CAMELLIA SINENSIS : AN ETHNOPHARMACOLOGICAL REVIEW

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Summary

Traditional medicines are and indomitable arena of pharmacognosy. *Camellia sinensis* commonly known as *TEA* belonging to family *Theaceae* is a perinial evergreen shrub and is always listed in Ayurvedic materia medica because of its various powers of healing with a wide spectrum of biological activity. During last few decades considerable progress have been achieved regarding the biological activity and medicinal applications of *Camellia sinensis* and so now considered as a valuable source of natural product for development of medicines against various diseases. The most important constituent of both black and green tea is the purine alkaloid, caffeine which accounts for the stimulating effect of tea liquor. This review consolidates the current trends and newer technologies and attempts to bring into focus various aspects of medicinally important plant *Camellia sinensis* so as to boost the modern enthusiastic natural product researcher to work more deeply on this plant.

Key words: *Camellia sinensis*, phytochemistry, pharmacology, tea, review

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Introduction

Medicinal plants are part and parcel of human society to combat diseases , from the dawn of civilization. The future of medicine is rooted in the past, before chemists undertook to synthesize synthetic silver bullets for all that ails, and before pharmaceutical companies hitched our collective health to what has become for them a multibillion-dollar wagon (1,2). In the past, almost all the medicines were from the plants, the plant being man's only chemist for ages. Herbs are staging a comeback , herbal 'renaissance' is happening all over the globe and more and more people are taking note of herbal therapies to treat various kinds of ailments in place of mainstream medicine (1,3). Herbal medicines are in great demand in developed as well as developing countries for primary health care because of their wide biological and medicinal activities , higher safety margins and lesser cost. A legend in India describes the story of Prince Siddhartha Gautama, the founder of Buddhism, who tore off his eyelids in frustration at his inability to stay awake during meditation while journeying through China. A tea plant is said to have sprouted from the spot where his eyelids fell, providing him with the ability to stay awake, meditate, and reach enlightenment (4).

Vernacular names (5)

Chai, chha (Bengal , hindi),Cha (Gujrat),Cha , chaha , theyale (Kannad),Chaya , theyila (Malyal),Chaha (Marathi),Chaha (Sanskrit),Chai (Urdu).

Synonyms (4)

Camellia assamica, camellia tea, camellia, *Camellia sinensis*, catechin, Chinese tea, tea for America, theifers, Thea sinensis, Thea bohea, Thea viridis

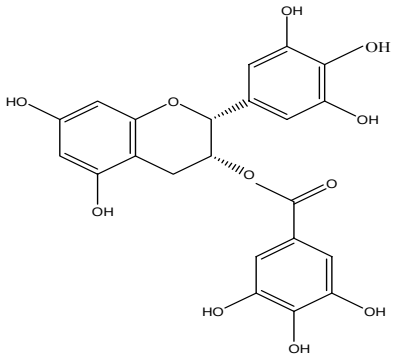
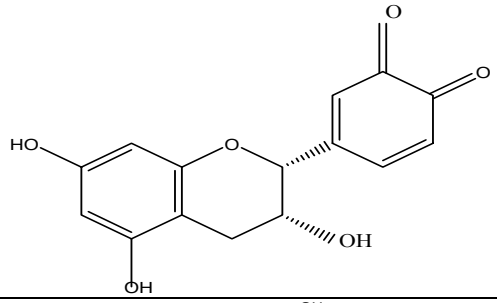
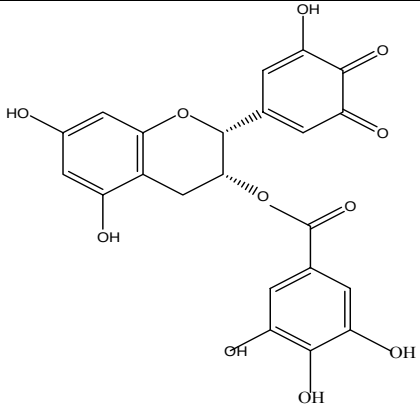
Taxonomy (6)

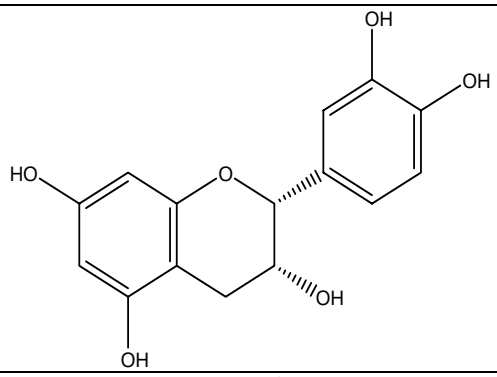
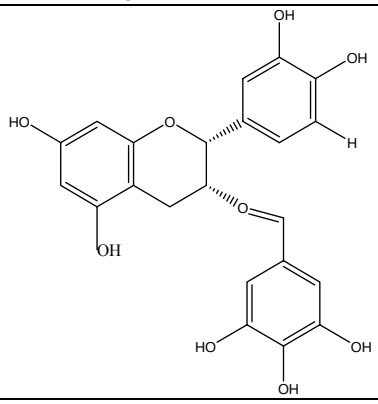
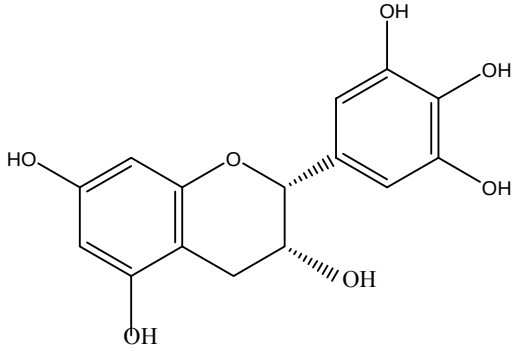
Kingdom : Plantae
Subkingdom : Tracheobionta
Division : Magnoliophyta
Class : Magnoliopside
Subclass : Dilleniidae
Order : Theales
Family : Theaceae
Genus : Camellia
Species : *Camellia sinensis* (L.) O.Kuntze

