

Review Article

Tea (*Camellia sinensis*): A Wonderful Medicinal Herb with Multiple Health Benefits

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Abstract

Green tea (*Camellia sinensis*) is reported to be one of the most popularly known healthy beverages. Herbal tea is rich in many bioactive constituents like polyphenols, flavanols, epigallo catechingallate, epicatechingallate etc. The active constituents in tea are found to possess many potent medicinal properties viz. anti-oxidative, reducing the risk of strokes, maintenance of blood pressure, immuno-stimulant, anti-diabetic, anti-stress, anti-inflammatory, anti-bacterial, anti-viral, anti-carcinogenic and many more. The popularity of this shrub is not attributed to its palatability/ flavor alone, but majorly depends upon the bunch of documented medicinal beneficial bioactivities. Studies on beverages, prepared from green tea, has warranted the evidence of a list of phytochemicals with a potential of reducing the risk of several ailments and improving the quality of life among people. This herb with huge number of therapeutic potentials in preventing and treating various diseases, provides immense health benefits and has become an integral part of modern healthy lifestyle.

The cautious and authenticated use of this herb is proven to have wonderful medicinal potential, but excessive consumption is found to produce detrimental effects as well. Many studies are being held for the determination of the safe dose rate for the consumption of tea to obtain the maximum healthy benefits. The present review emphasizes on the medicinal properties and the mechanism of action of various phytochemical constituents of tea.

Keywords: *Camellia sinensis*, tea, beverage, cancer, anti-oxidant

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Introduction

Tea (*Camellia sinensis*) is a medicinal shrub extensively used as a most popular beverage since ancient times. Green tea is a small shrub bearing white flowers, green leaves and fruits over it. The basic classification of this shrub includes Family-Theaceae, Genus-Camellia L.-camellia and species *Camellia sinensis* belonging to Plantae kingdom [1]. Tea is obtained from the leaves of the plant and found to have many pharmaceutical or therapeutic applications. Many studies have documented the beneficial effects of green tea against hypertension, cancers, diabetes, Parkinson disease and many more [2- 4]. A list of useful therapeutically known actions of this medicinal herb and its byproducts has already been concluded by many researchers. The constituents present in this plant has tremendous herbal uses including anti-mutagenic [5], anti-cancerous [6], anti-oxidative [7], anti-bacterial [8], anti-viral [9], cholesterol lowering activity [10], neuro-protective [11], anti-coagulant [12], anti-depressant, and anti-aging effects [13]. Established medicinal properties of green tea are attributed to the availability of critical constituents present in the leaves of this herb [14].

Distribution and varieties

This traditional beverage prepared from the tea was originated from the ancient China almost 5000 years ago [15, 16]. The composition of tea is influenced by the method of its fermentation. The constituents reported in tea are often found to stimulate the central nervous system and are required for the overall health of the human beings as depicted in previous studies by researchers [17]. Tea as beverage is consumed throughout the world but China and India both are the big producers of this crop [18, 19]. Commercial cultivation of tea is already established in many parts of India especially in hilly valleys like Assam and Himachal Pradesh. The other blooming zones for tea in Indian business include Tamil Nadu, Kerala and West Bengal. Darjeeling and Nilgiri hills in India are renowned globally for the finest tea producers in terms of delicacy, flavor and brightness [18, 20]. Tea business is a major source of income in many parts of the globe and is a popular consumable beverage among the population throughout the world [21-23]. There are 6 basic forms of tea manufactured from *Camellia sinensis* leaves and are listed in **Table 1**.

Table 1 Different forms of tea and their mode of processing [23, 24]

S. No.	Type	Nature of processing
1.	Green tea	Not oxidized and un-wilted
2.	White tea	Un-oxidized and wilted
3.	Oolong tea	Partially oxidized and wilted
4.	Black tea	Oxidized and completely wilted
5.	Yellow tea	Un-wilted and un-oxidized
6.	Post - fermented tea	Green tea that has been allowed to ferment/ compost

White tea is least processed tea and containing more catechins than green tea [1]. Throughout the world approximately 3.0 billion kg of tea leaves are produced annually. Out of this produced tea 78% black tea and 20% is green tea is consumed in India and Asian countries respectively [25, 26]. The rest of 2% Oolong tea is produced in Southern China by partial fermentation.

