



A Comprehensive Review on Biological Activity of Green Tea (*Camellia sinensis*)

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Abstract

Green tea, the commonly consumed beverage, is gaining increased attention in promoting overall health. In specific, green tea is considered a healthful beverage due to the biological activity of its polyphenols namely catechins. The main green tea polyphenols are catechins: (±)-catechin C, (-)-epicatechin EC, (+)-gallocatechin GC, (-)-epigallocatechin EGC, (-)-epicatechin gallate ECG, and (-)-epigallocatechin gallate EGCG. Among the polyphenols Epigallocatechin 3 gallate and Epicatechin 3 Gallate are the most predominant catechins. There are also human studies on using green tea catechins to treat chronic diseases such as obesity, type II diabetes, and cardiovascular risk factors. Long-term consumption of tea catechins could be beneficial against high-fat diet-induced obesity and type II diabetes and could reduce the risk of coronary disease. Several epidemiological studies have proved that green tea also has some general health benefitting properties like anti-obesitive agent, anti-oxidant, anti-aging, anti-diabetic, anti-hyperlipidemic, anti-hypertension, anti-cancer, anti-bacterial, anti-viral, anti-inflammatory, anti-parkinson's effects, anti-alzheimer's effects, anti-arthritic, anticollagenase, and antimutagenic etc. The properties of these catechins proved to be helpful in the treatment of chronic diseases like obesity, aging, diabetes, cardiovascular disease, hyperlipidemic, hypertension, cancer, microbial, parkinson's, alzheimer's, arthritis, and periodontal disease. There are numerous studies in humans, animal models, and cell lines which provide the concepts for underlying functional mechanisms of green tea catechins and their biological actions and to suggest potential health benefits from the consumption of tea, including prevention of cancer and heart diseases. The review highlights also the potentials of green tea, its health benefits in terms of their properties. The present review concentrates on the effects of green tea on different chronic disease and general health.

Keywords: Green tea, Polyphenols, Epidemiological, Catechins, Animal models

Introduction

Green tea is one of the most widely consumed beverages in the world. The increasing health benefits of Green tea have led to the inclusion of tea extracts in dietary supplements and functional foods. Green tea (non-oxidized), Oolong tea (partially oxidized), and Black tea (oxidized), three major categories of tea obtained from the plant *Camellia sinensis* (L.) Kuntze, belonging to the family Theaceae, differ in terms of their manufacturing and chemical composition¹⁻³. Green tea have a different biological activities such as anti-obesity, antioxidant/anti-aging, anti-diabetic, anti hyperlipidemic, anti-hypertension, anti-cancer, anti-bacterial, anti-viral, anti Parkinson's, anti alzheimer's, anti-arthritic, and deodorant activity which may be primarily responsible for the human health benefits. Several studies have been reported the effect of green tea consumption on health enhancement and prevention of different disease like cardiovascular disease(hyperlipidemic, hypertension), different types of cancer, diabetes mellitus, parkinson's disease, alzheimer's disease, arthritis, and the periodontal disease. The green tea consists of polyphenols, caffeine, different Flavonoids which are antioxidant and vitamins etc which are responsible for their activity. These caffeine and catechins are effective in reduce of weight by stimulation of thermogenesis and increase of energy expenditure and anti oxidant effect of catechin in green tea are more than vitamins⁴. Flavonoids are effective in

reducing inflammation and having antibacterial effect to prevent dental caries. The active constitute in green tea also effect in weight loss to prevent diabetes mellitus and cardiovascular disease in the long term⁶. Effective active ingredients of green tea to inhibit the carcinogenic stimuli caused by ultraviolet radiation and carcinogenic chemicals and protection role against the different types of cancer like lungs, liver, pancreas, skin, breast, urinary bladder, colon, and small intestine etc⁷. The effect of chlorophyll has show deodorizing effect. Polyphenols in green tea increase the anti bacterial activity against periodontal pathogens which is increase ability of anti oxidant oral fluid to prevent periodontal health and decrease inflammation by creating an impenetrable layer with polysaccharide⁸. A powerful catechin (EGCG) in green and white teas, can directly kill bacteria and viruses, including the influenza virus and HIV-1^{9,10}. Antioxidants in green tea help prevent against cell damage in the brain, which could cause Parkinson's, and prevent it¹¹. Effect of active constitute of green tea to inhibition of enzyme acetylcholinesterase and β -amyloidosis and prevent to alzheimer's disease¹². In the present review, we will discuss the current knowledge of different biological activities of Green tea specially tea polyphenols derivatives with their different mechanisms.

Composition of green tea

The chemical composition of green tea is complex. The components are illustrated in Table of which the green tea polyphenols especially catechins are more important for human health¹³.

Table 1 Composition of green tea

Contents	% dry weight
Phenolic compounds	30
Proteins	15-20
Amino acids	1-4
Caffeine	4
Crude fiber	26
Carbohydrates	7
Lipids	7
Pigments	2
Minerals	5

Phenolic compounds: According to belitz the content of phenolic compounds are 25-35% of the dry matter content of young, fresh tea leaves. Flavanol compounds are 80% of the phenols, while the remainder is proanthocyanidins, phenolic acids, flavonols and flavones. (-)-Epigallocatechin gallate(9-13), (-)-Epigallocatechin(3-6), (-)-Epicatechin gallate(3-6), (-)-Epicatechin(1-3), (+)-Catechin(1-2), (+)-Gallocatechin(3-4) % of the dry matter content of young, fresh tea leaves are present in grand total of phenol. Changes in the content of the phenols occur during tea leaf growth on the shrub: the concentration decreases and the composition of this fraction is altered. Therefore, good quality tea is obtained only from young leaves¹³.