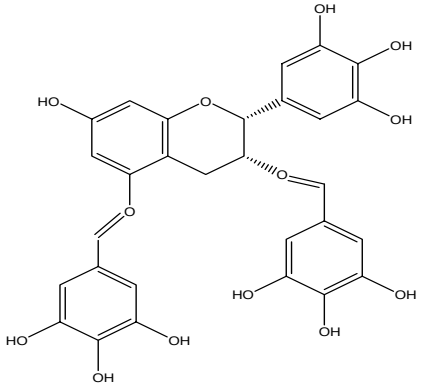
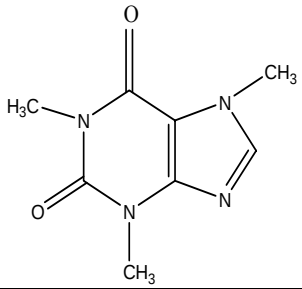
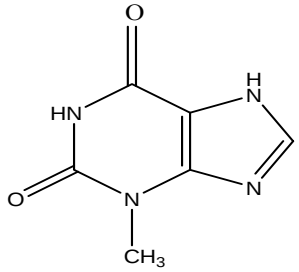
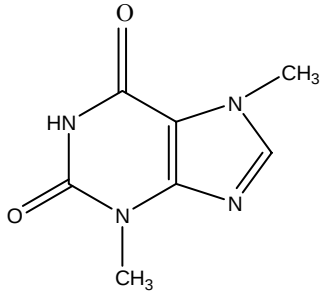
Phytochemistry

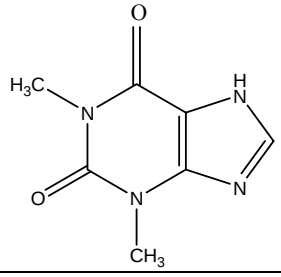
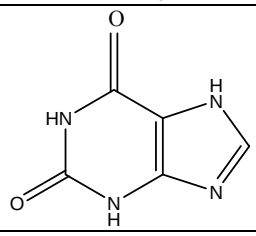
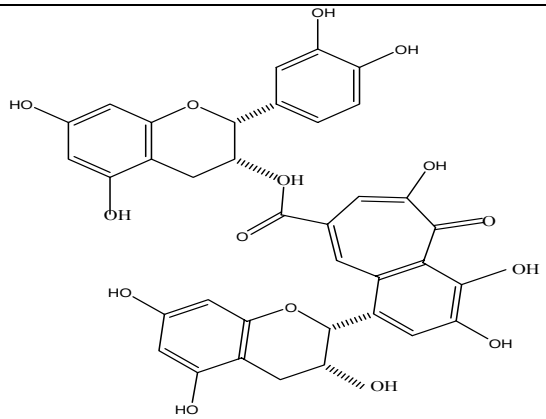
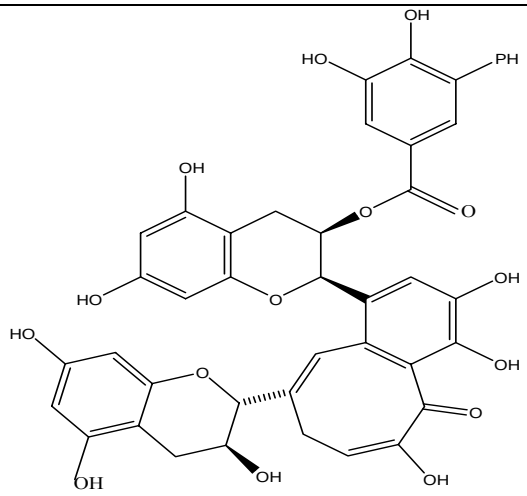
Fresh leaves from Assam contain 22.2% polyphenols, 17.2% protein, 4.3% caffeine, 27.0% crude fiber, 0.5% starch, 3.5% reducing sugars, 6.5% pectins, 2.0% ether extract and 5.6% ash. Per 100 g, the leaf is reported to contain 293 calories, 8.0 g H_2O, 24.5 g protein, 2.8 g fat, 58.8 g total carbohydrate, 8.7 g fiber, 5.9 g ash, 327 mg Ca, 313 mg P, 24.3 mg Fe, 50 mg Na, 2700 ug beta-carotene equivalent, 0.07 mg thiamine, 0.8 mg riboflavin, 7.6 mg niacin, and 9 mg ascorbic acid. Another report tallies 300 calories, 8.0 g H_2O, 28.3 g protein, 4.8 g fat, 53.6 g total carbohydrate, 9.6 g fiber, 5.6 g ash, 245 mg Ca, 415 mg P, 18.9 mg Fe, 60 mg Na, 8400 ug beta-carotene equivalent, 0.38 mg thiamine, 1.24 mg riboflavin, 4.6 mg niacin, and 230 mg ascorbic acid. Yet another gives 299 calories, 8.1 g H_2O, 24.1 g protein, 3.5 g fat, 59.0 g total carbohydrate, 9.7 g fiber, 5.3 g ash, 320 mg Ca, 185 mg P, 31.6 mg Fe, 8400 ug beta-carotene equivalent, 0.07 mg thiamine, 0.79 mg riboflavin, 7.3 mg niacin, and 85 mg ascorbic acid (7). Leaves also contain carotene, riboflavin, nicotinic acid, pantothenic acid and ascorbic acid. Caffeine and tannin are among the more active constituents (8). Ascorbic acid, present in the fresh leaf, is destroyed in making black tea. Malic and oxatic acids occur, along with kaempferol, quercitrin, theophylline, theobromine, xanthine, hypoxanthine, adenine, gums, dextrins, and inositol. Chief components of the volatile oil (0.007-0.014% fresh weight of leaves) is hexenal, hexenol, and lower aldehydes, butyraldehyde, isobuteraldehyde, isovaleraldehyde, as well as n-hexyl, benzyl and phenylethyl alcohols, phenols, cresol, hexoic acid, n-octyl alcohol, geraniol, linalool, acetophenone, benzyl alcohol, and citral. Does this mean that the leaves contain more dangerous substances than herb tea? More properly it only indicates that Camellia has been more intensively studied than most herb teas. Certain constituents, especially catechin, epigallocatechin, and epigallocatechin gallate are said to have antitoxidative properties (9). Other constituents are mentioned in the table 1.