Camellia sinensis var. *assamica* is native variety of tea to the Assam region in India and also cultivated at south eastern part of Asia viz. Australia and Malaysia. This variety is more often used as a black tea and contains more quantity of phenolic compounds as compared with other known varieties like *Camellia sinensis* var. *sinensis* which is a native plant to China [1]. *Camellia sinensis* var. *sinensis* also called China tea used to make white and green tea, majorly. This shrub is extensively grown in colder zones of globe namely China and Taiwan. Java bush (*Camellia sinensis* var. *cambodiensis*) is another known variety of tea, but not used so extensively or more common commercially unlike Assam and China tea [1, 27]. As per the studies conducted by Mcnaught [28], the tea obtained from *Camellia sinensis* leaves has also shown potential credibility against *Brucella* and organism responsible to cause typhoid fever [28, 29].



Figure 1 (a) Cultivation of tea shrubs near Kangra hills (b) Foliage of *Camellia sinensis* shrub (c) Leaves collected from *Camellia sinensis* and dried (d) Dark coloured black tea obtained from the leaves of *Camellia sinensis*

Constituents present in tea and their medicinal properties

A research conducted by Adnan et al. has suggested the predominant amount of moisture, protein, fat and crude fiber in green tea, whereas black tea was found to have higher concentration of ash and water extracts [30, 31]. There are approximately 4000 chemical compounds known to be present in tea. Among all known constituents, polyphenols are speculated to be highest in quantity [31]. Catechins are the basic flavonoids present in green and white tea with potential anti-oxidative properties. Some of the other compounds documented in tea include theanine, caffeine, theophylline, theobromine, negligible carbohydrates, fat and proteins [32]. Tea is a very rich source of almost all vitamins (including A, E and K) and minerals (P, Fe, Zn, Cu, Mn, Mg etc.), but rarely addresses the presence of vitamins C and B. Tea has more potent known anti-oxidative properties as compared with Vitamin C and E [33-35]. The various chemical constituents present in tea shoot includes total polyphenols, flavanols, epigallocatechingallate (EGCG), epicatechingallate (ECG), epigallocatechin (EGC), epicatechin, catechin, gallic catechin, flavonol glycosides, leucoanthocyanins, polyphenolic acids, caffeine, theobromine, theophylline, amino acids, monosaccharides, polysaccharides, cellulose, hemicelluloses, pectins, lignin, protein, lipids and chlorophyll pigments [32]. Catechins present in green tea are the flavanols consisting of six primary compounds such as epicatechin, gallategallaogatechin, ECG, catechin, EGC and EGCG [36, 37]. Studies have reported that a half cup of tea contains 45 milligrams of EGCG; whereas 7.5 ml/100 ml and 35 ml/100 ml EGCG is present in a half cup of black and green tea, respectively [5, 24, 38-40]. Polyphenols present in green tea prevent free radical formation by chelation of copper and iron metals; interact with oxidative enzymes to exhibit beneficial influence on protein phosphorylation. Whereas flavonoids inhibits P-450 catalyzed activity by acting pro-oxidants like ascorbic acid and tocopherol [41]. EGCG is most common and active polyphenol found in tea leaves. This active constituent has already been studied for its well-known beneficial properties. Some of the potential activities and mode of action of this constituent are summarized in **Table 2**.