Catechins: The active compounds in green tea are from a group of polyphenols called catechins. There are four kinds of catechins mainly find in green tea: epicatechin, epigallocatechin, epicatechin-3-gallate, and EGCG¹⁴. The percentage of catechins out of total catechins content is illustrated in Table¹⁵.

Catechins	Percentage
(-)Epigallocatechin-3 gallate(EGCG)	59 of total catechins
(-) Epigallocatechin(EGC)	19
(-) Epicatechingallate(EGG)	13.6
(-) Epicatechin(EC)	6.4

Amino acids: The content of free amino acids are 1-3% of the dry matter of the tea leaf. Of this, 50% is theanine (5-N-ethylglutamine) and the rest consists of protein-forming amino acids; β -alanine is also present. The content of theanine in Green tea is more than black tea.

Caffeine: Caffeine in green tea is 2.5-5.5% of the dry matter of tea leaves. Taste of tea is responsible for it. Theobromine (0.07-0.17%) and theophylline (0.002-0.013%) are also preset but in very low amounts. The concentration of caffeine

in tea beverage is about one-third of that in ordinary brewed coffee.

Carbohydrates: Glucose (0.72%), fructose, sucrose, arabinose and ribose are sugars present in tea leaves, and Rhamnose and galactose are bound to glycosides. Polysaccharides found include cellulose, hemicelluloses and pectic substances. Inositol occurs also in tea leaves.

Lipids: Lipids are present in green tea at low levels such as 7% of dry matter of the tea leaf. The polar fraction (glycerophospholipids) in young tea leaves is predominant, while glycolipids predominate in older leaves.

Pigments (Chlorophyll and Carotenoids): pigments are present in green tea at low levels such as 2% of dry matter of the tea leaf. Chlorophyll is degraded during tea processing. In fermented leaves Chlorophyllides and pheophorbides (brownish in color) are present, both being converted to pheophytines (black) during the firing step. 14 carotenoids have been identified in tea leaves. The main carotenoids are xanthophylls, neoxanthin, violaxanthin and β -carotene.

Minerals: Tea contains about 5% minerals. The major element is potassium, which is half the total mineral content. Some tea varieties contain fluorine in higher amounts (0.015-0.03%)¹³. The other minerals are calcium, phosphorus, manganese, Fluoride, Sodium, Aluminium, Chromium, Iron, and Selenium are also present in green tea at a very low levels¹⁶. The fluorine content of tea is 100 to 300 ppm, which is higher than the level found in most other plants. Each cup of tea beverage can provide 0.5 to 0.8 mg of fluorine, approximately one-fifth of the daily fluorine requirement for humans.

Vitamins: Green tea has about 600 mg vitamin C and 80 mg vitamin E per 100 g of freshly dried leaves. Vitamin B₂, β -carotene and folic acid also present in green tea. Ordinary green tea beverage is made with about 2 to 4 g of tea leaves and about 100 ml to 200 ml of hot water. Most of these green tea constituents are soluble in hot water and are major components in tea beverage. The antioxidant effect of catechin in green tea is more than the vitamin C, E, tocopherol and carotene¹⁷.

Biological activities of green tea

Various biological activities with mechanisms of action have been proposed for the observed beneficial effects of green tea especially tea polyphenols derivatives, based on studies in various cell line systems, human and animal models.

Weight loss: Several studies have suggested that oral consumption of green tea may protect against obesity-related disorders such as arteriosclerosis, diabetes, and hypertension. Mechanisms of Green tea polyphenols, flavonoids, caffeine, catechins which is EGCG may decrease energy intake, increase energy expenditure (stimulation of thermogenesis), induced cytochrome c oxidase activity, direct inhibite the gastric and pancreatic lipases, reduced thiobarbituric acid reactive substances levels in soleus muscle, modulate energy metabolism in obese sunbjects and reduce adipose tissue mass and prevent or treat obesity and its associated diseases, diabetes and hypertension. In humans, the effects on body weight and body fat in response to supplementation with green tea catechins rich in EGCG were explored in several intervention studies, in which the investigators approached the topic from slightly different angles, as outlined below. Please refer to Table for a summary of the studies which will be reviewed.

Human studies assessing the effect of green tea extract

Biological Activity	Type of study	mechanism	Model/ Population	Test components (daily dosage)	Duration of intake	Main outcomes		
						Weight (kg)	Fat mass (kg)	BMI
Weight loss	randomized cross-over	induced cytochrome c oxidase activity and reduced thiobarbituric acid reactive substances levels in soleus muscle 99	48 obese male mice 5-week-old, and assigned to 4 groups	400 mg TT/kg diet, GTP at 0.5% vol/wt in water dosage in mice corresponds to 4-6 cups per day of tea equivalent in human consumption.	14 weeks	Only GTP supplementation (P=.010) significantly reduced body weight and no interaction between TT and GTP was observed (P>.05). Tocotrienols(TT) and GTP, individually or synergistically have the potential to improve skeletal muscle metabolism in obese mice by improving glucose homeostasis, reducing lipid peroxidation, and increasing rate limiting enzymes of oxidative phosphorylation.		
	single-blind, placebo controlled, parallel	stimulation of the9rmigenesis	84 male and female subjects GT group (n = 41) and C group (n = 43), 18-50 years, BMI values of 24 - 35 kg/m ²	< 2 tea bag/day or < 4 g loose tea/day	12 weeks	According to the intragroup analyses, the trend of changes from baseline to 12 weeks after intervention were significant in both groups (P = 0.001); BW (79.88 ± 7.06 to 72.44 ± 6.82 kg) and (80.21 ± 7.16 to 77.07 ± 7.22 kg) , BMI (29.95 ± 1.79 to 26.86 ± 2.59 kg/m) and (29.69 ± 2.1 to 27.07 ± 2.22 kg/m) , waist circumference (87.77±6.06 to 83.913 ± 6.13 cm) and (86.94 ± 8.05 to 85.23 ± 7.89 cm), and hip circumference (102.41 ± 7.35 to 98.3 ± 7.54 cm) and (101.02 ± 8.47 to 99.31 ± 8.81 cm) in GT and C groups, respectively.		
	Controlled	BTPs increased pAMPK through increased SCFA production, GTPs increased AMPK in liver tissue	C57BL/6j mice	Average polyphenol consumption was 240 and 320 mg per kg body weight for mice fed decaffeinated GTP and BTP respectively	4 weeks	Testing period on 4 groups of mice: high-fat/high-sucrose (HF/HS), HF/HS + GTP or BTP, and low fat/high-sucroseGTP and BTP significantly induced weight loss. GTP and BTP induced significant increase in AMPK phosphorylation by 70 and 289% respectively		
	Controlled	modulate energy metabolism in high-fat fed obese mice.	Six-week-old 48 male C57BL/6 mice	FGT (500 mg/kg; dissolved in 0.1% methylcellulose) with HFD	8 weeks	FGT induced changes in the composition of the gut microbiota. These changes may be the mechanism responsible for the FGT-induced reduction in body		