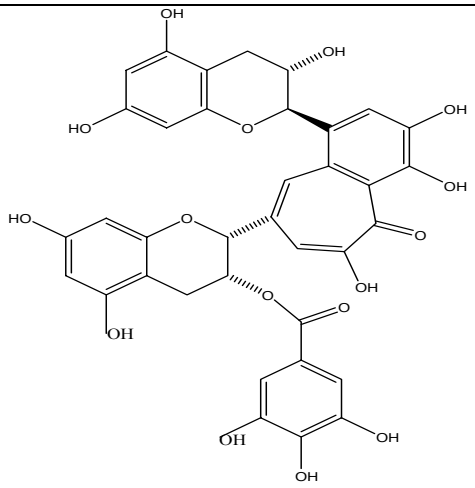
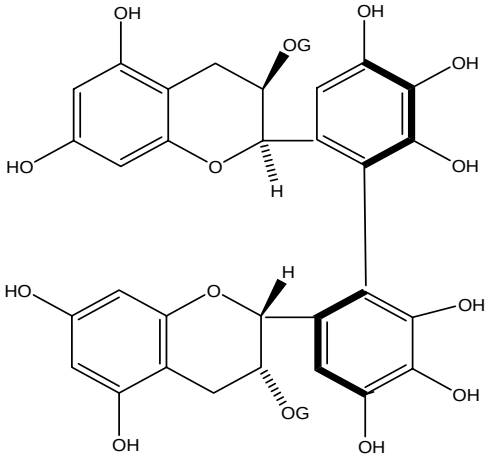
Table 1.: Chemical constituents of *Camellia sinensis*

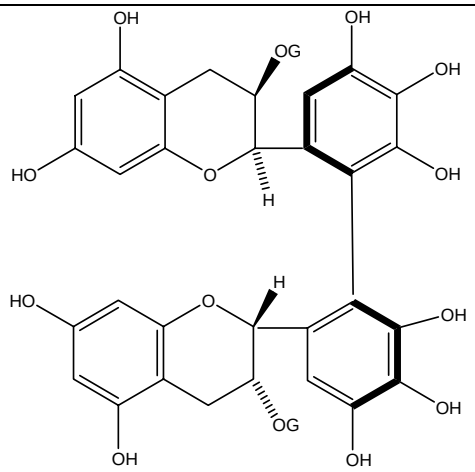
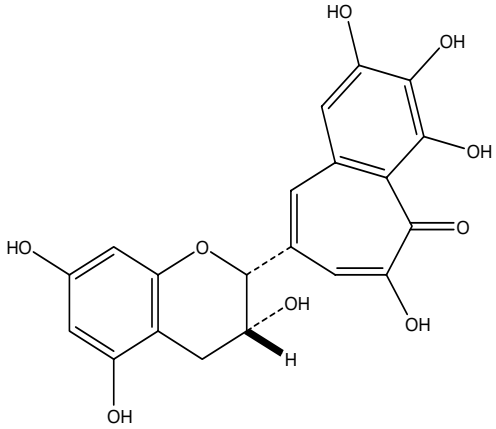
Sr. no .	Refrence no.	Name of compound	Structure
1	54	EPIGALOCATECHINGAL--LATE (EGCG)	
2	54	(-)-Epicatechin quinone (ECQ)	
3	54	(-)-epigallocatechin quinine (EGCGQ)	