Table 2 Medicinal activities and associated mode of action of Epigallocatechingallate (EGCG)

S. No	Properties	Mode of action	Reference
1.	Atherosclerosis inhibition	Modulate the cholesterol metabolism	[42]
2.	Anti-cancerous activity	Inhibit the initiation, promotion and progression of neoplastic cells in different stages of cell cycle in prostate cancer	[43]
3.	Anti- microbial activity	Limit the replication of <i>Candida albicans</i> , <i>Aspergillus fumigatus</i> , <i>Helicobacter pylori</i> , <i>Salmonella</i> spp. etc.	[44]
4.	Bone diseases (Rheumatoid arthritis and osteoarthritis)	Inhibit IL-1beta induced inflammatory response	[45]
5.	Anti-viral activity	Inhibition of JAK/STAT1 pathway of IFN gamma, bind to the HA unit of influenza viruses. Suppress the replication of Epstein-Barr virus, Adenoviruses and Herpes simplex virus also	[46]
6.	Anti-allergic action	Inhibition of tyrosine phosphorylation of cellular proteins thereby inhibiting mast cell degranulation	[47]
7.	Anti-HIV activity	Bind with CD-4 receptors and block binding with glycoprotein CD120	[48]
8.	Alzheimer's disease	Bind with hydrogen peroxide and beta amyloid protein	[49]

Tea exhibits anti-bacterial properties against various bacteria such as *Staphylococcus*, *Streptococcus*, *E.coli*, *Salmonella* spp, *Enterococcus* spp. etc. Polyphenols present in tea inhibits the growth of pathogenic bacteria of gut and regulates the friendly proliferation of commensal microorganisms. ECG and EGC are the major catechins present in tea and are found to show antimicrobial mechanisms [25]. Green tea inhibits the binding of viruses, prevents their entry to the cell, and protects the integrity of DNA and RNA to reduce mutations which can lead to drug resistance [1]. Polyphenols found in green tea effectively slow down the process of aging by protecting the serum lipids and proteins from the oxidative damage [5]. Tea has dual effect to prevent dental caries as it exhibits anti-bacterial properties and the polyphenols found in tea have anti-plaque properties [1]. EGCG has shown antiviral properties by inhibiting JAK/STAT1 pathway of IFN gamma, bind to the HA unit of influenza viruses, suppress the replication of Epstein-Barr virus, adenoviruses and herpes simplex virus. Ingestion of tea for longer duration can prevent the development of atherosclerosis as reported by Miura et al. [46] and Geleijnse [42], by preventing the oxidation of LDL cholesterol. The constituents present in tea also contribute to reduce the chances of coronary heart disease [50]. EGCG present in the tea has potent anti-allergic response [1], therapeutic potential against Parkinson's and Alzheimer's disease [51] and reduce the chances of arthritis as it protects chondrocytes from IL-1 β induced

inflammatory response [25]. Catechins present in tea enhances the metabolism of the body, boosts the immune system and lower down the anxiety. Green tea has shown potent synergistic antimicrobial activities with various antibiotics and expected to reduce the drug resistance problems (**Table 3**).

Table 3 Action of green tea in combination with other compounds against microorganisms/disease conditions [52-55]

S. No	Combination	Anti-microbial activity against
1.	Green tea + Penicillin	<i>Bacillus subtilis</i>
2.	Green tea + Probiotics	<i>Staphylococcus aureus</i> and <i>Staphylococcus pyogenes</i>
3.	Green tea + Levofloxacin	Enterohemorrhagic <i>E. coli</i>
4.	Green tea + Chloramphenicol	<i>Shigella dysenteriae</i>
5.	Green tea + Gentamicin	<i>Shigella dysenteriae</i>
6.	Green tea + Methicillin	<i>Shigella dysenteriae</i>
7.	Green tea + Nalidixic acid	<i>Shigella dysenteriae</i>
8.	Green tea + Rasagaline	Parkinson disease

Anti-carcinogenic action of tea

Tea has high concentration of catechins which plays an important role in cancer prevention as it exhibits similar structural properties as chaperones and their interactions with target molecules [56]. In various studies, it has been reported that green tea counters the proliferation, migration and angiogenesis of tumor cells. Green tea can lower down the risks of cancer of various organs such as colon, lung, small intestine, esophagus, stomach, kidney and mammary gland. The anti-carcinogenic effect of tea depends upon duration of drinking green tea, the number of cups consumed per day and EGCG content present in the tea. The green tea has been found to have anti-neoplastic action against prostate cancer by reducing the testosterone receptor activity of the cells [58]. The suppression of cutaneous tumours is associated with the alteration of expression of p53 and p21 stimulated by catechins present in green tea [58, 59]. Green tea has already been reported to inhibit the proliferation of chemically induced tumours in rats. EGCG in tea is found to inhibit the progression of various types of tumours by inducing the apoptotic mechanisms and thereby the proteins like Bcl-2, Bax etc. released through the mitochondrial disruption and finally destroy the tumorous cells [60, 61].