						weight gain and fat mass and improvement of glucose intolerance and fatty liver symptoms in HFD-fed obese mice.		
	Randomized, double-blind, placebo controlled	stimulation of thermogenesis and promote fat oxidant	23 M, 23 F BMI: 32.8 ±2.5 kg/m ² Age: 50.4 ± 8.3	Placebo treatment (one capsule, cellulose) Green tea extracts (one capsule, 379 mg catechins, whereof 208 mg was EGCG)	12 weeks	-	-0.67	-0.27
	single-center, placebocontrolled, double blind	lowers blood pressure and improves biomarkers of metabolic function in sedentary and overweight or obese men. The potential modifying effect of the COMT Val/Met genotype was also examined.	70 M BMI: 31.6 ±2.6 kg/m ² Age: 49.4 ± 5.6 years	Placebo treatment (two capsules, 1898 mg lactose) Decaffeinated green tea extracts (two capsules, 800 mg catechins, whereof 400 mg was EGCG and caffeine was 010 mg)	6 weeks	-1.17	-	-

Antioxidant/ Anti-Aging: Results of numerous investigations have confirmed that flavonols isolated from green, black and red tea leaves possess very strong antioxidant proprieties. The antioxidants in green tea have free radical- scavenging activities. Free radical mediated damage to DNA has been found in different cancer tissues. Antioxidants in green tea protect the skin from the harmful effects of free radicals, which cause wrinkling and skin aging. Mechanisms of Green tea which are to reduced oxidative DNA damage, blood

antioxidant, enhanced fatty acid oxidation, and enhanced biosynthesis of mitochondria, lower hippocampus reactive oxygen species concentrations, stimulation of thermogenesis, promote fat oxidant, inhibited LDL oxidation and elevated serum antioxidative activity to reduce the risk of different disease like cancer, cardiovascular disease, diabetes, hyperlipidemic etc. Several intervention studies are illustrated in Table.

Biological Activity	Type of study	mechanism	Model/ Population	Test components (daily dosage)	Duration of intake	Main outcomes
Antioxidant/ Anti aging	Pilot study-randomized, placebo, controlled	blood antioxidant	16 young males involved in CrossFit training	GTE capsule contained 250 mg of standardized green tea extract (245 mg polyphenols, including 200 mg catechins, among them 137 mg epigallocatechin-3-galate and additional substances such as caffeine < 4 mg, microcrystalline cellulose, and magnesium stearate).	6 weeks	consumption of GTE had marginal effect on aerobic capacity and serum BDNF level in CrossFit-trained men, but it caused a marked increase in the blood antioxidant capacity and a moderate attenuation of the training-induced lipid peroxidation
	Randomized, Double-Blind, Placebo-Controlled,	reduced oxidative DNA damage	10 obese men (age 37.12 ± 5.66 y; height 177	GTE (2 capsules per day)-250 mg GTE gelatin capsules r. One GTE capsule (55%	14 days	GTE supplementation significantly reduced oxidative DNA damage as measured by 8-OHdG after resistance exercise (RE)compared to PL (P < 0.05),

	Crossover		± 7.7 cm; BMI 32.53 ± 2.52)	EGCG) composed of 249 mg polyphenols which contain 200 mg catechins (137.5 mg EGCG)		and prevented oxidative DNA damage induced by RE in untrained obese men. However, the potential effects of GTE on oxidative stress after RE in obese people warrants further investigation.
	controlled	OTP + HFD group changed expression levels of PPARs, enhanced fatty acid oxidation, and enhanced biosynthesis of mitochondria in visceral WAT.	30 Eight-week-old male Sprague-Dawley (SD) rats is divided into 3 groups : LFD; HFD; HFD + OTP	Oxidized tea polyphenols (OTP) Diet containing 2% OTP.	12 weeks	decreased reduction of weight in the visceral white adipose, enhanced regulation of fatty acid β-oxidation by PPARα and enhanced biosynthesis of mitochondria in the visceral white adipose of the OTP rats compared with the HFD rats. Additionally, OTPs promoted the excretion of lipids

Anti diabetic: Green tea may protect against the development of long-term complications of diabetes. The underlying mechanisms and pathways by which green tea catechins could potentially improve glucose haemostasis have been explored in in vitro and animal based studies. The reduction of carbohydrate absorption by inhibition of various digestive enzymes is of considerable interest in the prevention of diabetes. . It has been shown that green tea catechins reduced

the blood glucose levels by intestinal glucose glucose absorption, regenerated -cells to release more insulin from pancreas, LDL oxidation inhibit, Prooxidative effects, Glucose oxidase, and insulin-stimulated glucose uptake of adipocytes etc. Overall, the harmonizing effects of green tea catechins on disorders of glucose metabolism implicated in type-2 diabetes seem to be mediated by various mechanisms are illustrated in table.