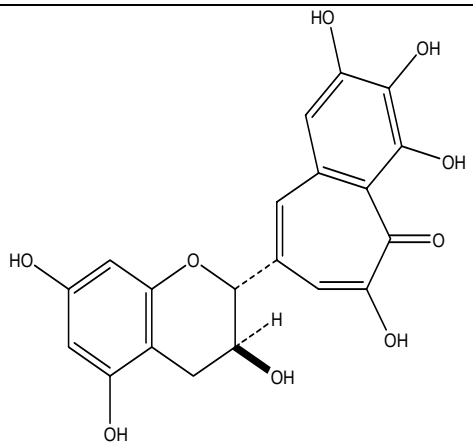
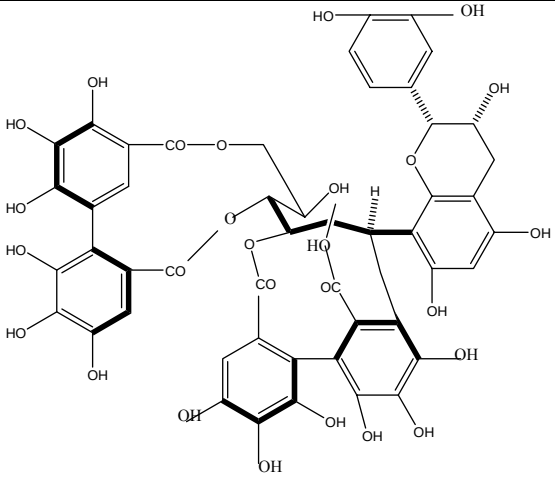
4	55	(-)-EPICATECHIN (EC)	
5	55	EPICATECHINGALLATE (ECG)	
6	55	EPIGALLOCATECHIN (EGC)	

7	55	(-)-EPIGALLOCATECHIN-3,5-DI-O-GALLATE (EGCDG)	
8	54	CAFFEINE	
9	54	3-METHYL XANTHINE	
10	54	THEOBROMINE	

11	55	THEOPHYLINE	
12	55	XANTHINE	
13	55	THEAFLAVATE B	
14	55	ISOTHEAFLAVIN-3-O-GALLATE	

15.	55	NEOTHEAFLAVIN-3-O-GALLATE	
16.	55	THEASINENSIN A	

17	55	THEASINENSIN D	
18	39	THEAFLAGALLIN	

19	39	EPI THEAFLAGALLIN	
20	39	CAMELLIATANNIN A	

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<tr><td>21</td><td>39</td><td>CAMELLIANIN</td><td>
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<tr><td></td><td>R</td></tr>
<tr><td>Camellianin A</td><td>Glu(6"- Ac) (4→1)Rha</td></tr>
<tr><td>Camellianin B</td><td>Glu(4→1)Rha</td></tr>
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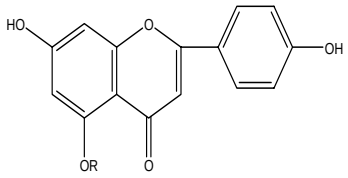

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<tr><td>22</td><td>39</td><td>CAMELLIASIDE</td><td>
<table>
<tr><td></td><td>R</td></tr>
<tr><td>CAMELLIASIDE A</td><td>Glu[(2→1)Gal] (6→1) Rł</td></tr>
<tr><td>CAMELLIASIDE B</td><td>Glu[(2→1)Xyl] (6→1) Rl</td></tr>
<tr><td>CAMELLIASIDE C</td><td>Glu (2→1)Gal</td></tr>
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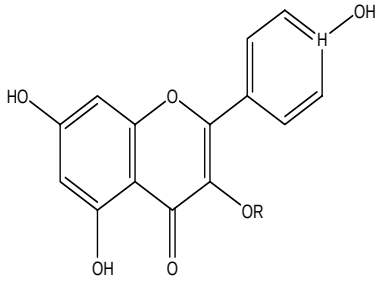

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<tr><td>23</td><td>55</td><td>ISOTHEASAPONIN</td><td>
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<tr><td></td><td>R1</td><td>R2</td><td>R3</td><td></td></tr>
<tr><td>Isotheasaponin B1</td><td>(E)-Cin</td><td>H</td><td>Ac</td><td></td></tr>
<tr><td>Isotheasaponin B2</td><td>Ac</td><td>(E)-Cin</td><td>H</td><td></td></tr>
</table>
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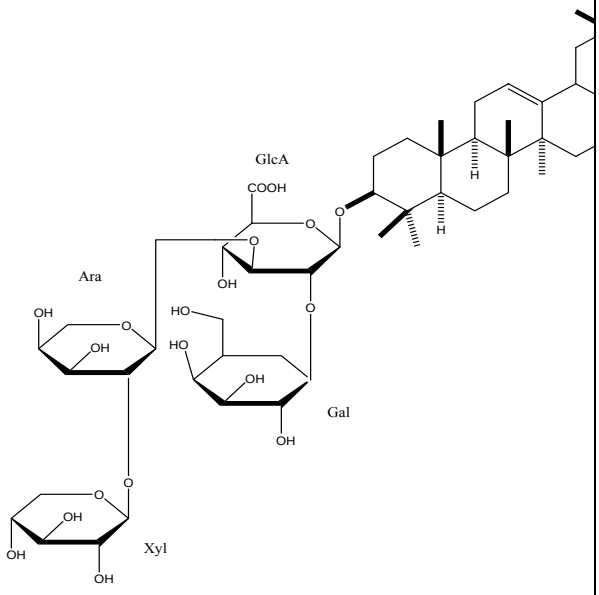
			Isotheasaponin B3	Ang	(E)-Cin	H
			Theasaponin B1	(E)-Cin	Ac	H



Experiments on the incorporation of 14 Carbon adenine into purine alkaloids by C. sinensis leaves showed that caffeine synthesis occurs only in young tissues (12,13,17). Seasonal variations in caffeine biosynthetic activity have been investigated using leaf discs, prepared at monthly intervals over the course of a one year period, from plants grown under natural field conditions in Japan (14,15,18). Incorporation of radioactivity into theobromine and caffeine occurred only in the young leaves harvested between April and June (16,19). In young tea leaves, [8-14C]theophylline and [2-14C]xanthine are also utilised for caffeine biosynthesis via 3-methylxanthine (20). Caffeine biosynthesis has been detected in pericarp and seeds of tea fruits with the highest biosynthetic capacity occurring in young tissues (21). It is well established that artificial shading of tea plants prior to harvest produces young shoots that yield a higher quality beverage (22). The biosynthesis of the flavan-3-ols, (–)-epicatechin and (–)-epicatechin-3-gallate, (–)-epigallocatechin and (–)-epigallocatechin- 3-gallate in young tea leaves is enhanced by light (23). In contrast, shading generally increases caffeine levels in tea leaves when expressed as percentage of dry weight (24).