Table 4 Mechanism of action of tea constituents against carcinogenic mediators

S. No.	Activity	Mode of action	Reference
1.	Inhibition of transcription factors	Inhibition of activator protein-1 (AP1)	[62-65]
		Inhibition of NF- κ B nuclear factor	[66, 67]
2.	Inhibition of receptor tyrosine kinase (RTKs) pathway	EGCG down regulates the production of VEGF by blocking the STAT-3 and NF- κ B pathways Catechins suppress the RTKs and thereby the signals to phosphatidylinositol-3 and RAS pathways and finally prevent the proliferation of cells	[67-70]
3.	Modulation of immune system	Enhancement of cell mediated (CMI) and humoral mediated immunity (HMI) EGCG reduces the levels of tumour necrosis factor (TNF)	[71, 72]
4.	Anti-oxidant activity	Catechins act as a potent free radical scavenger	[73, 74]
5.	Activation of apoptotic pathways	The levels of Bcl-2 and Bcl-XL are reduced; while the levels of caspase-3 and Bax are elevated by EGCG EGCG induces apoptosis via activation of ROS, caspase-3 and caspase 9	[75-78]
6.	Other beneficial effects	EGCG suppresses the epigenetic mechanisms via modification of histone proteins in tumour cells The preventive action of the constituents present in tea is seen against blood pressure, obesity and anxiety	[3, 79]

The constituents like EGCG and polyphenols are documented to have anti-proliferative potential against mammary tumours via inducing apoptosis of neoplastic cells and also found to prevent metastases of tumourous cells [57, 80, 81]. The activity of some of the tumour suppressor genes (cyclin-dependent kinase inhibitors like p27 and p21; p53) is also found to be stimulated by EGCG and thereby again contributing to prevent the carcinogenesis. The anti-proliferative activity of EGCG is also influenced by the other constituents present in tea and these constituents are reported to serve synergistically with EGCG [57]. EGCG is also reported to inhibit the activity of telomerase enzyme, which is usually found to be increased during cancer progression [82]. The angiogenesis and metastases of different kind of tumours is reported to be regressed by EGCG through the inhibition of vascular endothelial growth factors (VEGF) and various matrix metalloproteinases (MMPS-3, 9), respectively [83-85]. EGCG is speculated to alter the DNA methyltransferase and transcription factor hypoxia-inducible factor, thereby leading to the direct inhibition of DNA hypermethylation and angiogenesis, respectively. The neovascularization or angiogenesis is a key factor associated with tumour development and the suppression of this mechanism by EGCG is mediated by STAT3 pathway blockade [86, 87].