Biological Activity	Type of study	mechanism	Model/ Population	Test components (daily dosage)	Duration of intake	Main outcomes
Anti diabetic	Controlled	reduced the blood glucose levels by intestinal glucose absorption, regenerated -cells to release more insulin from pancreas	42 Male Rats (200-220 g b wt.) (30 diabetic surviving and 12 normal)	Control (water) GTE (300 mg/kg b.wt.)	30 days	Significant reduction in the levels of plasma glucose, glycosylated hemoglobin (HbA1c) and increase in the levels of insulin and hemoglobin.
Anti diabetic/ Anti hyperlipidemic/ Antioxidant	Controlled	reduced the blood glucose levels by intestinal glucose absorption, LDL oxidation inhibit, promote fat oxidant	28 Male albino Wistar rats, 250-300 g	EGCG 25 mg/kg/day	8 weeks	EGCG produced a hypoglycemic effect and there were appropriate changes regarding serum lipids in treated diabetic group. EGCG produced a hypoglycemic effect and there were appropriate changes regarding serum lipids in treated diabetic group.
	Controlled	regenerated -cells to release more insulin from	22 healthy subjects	Control (water) 1.5 g Green tea powder (84 mg EGCG) after an oral glucose	Single administration	Plasma glucose was significantly reduced after an OGTT

		pancreas				
	Controlled	reduced the blood glucose levels by intestinal glucose absorption	18 Male rats (250/300 g b wt.)	Control (water) 250 g Green tea powder (50,100 mg/kg b.wt. GTP) after an oral glucose	18 days, Single administration	alloxan treatment the percent reduction in serum glucose was 44.1%. Blood glucose levels in the control (alloxan treated) and normal (alloxan non-treated) group was remained unchanged over this period

In Cardiovascular disease (Anti hyperlipidemic/Anti hypertension): several studies suggest that drinking green tea may protect against cardiovascular diseases. The protective effect of green tea in cardiovascular diseases is also thought to stem from its antioxidant activity. The green tea extract administered in drinking water by human volunteers increased resistance of plasma LDL to oxidation *in vivo*, an effect that may lower the risk of arterogenesis. Green tea

prevents heart disease and stroke by lowering the level of cholesterol. Even after heart attack, it prevents cell deaths and speeds up the recovery of heart cells. The Green tea extract also attenuated blood pressure increases in spontaneously hypertensive rats, an effect attributed to its antioxidant properties. Green tea help to blood pressure down by repressing angiotensin, which leads to high blood pressure. Several investigated studies are summarized in below Table.

Biological Activity	Type of study	mechanism	Model/ Population	Test components (daily dosage)	Duration of intake	Main outcomes
In Cardiovascular disease (Anti hyperlipidemic, Anti hypertension)	Controlled	LDL oxidation inhibite	50 male rats aged six weeks with (200±10 g b wt.) - treated with GTE (group-D 10 M rats)	GTE -100 mg/kg/day	56 days	In group (D), total cholesterol, LDLc, HDLc, and triglyceride levels were significantly decreased by 33.3%, 30.2%, 40%. The extract of green tea has a hyperlipidemic lowering effect.
	Randomized, parallel, doubleblind, placebo controlled	LDL oxidation inhibite	Participants: 100 BMI: > 27	Placebo [1200 mg cellulose] GT 1200 mg [491 mg catechins (302 mg EGCG)]	12 weeks	GT consumer slightly reduces body weight and body fat, whereas significant reduces LDH-cholesterol and triglyceride levels.
	Randomized doubleblind parallel multicenter trial	LDL oxidation inhibite	140-M and 100-F obese, BMI- 24 to 30 kg/m ²	583 mg of catechins (catechin group) or 96 mg of catechins (control group)	12-weeks	Reduces body fat, cholesterol levels, and blood pressure in women and men. The ingestion of a GTE high in catechins might prevent obesity and decrease the risk of cardiovascular disease
	Randomized, doubleblind, placebocontrolled, parallel	LDL oxidation inhibite	240 M and F	Green tea extract (375 mg)	12 weeks	Reduce LDL- C in hypercholesterolemic adults

Anti-Cancer: Green tea is used in cancer prevention due to induced apoptosis increases normal cell growth while promoting programmed cell death *Chaun Xu et al.(2007)*. Green tea catechins which is EGCG has been shown to inhibit angiogenesis of tumor cell thus not allowing them to become cancerous. This is achieved by stopping the production of

angiogenic compounds in the tumor cells. Several studied show that the Green tea Inhibite of COMT in rats, inhibited the growth of all HCC cell lines in mice, Monoclonal antibody inhibition in mice, Lipid peroxidation, and antioxidation which are mechanisms to help for prevent and treat of cancer in human and animal models are illustrated in Table.