Metabolism of theacrine has not yet been investigated in kucha. Relatively little information is available for the catabolism of purine alkaloids in C. sinensis although the pathways have been investigated using various 14C-labelled purine alkaloids (25). In green tea manufacture, the enzymes are inactivated immediately after harvesting of fresh tea leaves, and therefore, the composition of green tea polyphenols, are mainly comprised of (-)-epicatechin, (-)-epigallocatechin and their galloyl esters, similar to those in fresh leaves. On the other hand, in black tea manufacture, the tea catechins are first oxidized with the aid of enzymes, which are then inactivated. The oxidation reactions generate B-ring o-quinones of the catechins and cross-coupling reactions of the quinones produce a complex mixture of black tea polyphenols (26,27). Although dimeric products, including theaflavins and theasinensins, are known to be important (28) the major components of the oxidation products, especially those with an oligomeric nature, so called thearubigins, have yet to be clarified despite assiduous efforts (29). The compound (-)-epigallocatechin-3-gallate (EGCG) is the major catechin found in green tea [*Camellia sinensis* L. Ktze. (Theaceae)] (30,31). This polyphenolic compound and several related catechins are believed to be responsible for the health benefits associated with the consumption of green tea. The potential health benefits ascribed to green tea and EGCG include antioxidant effects, cancer chemoprevention, improving cardiovascular health, enhancing weight loss, protecting the skin from the damage caused by ionizing radiation, and others. The compound EGCG has been shown to regulate dozens of disease-specific molecular targets. Many of these molecular targets are only affected by concentrations of EGCG that are far above the levels achieved by either drinking green tea or consuming moderate doses of green tea extract-based dietary supplements (32). Several other polyphenolic compounds known as catechins are also found in lower abundance in green tea. These other catechins include (-)-epicatechin- 3-gallate (ECG), (-)-epigallocatechin (EGC), (-)-epicatechin (EC) and (+)-catechin. More than 50% of the mass of this catechin combination is composed of EGCG and a vast body of scientific research suggests that EGCG (and other catechins) is responsible for the majority of the potential health benefits attributed to green tea consumption (32).

Morphology

Small evergreen tree to 16 m tall, usually pruned back to shrubs in cultivation, with strong taproot giving rise to a surface mat of feeders with endotrophic mycorrhizae; leaves alternate, exstipulate, lanceolate to obovate, up to 30 (usually 4-15) cm long, 2-5 (7-12) cm broad, pubescent, sometimes becoming glabrous, serrate, acute or acuminate; flowers 1-3, in axillary or subterminal cymes, deflexed, 2-5 cm broad, aromatic, white or pinkish, actinomorphic, sepals and petals 5-7, pedicels 5-15 mm

long; stamens numerous; ovary 3-5-carpellate, each carpel 4-6-ovulate; capsules depressed-globose, brownish, lobate, to 2 cm broad, valvate, with 1-3 subglobose seeds in each lobe; approximately 500 seeds per kg (10).

Photo of *Camellia sinensis* (11)

Geographical source

Native to Southeast Asia, from Sri Lanka and India to Assam and China, tea has been planted widely in tropical and subtropical areas. Near the Equator, it ranges up to nearly 2,000 m elevation (10).

Genetics and molecular biology

Pheno epigallocatechin gallate from green tea inhibits IL-1beta-induced glycosaminoglycan release from human cartilage explants in vitro and also mRNA & protein expression of matrix metalloproteinase-1 & -13 in human chondrocytes suggesting its possible use in arthritis (33). A constituent of green tea, (-)-epigallocatechin-3-gallate inhibits cervical cancer cell growth in human papillomavirus -16 associated cervical cancer cell line, CaSki cells through induction of apoptosis and cell cycle arrest as well as regulation of gene expression in vitro and in vivo (34). (-)-Epigallocatechin-3-gallate markedly increases AP1 factor-associated responses in normal human keratinocytes via a MAPK signaling mechanism (35). Green tea catechins (-)-epicatechin (EC), (-)-epigallocatechin

(EGC), (-)-epicatechin gallate (ECG) and (-)-epigallocatechin gallate (EGCG) partially protect DNA from (.)OH radical-induced strand breaks and base damage through fast chemical repair of DNA radicals (36). Epigallocatechin gallate (EGCG) from green tea is a beta-ketoacyl reductase related inhibitor of fatty-acid synthase from chicken liver (37).