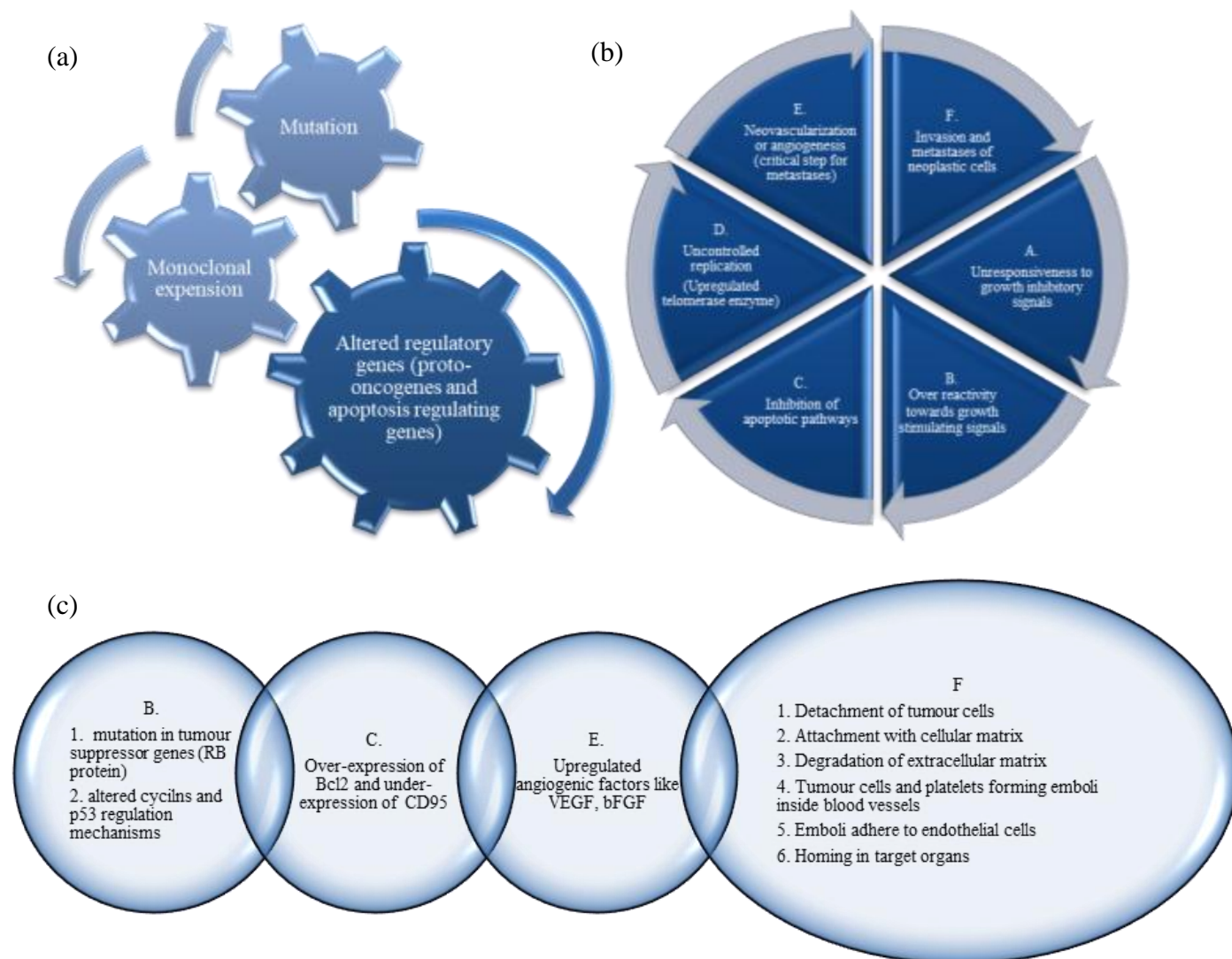


Figure 5 (a) Steps in carcinogenesis (b) General mechanism in carcinogenesis (c) Basic points related with steps B, C, E and F depicted in Fig 5b

Many experimental studies conducted on rat/animal models have shown adverse effects of tea due to oxidative damage to vital organs like liver and pancreas [88]. The negative impact of caffeine and methylxanthine present in tea has been documented to alter the iron availability and causing the accumulation of aluminium. Caffeine and methylxanthine in tea are observed to contribute to neurological alterations in animals, as a consequence of cytotoxicity produced by them [89-91]. Thus, in spite of having several medicinal benefits of tea, only the recommended validated doses must be consumed on routine basis, in order to check the maladaptive syndromes in human beings

Conclusion

Tea is one of the most commonly used affordable beverages having a magnified range of chemical constituents with versatile beneficial effects to the body. This shrub has been found to limit many pathological and physiological alterations in the body and also reported to exhibit synergistic effect with various known compounds. The various health benefits of this shrub viz. anti-carcinogenic, anti-inflammatory, anti-oxidative, anti-arthritis potential etc. are due to the multiple constituents evident in this plant. The main aim of present article is to comprehend the immense health benefits of tea against various health ailments and to summarize the phytochemical constituents present in this wonderful medicinal herb.

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