Biological Activity	Type of study	mechanism	Model/ Population	Test components (daily dosage)	Duration of intake	Main outcomes	Ref. articles/ year
Anti-cancer	Synergistic Anticancer Activity of Curcumin and Catechin:	curcumin and catechin in combination can inhibit the proliferation of HCT 15, HCT 116, as well as Hep G-2 cells efficiently through induction of apoptosis	HCT 15, HCT 116 (human colon adenocarcinoma cells), and Hep G-2 (human larynx cancer cells)	curcumin (50 IM), catechin (50 IM), and combination of both (50 IM and 25 IM, respectively)	incubated for 48 h	In the cytotoxicity assay the combination of both curcumin and catechin, destruction of monolayer was observed significantly when compared to the untreated cells, cell lines exhibited increased chromatin fluorescence, condensed nuclear morphology, and changes of DNA fragmentation. The anticancer activity shown is due to cytotoxicity, nuclear fragmentation as well as condensation, and DNA fragmentation associated with the appearance of apoptosis.	Manikandan et al. (2011)
	Controlled	Apoptosis	y Kunming male mice (SPF grade) with body weight between 24 and 26 g, 5 group 10 mice each.	Control Saline solution i.g. (0-18 days) + DMSO i.p. (6-18 days) II MC-LR Saline solution i.g. (0-18 days) + MC-LR 10g/kg i.p. (6-18 days) III MC-LR + GTP50 GTP 50 mg/kg i.g. (0-18 days) + MC-LR 10g/kg i.p. (6-18 days) IV MC-LR + GTP100 GTP 100 mg/kg i.g. (0-18 days) + MC-LR 10g/kg i.p. (6-18 days) V MC-LR + GTP200 GTP 200 mg/kg i.g. (0-18 days) + MC-LR 10g/kg i.p. (6-18 days)	18 days	The first time that tea polyphenols possess potent preventive effects against MC-LR-induced hepatotoxicity through modulating aforementioned biochemical mediators to block or reverse cell damages. Taking into consideration that metabolism of MCs and GTP is the same in animals as in human being, GTP could be novel compounds to be developed as chemoprotectant against MCs-induced liver injury.	Chaun Xu et al. (2007)
	Controlled	inhibited the growth of all HCC cell lines	20 nude mice	Purified EGCG (50-100 µg/ml)	24-96 h	EGCG inhibited the growth of all HCC cell lines. Oral administration of EGCG showed similar effects in HLE xenograft tumors and it enhanced TRAIL induced apoptosis.	Nishikawa et al. (2006)

Anti-bacterial/Anti viral: There are numerous studies on the antimicrobial activity of tea extracts, catechins and other polyphenols. Green tea catechins especially EGCG, a powerful catechin antioxidant found in green and white teas, can directly kill bacteria and viruses, including the influenza virus and HIV virus. Catechins are found to be inhibitory against *Streptococcus mutans* and *Streptococcus sobrin* at minimum inhibitory concentration (MIC) ranging between 50-1000 µg/ml. Green tea Inhibite the growth of multi-drug resistant (MDR) pathogens, inhibite the growth of MBL

(Metallo-β-lactamase) producing bacteria was drastically reduced when used in combination with GTE, inhibit varieties of pathogenic bacterial growth cause inflammation. Tea leaves flavonoids show also germicidal and antiviral proprieties. It was stated that both green and black tea leaves components damage bacteria's cellular membrane. Green tea also inhibit HIV-1 replication into host DNA and linhibitors of influenza virus replication in MDCK cell culture, and it also suppressed viral RNA synthesis in MDCK cells which are illustrated in Table

Biological Activity	Type of Study	Bacteria/Virus	mechanism	Test components	Main outcomes
Anti-bacterial/ Anti viral	GTE and synergistic effects of epigallocatechingallate (EGCG) with gentamicin against MDR pathogens	Multi-drug resistant (MDR) pathogens - Gram positive and Gram negative pathogens. <i>Staphylococcus aureus</i> and <i>Escherichia coli</i>	Inhibite the growth of multi-drug resistant (MDR) pathogens	Concentrations of EGCG extracts ranged from 4.75 µg/mL to 2500 µg/mL	MIC value of green tea extract was found at 125 µg/mL in case of MDR <i>E. coli</i> , MDR <i>S. aureus</i> and their reference strains and MBC at 500 µg/mL against <i>S. aureus</i> . No MBC value was found against <i>E. coli</i> . EGCG showed better activity on Gram positive pathogen compared to that of Gram negative. MBC value of this compound was 1250 µg/mL for <i>E. coli</i> where 625 µg/mL for <i>S. aureus</i> . Strong synergistic relation (FICI 0.325) was found against pathogens in the combination of EGCG with gentamicin
Anti-bacterial/ Anti viral/ anti inflammatory	Cariogenic bacteria study	20 strains of each of bacteria like <i>Actinomyces</i> , <i>actinomycetemcomitans</i> <i>p. gingivalis</i> , <i>Prevotella intermedia</i> , <i>Streptococcus mutans</i>	inhibit varieties of pathogenic bacterial growth cause inflammation	GTE (50mg/ml)-stock solution	MIC of green tea extract for <i>S. mutans</i> was 3.28 ± 0.7 mg/ml and for <i>A. actinomycetemcomitans</i> 6.25, for <i>P. gingivalis</i> and <i>P. intermedia</i> 12.5 mg/ml. green tea extract exhibited strong antibacterial activity on <i>S. mutans</i> , <i>A. actinomycetemcomitans</i> , <i>P. gingivalis</i> and <i>P. intermedia</i> to prevention of dental caries and periodontal diseses.
	time-of-addition	HIV (HIV-1(IIIB) and HIV-2(EHO))	inhibit HIV-1 replicatio into host DNA	EC50 (EGCG) = 1.6~2.0 µM	EGCG suppressed both HIV-1(IIIB) and HIV-2(EHO) infection in HeLa-CD4-LTR-β-gal cells, with relatively low 50% effective concentrations of 1.6 and 2.0 µM. EGCG appears to act mainly as an allosteric reverse transcriptase inhibitor that directly interact with the non-nucleoside reverse transcriptase inhibitor binding pocket. Furthermore, synergistic inhibition was observed in EGCG with AZT(3'-azido-3'-deoxythymidine).
	Influenza virus	Influenza A/Chile/1/83 (H1N1),	linhibitors of influenza	EC50 (EGCG) = 22-28 µM,	Activity reduction of viral neuraminidase and RNA