Pharmacology

Black tea lowered the blood glucose levels significantly in these patients (NIDDM type of diabetic patients) after its consumption for four weeks. Results indicate that black tea can be used therapeutically in diabetic patients as a substitute for oral hypoglycaemic agents (38). Plant decoction showed prolonged hypertensive effect in rabbits. Gallocatechin galate reduced blood pressure in rabbits (39) . Chinese green tea extract inhibited induced peroxidation in rat liver microsomes and mutagenecity of benzo[a] pyrene and aflatoxin B_1 and suppressed benzo[a]pyrene hydroxylase activity (39). Green tea infusion markedly inhibited NDEA induced tumorigenesis. It decreased lung tumor incidence and stomach tumor multiplicity (39).
Catachins, gallates and all theaflavin inhibited growth of both spores and vegetative cells of Clostridium botulinum (39). Crude polyphenolic fraction of tea inhibited attachment of Streptococcus mutans stain formation of water soluble glucan from sucrose by bacterial glucosyl-transferase and dental caries (39). Tea flavonols reduced incidence of ischemia reperfusion arrhythmias in rat heart by 70% (39).The diuretic property of tea is useful in the therapy of cardiac oedema (39). It seems to reduce serum lipid, induce synthesis and secretion of catecholamines and prevent atherosclerosis (39).Tea polyphenols may inhibit the absorbtion of dietary cholesterol and prevent degradation of triglycerides in adipose tissue thereby reducing weight (39). Dimeric compounds particularly theaflavins produced oxidatively, in the manufacture of black tea inhibit angiotensin 1 converting enzyme (39). Tea flavonoids possess anticoagulant activity and inhibit platelet aggregation in rabbits (39). Tea may be used in relieving bronchial asthama due to muscle relaxant effect of caffeine (39). Tea polyphenols strengthen the walls of blood vessels and regulate their permeability , an activity associated with o-dihydroxybenzene group collectively termed vitamin P or biflavonoids (39). Tea polyphenols protect ascorbic acid from oxidation in rat tissue homogenates due to their antioxidant properties (39). Green tea polyphenols have been found to normalize thyroid hyperfunction which induces thyrotoxicosis ; this has been attributed to flavanols , especially gallocatechins (39). Green tea infusion shoes anti bacterial activity against a number of bacteria and is an effective cure against dysentery (39). EGCG from green tea prevents formation of tumor cells (39).

Consumption of 5 g of tea every day can reduce the synthesis of nitrosamine which is a major carcinogen (39). Green tea extract has been reported to be more effective in preventing tooth decay than fluoride compounds (39).Green tea extract strongly inhibits the formation of dextran and levan from sucrose by the carcinogenic bacteria (39). Tea is considered a cure for cold and removes phlegm (39). Tea prevents the formation of stones in bladder , liver , kidney (39). Catechin preparations are usefull in treating nephritis and chronic hepatitis. Tea is successfully used in treating severe abdominal , intestinal , cerebral haemorrhages (39).
Green tea tannin may be used in treating toxic goiter (39). Tea drinking, by providing antioxidants,may become valuable in several chronic disease known as oxidative stress conditions, such as the cardiovascular diseases (CVD). An increase in daily tea drinking of 711 ml was also reported to decrease the risk of myocardial infarction by 11% (40).

Antimutagenicity of green tea polyphenols against tobacco as a mutagen (41):
Green tea polyphenols was found to produce inhibition of mutagenicity induced by tobacco in a concentration dependent manner. At concentration of 10.0 mg of green tea polyphenols per plate, 100% of inhibition in the revertant colony formation was observed. Addition of green tea polyphenols at concentrations 1.0 mg and 5.0 mg per plate have produced 27.8% and 45.6% of inhibition, respectively.

Effect of green tea polyphenols on urinary mutagenicity induced by tobacco (41):
Green tea polyphenols was found to inhibit urinary mutagenicity induced by tobacco in rats. Urine collected from rats treated with tobacco was found to be significantly mutagenic to S. typhimurium strain TA 102 as seen from the number of revertant formation. Administration of green tea polyphenols could significantly inhibit urinary mutagenicity induced by tobacco in rats .

Effect of green tea polyphenols on nitrosation reaction (41):
Nitrosation of methyl urea with sodium nitrite at acidic condition was found to increase the mutagenicity as seen from the increased revertant formation. Incubation of bacteria with the reaction mixture produced 632.0±14.5 revertant colonies. Addition of green tea polyphenols to the medium at concentrations of 0.1 mg, 0.2 mg, 0.5 mg, 1.0 mg produced 11%, 27.7%, 55.4%, 81.1% inhibition in revertant formation. The potential protective role played by green tea against injurious effects of reactive oxygen species in human microvascular endothelial cells was evaluated and the results showed that green tea polyphenol can act as a biological antioxidant in a cell culture experimental model and prevent oxidative stress-induced cytotoxicity in endothelial cells (42).

Curative effect of tea extract on STZ-induced hyperglycemia in rats (43):
Tea extract (both black and green) administration to rats, which were made hyperglycemic by STZ injection, significantly reduced the blood glucose level as compared to STZ control rats which received distilled water. Black tea extract was marginally more effective in reducing the blood glucose when compared to green tea extract .

Preventive effect of tea extract on STZ-induced hyperglycemia in rats (43):
Injection of STZ (40 mg/kg i.v.) produced a gradual increase in blood glucose level in control rats. At the end of the third week after STZ injection the increase reached a maximum (92.5%). The blood glucose level declined gradually thereafter and reached the basal level at the end of fifth week after STZ injection . While the elevation of blood glucose level in STZ-control group was found to be 92.5% and 20% in the 3rd and 4^{th} week after STZ administration, the elevation of blood glucose level at the corresponding periods in the black tea treated group was found to be 5%. and 8%. The inhibitory effect of black tea extracton hyperglycemia induced by STZ was statistically significant. A similar regimen of green tea extractadministration completely inhibited the STZinducedincrease in blood glucose level .

