194–210.
43. Khan SG, Katiyar SK, Agarwal R, Mukhtar H. Enhancement of antioxidant and phase II enzymes by oral feeding of green tea polyphenols in drinking water to SKH-1 hairless mice: possible role in cancer chemoprevention. Cancer Res., 1992; 52: 4050–2.
44. Wu, L.Y., Juan, C.C., Ho, L.T., Hsu, Y.P. and Hwang, L.S. (2004) Effect of green tea supplementation on insulin sensitivity in Sprague Dawley rats. J. Agric. Food Chem., 52: 643–648.
45. Waltner-Law, M.E., Wang, X.L., Law, B.K., Hall, R.K., Nawano, M. and Granner, D.K. (2002) Epigallocatechin gallate, a constituent of green tea, represses hepatic glucose production. J. Biol. Chem., 277: 34933–34940.
46. Nakayama M, Suzuki K, Toda M, Okubo S, Hara Y, Shimamura T. Inhibition of the infectivity of influenza virus by tea polyphenols. Antiviral Res., 1993; 21: 289–99.
47. Rowe CA, Nantz MP, Bukowski JF, Percival SS. Specific formulation of Camellia sinensis prevents cold and flu symptoms and enhances gamma, delta T cell function: a randomized, double-blind, placebo-controlled study. J Am Coll Nutr., 2007; 26: 445–52.
48. Blanco, A. R., Sudano-Roccaro, A., Spoto, G. C., Nostro, A., and Rusciano, D. (2005). Epigallocatechin gallate inhibits biofilm formation by ocular staphylococcal isolates. Antimicrob. Agents Chemother, 49: 4339–4343. doi: 10.1128/AAC.49.10.4339-4343.2005
49. Sugita-Konishi, Y., Hara-Kudo, Y., Amano, F., Okubo, T., Aoi, N., Iwaki, M., et al. (1999). Epigallocatechin gallate and gallocatechin gallate in green tea catechins inhibit extracellular release of vero toxin from enterohemorrhagic Escherichia coli O157:H7. Biochim. Biophys. Acta, 1472: 42–50. doi: 10.1016/S0304-4165(99)00102-6
50. Sakanaka, S., and Okada, Y. (2004). Inhibitory effects of green tea polyphenols on the production of a virulence factor of the periodontal-disease-causing anaerobic bacterium Porphyromonas gingivalis. J. Agric. Food Chem., 52: 1688–1692. doi: 10.1021/jf0302815
51. Chinnam, N., Dadi, P. K., Sabri, S. A., Ahmad, M., Kabir, M. A., and Ahmad, Z. (2010). Dietary bioflavonoids inhibit Escherichia coli ATP synthesis in a differential manner. Int. J. Biol. Macromol, 46: 478–486. doi: 10.1016/j.ijbiomac.2010.03.009
52. Sugatani J, Fukazawa N, Ujihara K, Yoshinari K, Abe I, Noguchi H, Miwa M. Int Arch Allergy Immunol, 2004; 134: 17. [PubMed: 15051936]