		A/Sydney/5/97 (H3N2) and B/Yamagata/16/88	virus replication in MDCK cell culture, and it also suppressed viral RNA synthesis in MDCK cells	EC50 (EGC) = 22–40 μM, EC50 (EGC) = 309–318 μM,	synthesis of viral genome- The 50% effective inhibition concentration (EC50) of EGCG, ECG, and EGC for influenza A virus were 22–28, 22–40 and 309–318M, respectively. EGCG and ECG exhibited hemagglutination inhibition activity, EGCG being more effective.
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Anti-inflammatory: There are numerous studies on the anti-inflammatory activity of tea extracts, catechins and other polyphenols. Green tea catechins were reported to be effective also in preventing gingival and periodontal inflammation. Green tea catechins help to reduce inflammation by blocking nuclear factor-kB activation in rats. Green tea polyphenols and

Low EGCG improved antioxidants pools, decreased inflammatory cytokines. Green tea (20% and 10%) showed an inhibition of 71.7% and 50%, respectively, in comparison to the standard drug indomethacin that showed an inhibition of 98.3%. Several studies are summarized below in Table.

	Controlled	by blocking nuclear factor-kB activation	Male Wistar rats (n = 16, 230–245 g), 2 groups	All animals received AOM (15 mg/kg body wt ip) once each week for two weeks. The rats were randomly divided into two groups, which received the same isoenergetic diet . This diet contained 13.5% proteins as casein and fish protein, 62% carbohydrates as wheat starch, 3% lipids as soya and fish oil, 6% salt mixture, and 1% vitamin mixture.	6 weeks	Polyphenols exhibit anti-inflammatory action in several experimental models. An antioxidant-rich polyphenolic fraction isolated from green tea has been shown to possess anti-inflammatory properties on collagen-induced arthritis in mice . The flavonoid oroxylin A has been shown to inhibit COX-2 gene expression in macrophages by blocking nuclear factor-kB activation	Nadia Metz et al. (2000)
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Anti-Parkinson's /Anti-Alzheimer's: Antioxidants in green tea help prevent against cell damage in the brain, which could cause Parkinson's, and thus prevent it. Parkinson's disease is a progressive, degenerative disorder of the central nervous system, resulting from the loss of dopamine-producing brain cells, and there is presently no cure. Certain researchers have indicated that green tea possesses neuroprotective effects, suggesting its role in the prevention of Parkinson's disease. Oxidative stress is believed to be a major contributor to the pathogenesis of Parkinson's disease, especially the death of dopaminergic neurons. Various studies have shown that green tea catechins especially EGCG significantly prevent these

pathologies in Human and animal models are illustrated below in Table. Green tea has a primary target for treatment of Alzheimer's disease is inhibition of enzyme acetylcholinesterase and β-amyloidosis. In an in vitro study, it was found that green tea inhibited acetylcholinesterase in rats. Thus the inhibitory effect of green tea catechins on Alzheimer's disease targets and the neuroprotective effect of their antioxidative activity strongly suggest that these catechins have potential application in the treatment of Alzheimer's disease. All the investigated studies are summarized in Table.

Biological Activity	Type of study	mechanism	Model/ Population	Test components (daily dosage)	Duration of intake	Main outcomes
Anti-Parkinson's /Anti-Alzheimer's	sham-operated Controlled	oxidative stress mechanism- decreased lipid peroxidation found in the substantia	Male Wistar rats (200–250 g) divided into SO (untreated 6-OHDA-	CS (25, 50, or 100 mg/kg), EC (10 mg/kg), or EGCG (10 mg/kg)	2 weeks	The results showed that CS and catechins reverted behavioral changes, indicating neuroprotection

		nigra of PD patients and neuroinflammatory mechanisms	lesioned and 6-OHDA-lesioned treated)			manifested as decreased rotational behavior, increased locomotor activity, antidepressive effects, and improvement of cognitive dysfunction, as compared to the untreated 6-OHDA-lesioned group. The antioxidant and anti-inflammatory properties, pointing out the potential of CS and its catechins for the prevention and treatment of PD.
	Controlled	Antioxidant	Male ICR mice (weighing 18–22 g upon arrival) 5 groups and 8 mice each.	Five groups of mice orally received saline, GTP (5, 10, and 20 mg/kg) or venlafaxine (10 mg/kg) as a positive control. The mice received the drugs orally once daily for consecutive 7 days. On day 7, 60 min after the last treatment, mice were subjected to TST for 6 min (n = 9–11 per group). Another independent five groups of mice were treated with a single dose of saline, GTP (5, 10, and 20 mg/kg) or venlafaxine (10 mg/kg) 60 min	7 days	In conclusion, oral GTP administration exerted significant antidepressant-like effects in the FST and TST and was associated with normalization of HPA axis dysfunction induced by stress. Regular dietary intake of green tea can maintain a stable GTP concentrations in the body and may have valuable effects on health because of good oral bioavailability and few adverse effects
	Controlled	Antioxidant	The two different age groups, Male Wistar albino rats young rats (2 months old, approximately 100 g weight) and older rats (12 months, 300 g weight), 2 subgroups 6 mice in each	Male Wistar albino rats that belong to two different age groups, young rats and older rats were used to study the effect of eight week treatment with 0.5% green tea extract (GTE) in the drinking water. The animals were divided randomly into two subgroups of six animals each namely control group and treated group. Control group animals were given plain drinking water ad libitum whereas treated group animals were given 0.5% GTE in the drinking water.	8 weeks	The study concludes that green tea extract administration is effective in enhancing learning and memory in aged rats and also demonstrates selectivity for inhibition of acetylcholinesterase. Hence, green tea administration might serve useful in reversing age-related deficits in learning and memory.
	Controlled	GTP might protect dopamine neurons through inhibition of Nitric oxide (NO) and reactive oxygen species (ROS).	42 Male Sprague-Dawley rats (220–230g)	GTP 450 mg/kg/day-fed	7 days	GTP treatment dose-dependently protected dopaminergic neurons by preventing from midbrain and striatal 6-OHDA-induced increase in 1) both ROS and NO levels, 2) lipid peroxidation, 3) nitrite/nitrate content, 4)