Side effects of green tea

Green Tea can cause allergic reactions. Green tea contains caffeine which has been shown to increase anxiety and impair sleep. Caffeine can interfere with many prescription medications causing adverse reactions or dangerous interactions. Results suggest that tea consumption inhibits the utilization of thiamin(44). Findings confirm that alcohol consumption is associated a greater number of errors and provide some evidence for task-specific antagonism of alcohol's cognitive effects by caffeine(45). Green Tea has been associated with documented reports of potential interactions with warfarin(46). Overconsumption may cause irritability, insomnia, nervousness, and tachycardia. Because studies on its possible teratogenic effect are inconclusive, caffeine consumption is contraindicated during pregnancy. Lactating women should also limit caffeine intake to avoid sleep disorders in infants(47).Studies of the side effects of green tea specifically are limited. However, green tea is a source of caffeine, for which multiple reactions are reported. Caffeine is a stimulant of the central nervous system, and may cause insomnia in adults, children, and infants (including nursing infants of mothers taking caffeine). Caffeine acts on the kidneys as a diuretic (increasing urine and urine sodium/potassium levels, and potentially decreasing blood sodium/potassium

levels), and may worsen urge incontinence. Caffeine-containing beverages may increase the production of stomach acid, and may worsen ulcer symptoms. Tannin in tea can cause constipation. Certain doses of caffeine can increase heart rate and blood pressure, although people who consume caffeine regularly do not seem to experience these effects in the long-term (48).

An increase in blood sugar levels may occur. Caffeine-containing beverages such as green tea should be used cautiously in patients with diabetes. In contrast, lowering of blood sugar levels from drinking green tea has also been reported in preliminary research. Additional study is needed in this area (48). People with severe liver disease should use caffeine cautiously, as levels of caffeine in the blood may build up and last longer. Skin rashes have been associated with caffeine ingestion. In laboratory and animal studies, caffeine has been found to affect blood clotting, although effects in humans are not known (48). Caffeine toxicity is possible with high doses. Chronic use can result in tolerance, psychological dependence, and may be habit forming. Abrupt discontinuation may result in withdrawal symptoms (48). Several population studies initially suggested a possible association between caffeine use and fibrocystic breast disease, although more recent research has not found this connection. Limited research reports a possible relationship between caffeine use and multiple sclerosis, although evidence is not definitive in this area. Animal study reports that tannin fractions from tea plants may increase the risk of cancer, although it is not clear that the tannin present in green tea has significant carcinogenic effects in humans (48). Drinking tannin-containing beverages such as tea may contribute to iron deficiency, and in infants, tea has been associated with impaired iron metabolism and microcytic anemia (48). In preliminary research, green tea has been associated with decreased levels of estrogens in the body. It is not clear if significant side effects such as hot flashes may occur (48).

Toxicity

Camellia sinensis Conception may be delayed in women who consume large amounts of caffeine. Seizure, muscle spasm, life-threatening muscle breakdown (rhabdomyolysis), and life-threatening abnormal heart rhythms have been reported with caffeine overdose. Extremely high doses may be fatal. It has been found to affect blood clotting, although effects in humans are not known. Tea polyphenols (40 microgram/ml) and (-)-epigallocatechin gallate (10 microgram/ml) enhanced the cytotoxicity of doxorubicin on KB-A-1 cells by 5.2 and 2.5 times respectively and also showed reversal effects on the multidrug resistance phenotype (49). Analysis of 48 black tea (*Camellia sinensis*) samples from Oman revealed

contamination with 5 species of Aspergillus niger ranging from 0.66% and 30.34%. Other fungi isolated were Aspergillusflavus, Penicillium spp. and Pacelomyces spp. Such contamination might pose health hazards (50).

Pregnancy and breast feeding (51)

Large amounts of black tea should be used cautiously in pregnant women, as caffeine crosses the placenta and has been associated with spontaneous abortion, intrauterine growth retardation, and low birth weight. Heavy caffeine intake during pregnancy may increase the risk of later developing SIDS (sudden infant death syndrome). Very high doses of caffeine have been associated with birth defects, including limb and palate malformations. Caffeine is readily transferred into breast milk. Caffeine ingestion by infants can lead to sleep disturbances/insomnia. Infants nursing from mothers consuming high levels of caffeine daily have been reported to experience tremors and heart rhythm abnormalities. Components present in breast milk may reduce infants' ability to metabolize caffeine, resulting in higher than expected blood levels. Tea consumption by infants has been associated with anemia, reductions in iron metabolism, and irritability.

Interactions with drugs (52)

Studies of the interactions of black tea with drugs are limited. However, black tea is a source of caffeine, for which multiple interactions have been documented. The combination of caffeine with ephedrine, an ephedra alkaloid, has been implicated in numerous severe or life-threatening cardiovascular events such as very high blood pressure, stroke, or heart attack. This combination is commonly used in over-the-counter weight loss products, and may also be associated with other adverse effects, including abnormal heart rhythms, insomnia, anxiety, headache, irritability, poor concentration, blurred vision, and dizziness. Stroke has also been reported after the nasal ingestion of caffeine with amphetamine.