						inducible nitric oxide synthase, and 5) protein-bound 3-nitro-tyrosine. Moreover, GTP treatment dose-dependently preserved the free radical scavenging capability of both the midbrain and the striatum.
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Anti-arthritis: Green tea can help prevent and reduce the risk of rheumatoid arthritis. Green tea help to suppression both of the proinflammatory cytokine IL-17 and of the antibodies to Bhs65 combined with an increase in the anti-inflammatory cytokine IL-10. Thus, green tea induced changes in arthritis-

related immune responses. Green tea polyphenols rich in antioxidants reduce the frequency of pathogenic Th1-type cells and associated pathogenic CII-specific IgG2a antibody in the affected joints. The various investigated studies are illustrated in Table.

Biological Activity	Type of study	Mechanism	Model/ Population/ cell lines	Test components (daily dosage)	Duration of intake	Main outcomes
Anti-arthritis	controlled	EGC-NPs suppressed the expression of TNF- α , IL-1 β , IL-6, and IL-8 in arthritic rats	Collagen-induced arthritis (CIA) 24 Female Wistar rats, 6 weeks old (130–170 g) are divided into 4 groups	(1) rats with CIA receiving saline (0.1 mL/100 g once daily) (2) rats with CIA receiving EGC-NPs (EGCG 80 mg/kg + GA 800 mg/kg); (3) rats with CIA receiving EGCG-GA (EGCG 80 mg/kg + GA 800 mg/kg); (4) rats with CIA receiving celecoxib (25 mg/kg).	9 weeks	Anti-arthritis effect of the EGC-NPs was significantly higher than that of EGCG-GA mixture. In the EGCG-GA group, EGC-NP group, and celecoxib group, the radiographic scores of the right paws were 3.12, 1.28, and 1.16 points. The therapeutic effect of the EGC-NPs was significantly better than that of the EGCG-GA mixture and comparable to the antiarthritic effect of celecoxib. The enhanced antiarthritic activity in vivo was consistent with that in vitro. The EGC-NPs demonstrate potential as a food supplement for the treatment of arthritis.
	Controlled	reduced levels of Mmp1, Mmp3, Mmp8, Mmp13, Adamts5, interleukin 1 beta (Il1b) and tumor necrosis factor alpha (Tnfa) mRNA and elevated gene expression of the MMP regulator Cbp/p300 interacting transactivator 2 (Cited2).	C57BL/6, 36 mice (males 5 to 6 months of age) were subjected to surgical destabilization of the medial meniscus (DMM) or sham surgery	EGCG (25 mg/kg) or vehicle control was administered daily for 4 or 8 weeks by intraperitoneal injection starting on the day of surgery.	4 or 8 weeks	This study provides the first evidence in an OA animal model that EGCG significantly slows OA disease progression and exerts a palliative effect. Four and eight weeks after DMM surgery, compared to vehicle controls, mice treated with EGCG exhibited reduced OA-associated pain, as indicated by higher locomotor behavior (that is, distance traveled). Moreover, expression

						of the chemokine receptor Ccr2 and proinflammatory cytokines Il1b and Tnfa in the DRG were significantly reduced to levels similar to those of sham-operated animals.
	Controlled	Induced B-lymphocyte apoptosis via upregulation of BAFF/PI3K/AKT/mTOR pathway	50 Sprague-Dawley (SD) rats (male, 150–180 g.) were immunized to induce collagen-induced arthritis (CIA) divided into 5 groups.	Different groups of CIA rats treated with EGCG (40, 80 mg/kg), Paeoniflorin (100 mg/kg) .	18 to day 38	This study showed that, BAFF/BAFF receptor might regulate B cell anti-apoptosis through PI3K/Akt/mTOR pathway. This study would be useful for treatment selection of rheumatoid arthritis patients in different clinical pathological condition.
	Controlled	antiarthritic activity via suppression both of the proinflammatory cytokine IL-17 and of the antibodies to Bhs65 combined with an increase in the antiinflammatory cytokine IL-10.	5–6 wk old, 8 Inbred male Lewis rats	Rats consumed green tea (2–12 g/L) in drinking water	2 weeks before to Mycobacterium tuberculosis H37Ra (Mtb) injection	Feeding 8 g/L PGT to Lewis rats for 9 d significantly reduced the severity of arthritis compared with the water-fed controls. PGT feeding also suppressed the anti-Bhs65 antibody response. Thus, green tea induced changes in arthritis-related immune responses. suppressed the anti-Bhs65 antibody response
	Controlled	polyphenolic fraction of green tea reduces the incidence and severity of collagen-induced arthritis in DBAy1 mice.	6- to 7-week-old DBAy1, 36 male mice	GTP (0.2% solution as the sole source of drinking water)	1 week after arrival	GTPs rich in antioxidants reduce the frequency of pathogenic Th1-type cells and associated pathogenic CII-specific IgG2a antibody in the affected joints. The antioxidant-rich polyphenolic fraction of green tea reduces the incidence and severity of collagen-induced arthritis in DBAy1 mice.