Caffeine may add to the effects and side effects of other stimulants including nicotine, beta-adrenergic agonists such as albuterol (Ventolin®), or other methylxanthines such as theophylline. Conversely, caffeine can counteract drowsy effects and mental slowness caused by benzodiazepines like lorazepam (Ativan®) or diazepam (Valium®). Phenylpropanolamine and caffeine should not be used together due to reports of numerous potentially serious adverse effects, although forms of phenylpropanolamine taken by mouth have been removed from the U.S. market due to reports of bleeding into the head. When taken with caffeine, a number of drugs may increase caffeine blood levels or the length of time caffeine

acts on the body, including disulfiram (Antabuse®), oral contraceptives (OCPs) or hormone replacement therapy (HRT), ciprofloxacin (Cipro®), norfloxacin, fluvoxamine (Luvox®), cimetidine (Tagamet®), verapamil, and mexiletine. Caffeine levels may be lowered by taking dexamethasone (Decadron®). The metabolism of caffeine by the liver may be affected by multiple drugs, although the effects in humans are not clear. Caffeine may lengthen the effects of carbamazepine or increase the effects of clozapine (Clozaril®) and dipyridamole. Caffeine may affect serum lithium levels, and abrupt cessation of caffeine use by regular caffeine users taking lithium may result in high levels of lithium or lithium toxicity. Levels of aspirin or phenobarbital may be lowered in the body, although clinical effects in humans are not clear. Although caffeine by itself does not appear to have pain-relieving properties, it is used in combination with ergotamine tartrate in the treatment of migraine or cluster headaches (for example, Cafergot®). It has been shown to increase the headache relieving effects of other pain relievers such as acetaminophen and aspirin (for example, Excedrin®). Caffeine may also increase the pain relieving effects of codeine or ibuprofen (Advil®, Motrin®). As a diuretic, caffeine increases urine and sodium losses through the kidney, and may add to the effects of other diuretics such as furosemide (Lasix®). Black tea may contain vitamin K, which when used in large quantities can reduce the blood thinning effects of warfarin (Coumadin®), a phenomenon that has been reported in a human case. Based on preliminary data, theanine, a specific glutamate derivative in green tea (which is the same species as black tea), may reduce the adverse reactions caused to the heart and liver by the prescription cancer drug doxorubicin. Further research is needed to confirm these results. Based on preliminary data, ingestion of green tea may lower LDL cholesterol, and thus may theoretically interact with other cholesterol-lowering drugs. Other potential interactions may include drugs such as adenosine, alcohol, antidiabetics, antipsychotics, fluconazole, hydrocortisone, levodopa, MAOI antidepressants, phenytoin, proton pump inhibitors (PPIs), riluzole and timolol.

Interactions with herbs and dietary supplements (52)

Studies of green tea interactions with herbs and supplements are limited. However, green tea is a source of caffeine, for which multiple interactions have been documented. Caffeine may add to the effects and side effects of other stimulants. The combination of caffeine with ephedrine, which is present in ephedra (ma huang), has been implicated in numerous severe or life-threatening cardiovascular events such as very high blood pressure, stroke, or heart attack. Cola nut, guarana (*Paullina cupana*), and yerba mate (*Ilex paraguariensis*) are also sources of caffeine, and may add to the effects and side effects of caffeine in green tea. A

combination product containing caffeine, yerbe mate (*Ilex paraguariensis*), and damiana (*Turnera difussa*) has been reported to cause weight loss, slowing of the gastrointestinal tract, and a feeling of stomach fullness. As a diuretic, caffeine increases urine and sodium losses through the kidney, and may add to the effects of other diuretic agents. Based on preliminary data, ingestion of green tea may lower LDL cholesterol, and thus may theoretically interact with other cholesterol-lowering herbs and supplements. Bitter orange, calcium, iron, MAOIs, and tannin-containing herbs and supplements may also interact with green tea.

Interactions with food (52)

The bioavailability of catechins, constituents of green tea, may decrease when ingested with food. Green tea may also interact with grapefruit juice or milk.

Contraindications (53)

Accumulated fluoride in the leaves of tea is a potential source of high fluoride ingestion & recommendations should be made to reduce consumption in patients who may be at risk of dental fluorosis.

Phtochemical analysis

HPTLC methods for identification of green tea and green tea extract on silica gel 60 with ethyl formate, toluene, formic acid, water (30:1.5:4:3) as mobile phase, the flavonoid fingerprint of green tea can give information about the geographical origin of the material. The mobile phase toluene, acetone, formic acid (9:9:2) allows the discrimination of green tea from black and other specialty teas, based on the polyphenol pattern. The latter method has been validated, addressing specificity, stability, reproducibility, and robustness. For additional quality control of extracts, ethyl acetate, methanol, and water (20:2.7:2) can be used as mobile phase to investigate the alkaloid profile, whereas, 1-butanol, acetone, acetic acid, water (7:7:2:4) provides an amino acid profile.(54,55)

Discussion

There are lack phyto-chemical and phyto-analytical studies of this plant. With the availability of primary information, further studies can be carried out like phyto-pharmacology of different extracts, standardization of the extracts, identification and isolation of active principles and pharmacological studies of isolated compound. Alternative systems of medicine viz. Ayurveda, Siddha, and Chinese

Medicine have become more popular in recent years (56,57). Medicinal plants have provided copious leads to combat diseases, from the dawn of civilization(58).As the global scenario is now changing towards the use of nontoxic plant products having traditional medicinal use, development of modern drugs from *Camellia sinensis* should be emphasized for the control of various diseases. In the present review we have made an attempt to congregate the botanical, phytochemical, ethnopharmacological, pharmacological and toxicological information on *Camellia sinensis*, a medicinal herb used in the Indian system of medicine.

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