In Oral Disease or periodontal Disease: Green tea also promotes periodontal health by reducing inflammation, preventing bone resorption and limiting the growth of certain bacteria associated with periodontal diseases. Green tea demonstrated strong deodorant activities in halitosis, green tea was very effective in reducing oral malodor temporarily because of its disinfectant and deodorant activities, whereas other foods were not effective. The mouth wash with a dilute catechin of green tea solution reduced the mouth odor (halitosis) associated with periodontal disease. Green tea catechin inhibit the growth of *P. gingivalis*, *Prevotella intermedia* and *Prevotella nigrescens* and adherence of *P. gingivalis* on to human buccal epithelial cells. Green tea catechins with steric structures of 3-galloyl radial, EGCG, ECg

and gallicocatechin gallate, which are major tea polyphenols, inhibit production of toxic end metabolites of *P. gingivalis*. A study showed that green tea catechin, EGCG and ECg inhibit the activity of *P. gingivalis*-derived collagenase. EGCG may prevent alveolar bone resorption that occurs in periodontal diseases by inhibiting the expression of MMP-9 in osteoblasts and formation of osteoclast. Oxidative stress plays an important role in the pathogenesis of periodontal disease as well as many other disorders, and it is believed that antioxidants can defend against inflammatory diseases. Various authors have studied the inhibitory effects of catechin contained in green tea on periodontal pathogens, which may provide the basis for beneficial effect of daily intake of green tea on periodontal health.

Biological Activity	Type of Study	mechanism	Model/Population/cell Lines/Bacteria	Test components / Duration	Main outcomes
In Oral Disease or periodontal	In-vitro	EGCG increased the ROS level and inhibited the cell proliferation of hPDLs, increased extracellular matrix mineralization, generated the most mineralizing nodules.	Periodontal ligaments were obtained from human premolars that were extracted for orthodontic reasons. followed by treatment with 1 mg/mL type I collagenase for 30 min	EGCG at concentrations of 0 (the control group), 2, 4, 6, 8 and 10 μ M and. The medium was renewed every 3 days	This study showed that, EGCG showing the strongest osteogenic enhancement without cytotoxicity, indicating a promising role for EGCG in periodontal regeneration in patients with deficient alveolar bone in the future
	randomized clinical	antioxidant, antimicrobial, and anticollagenase activities on periodontal health.	840 patients who were suffering from chronic periodontitis divided into 2 groups	rinse with 10–20 ml of 2% green tea 3 times/day for 1 and 3 months.	The three dependent variables, namely, PD, CAL, and BOP showed statistically significant reductions following introduction of green tea as a conjunct oral hygiene measure in study group as compared to control group. Green tea has shown the antioxidant, antimicrobial, and anticollagenase activities on periodontal health.
In Oral Disease or periodontal- Deodorant activity	Halitosis	Halitosis caused by VSCs such as H ₂ S and CH ₃ SH. Oral microorganism degrade proteinaceous substrates to cysteine and methionine which are then converted to VSCs. GT strongly inhibited Halitosis VSCs production in a saliva-putrefaction.	Oral microorganisms	670 mg green tea powder and the subjects (n=15) and the other test component were mint, chewing gum, parsley seed oil and toothpaste	Deodorant activity by each product was shown as reduction of H ₂ S. Toothpaste and green tea demonstrated significant reduction (p <0.01, respectively) compared to the control. However, mint, chewing gum and parsley seed oil product demonstrated very low activities. Green tea was very effective in reduction oral malodor because of its disinfectant and deodorant activities.
In Oral Disease or periodontal- (Anti-bacterial/ Anti-inflammatory)	Cariogenic or periodontal bacteria	EGCG-prevent alveolar bone resorption that occurs in periodontal diseases by inhibiting the expression of MMP-9 in osteoblasts and formation of osteoclast	<i>Porphyromonas gingivalis</i> ,	gene expression of MMPs was examined by treating mouse calvarial primary osteoblastic cells with EGCG (20 μ M) in the presence of sonicated P. gingivalis extracts.	Treatment with the sonicated P. gingivalis extracts stimulated the expression of MMP-9 mRNA and this effect was significantly reduced by EGCG, whereas the transcription levels of MMP-2 and MMP-13 were not affected by either the sonicated P. gingivalis extracts or EGCG. In addition, EGCG significantly inhibited osteoclast formation in the co-culture system at a concentration of 20 μ M.
	Cariogenic or periodontal bacteria	Inhibite of collagenase activity	<i>Porphyromonas gingivalis</i> ,	GTP (EGCG 250-500 μ g/ml)	GTP inhibite the growth of p. gingivalis and the MIC was 1000 μ g/ml

Conclusion

Drinking green tea that is already known to possess health-related benefits. Several animals and epidemiological studies have the efficacy of tea constituents in the prevention of chronic diseases. Green tea catechins, in particular EGCG, are ingested in considerable amounts through consumption of green tea beverages. Human, animal, and cell lines studies show anti-obesity, anti-oxidant, anti-aging, anti-diabetic, anti-hyperlipidemic, anti-hypertension, anti-cancer, anti-bacterial, anti-viral, anti-inflammatory, anti-parkinson's effects, anti-alzheimer's effects, anti-arthritis, anticollagenase, and antimutagenic, and cardio-protective effects of green tea and content catechins against obesity, aging, diabetes, cardiovascular disease, hyperlipidemic, hypertension, cancer, microbial, parkinson's, alzheimer's, and arthritis. Among the tea constituents, catechins, especially EGCG, and caffeine have been well studied. The biochemistry and biological activity of green tea well studied. This efficacy is supported by conclusive evidence from animal studies which have also provided the concepts for underlying functional mechanisms. To determine the optimal doses relevant for use in prevention, early management and treatment of the rising health burden of chronic disease. Green tea extract may have numerous effects on periodontal pathogens and periodontal tissues. Greater the concentration of catechins better the health benefits. So the consumption of green tea in comparison to other beverages may be widely recommended. By interfering with the body's inflammatory response to periodontal bacteria, green tea may actually help promote periodontal health and ward off further disease. Continuous use of green tea catechin on a daily basis may be a useful and practical method for the prevention of periodontal disease, but should be carried out with caution to avoid side-effects. Therefore, let us start sipping green tea and grow healthier. Overall, the scientific evidence supports the rewards of ingesting green tea catechins, with special attention to EGCG.

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