BENEFICIAL PROPERTIES OF TEA ON HUMAN HEALTH: A MINI REVIEW

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ABSTRACT

Green tea is un-fermented product of Camellia species. Leaves of Camellia sinensis and Camellia assamica are used for the production of green tea but C. assamica is widely used for black tea. It contain many active compounds such as theaflavins, tea polyphenols, epigalloctocatenin (EGCG), epicatechin (EC), epigallocatechin (EGC), gallo-catechin gallate (GCG) and tea catechins. Tea possesses antimicrobial activity against Staphylococcus aureus, Bacillus cereus, MRSA, Clostridium perfringes, Vibro parahaemolyticus and Heliobacter pylori. It also bears antioxidant, immunomodulatory and anti-cancerous properties. It also works to LDL oxidation and shows hypoglycemic action of tea polyphenols. Therefore, both the species of Camellia can be useful to protect human beings from various ailments.

KEYWORDS: Camellia sinensis, Camellia assamica, Epigalloctocatenin (EGCG), Epigallocatechin (EGC), Galloocatechin gallate (GCG)

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INTRODUCTION

Tea (*Camellia*) is one of the most popular and liked beverages in India and other countries due to its health benefits. Among many species of *Camellia*, only two species are widely used as beverages. *Camellia sinensis* L. (Chinese tea) originated from China and *C. assamica* L. (Indian tea) from Assam (India). *Camellia* is a branched tree belonging to the family Theaceae. *C. sinensis* is a dwarf, slow growing and shrub like plant having small, erect narrow, serrate and dark green leaves. But *C. assamica* is a tall and quick growing tree having large, horizontal, broad, mostly non-serrated and light green leaves. The phenolic compounds of tea plants vary due to their harvesting, handling and storage conditions. The black tea is the fermented product, while the green tea contains about one-fourth caffeine as compared to black tea. Green tea is not oxidized by oxidation process, hence its polyphenols are preserved in leaf tissues. Leaf harvesting, processing, geographic location and tea preparation affect the tea catechins.

Green tea is an unfermented product which is pale in colour with bitter flavor. It is prepared by organic processes. Much emphasis has been paid on its use due to its health improving traits such as brain health, lowering blood sugar level, reducing cholesterol level, promoting oral health, maintaining body weight, supporting skin health, lowering blood pressure, reducing the risk of cancer, keeping bone strong and fighting against ageing.

According to the medicine theory of Chinese, it has a cooling characteristic due to sweet and bitter taste. In laboratory studies proved tea showed some immunological properties. Recently, it has been approved for health benefits in some countries like the United States. It has also been reported as the most preferable drink. Green tea is a non-fermented beverage that contains high amount of bioactive compounds such as EGCG (epigallocatectenin gallate), flavanols, flavadiols, and phenolic acids and the most active content which is 10% of dry weight. Six types of catechins bearing biological activity have been reported in green tea that bears the biological activity such as (+)-catechin (C), (-) epicatechin (EC), (-)-epigallocatechin (EGC), (-)-gallocatechingallate (GCG), (-)-epigallocatechin gallate (EGCG) and epicatechin gallate (ECG). EGCG is the most common and abundant component found in green tea with about 59% catechins. Green tea consists of about 13.6% ECG and 6.4% EC. It acts as antioxidant and enhances immune system to play a significant role against foreign bodies. EGCG has potent bioactive compound that performs activity against cancer and cardiovascular diseases.

Tea has also been found to be effective in the clinical treatment of amoebic dysentery, bacillary dysentery, gastro-enteritis and hepatitis. The antibacterial activity of *C. sinensis* against food borne bacteria and enteric pathogenic bacteria such as *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus cereus*, etc. has been reported by various researchers. The plant derived phytochemicals provide a useful intervention to reduce pathogenic bacteria in food. The antimicrobial activities of green tea catechins inhibit the growth of *Bacillus cereus*, *Salmonella typhi* and *Salmonella typhimurium* exhibited greater susceptibility to the alcoholic extracts of *C. sinensis* than *Salmonella paratyphi*. The ECGC present in
green tea extract were found inhibitory to *Staphylococcus aureus*, a Gram-positive toxin producing food borne bacteria, contaminates food and affects skin, lungs, heart and other organs.

1. **Processing of Tea Leaves**

   The green and black teas are the products of the same plant but the basic difference lies in their processing. Black tea is the fermented product and undergoes fermentation process before drying whereas black tea is made by oxidation process. After plucking, leaves are subjected to the process of withering (removal of moisture by air flow), pre-conditioning, fermentation and drying which are involved to make a finished product. The colour of tea leaves changes after all the steps from green to copper brown and gives a floral smell. The leaves are heated immediately, mechanically wound, compressed and then shade dried to preserve their natural components and colour.

2. **Black tea processing**

   The major steps of black tea processing are as below:

   Fresh leaves → Withering → Rolling by tea roller or CTC → Fermenting → Drying

   After following these steps, the fermentation step plays a crucial role in maintaining quality of black tea. The oxidation process predominantly oxidizes the catechins present in tea leaves. The moisture content in the tea leaves is evaporated and leaves become flaccid. The black tea is made by a CTC (crushing, tearing, curling) machine. In many countries such as India, Kenya and Sri Lanka, CTC process of tea making are being followed. But, China follows its traditional “orthodox rollers” process. For the fermentation of black tea, warm temperature (25-35°C) and high humidity (~95%) are required. The fermentation process depends on the variety of plant and age of tea leaves. It takes half hour to three hours to complete the fermentation process. Generally, CTC machine takes less time (30 to 60 minutes), while orthodox roller takes 2-3 hours.

3. **Green tea processing**

   The major steps of green tea processing are as below:

   Fresh leaves → sorting and cleaning → withering (often) → panfrying or steaming → drying or rolling shape

   The discrete feature of green tea processing is that the leaves are never subjected to fermentation process. Instead, the leaves are steamed (95-100°C) for 30-45 seconds immediately after harvesting, to inactivate the enzymes and protect degradation of vitamins. This is why the green tea contains more vitamin contents in comparison to black tea. The fresh leaves contain 78-80% polyphenols, which decreases to about 10% during rolling process. The drying process is necessary to preserve the aroma and storage capacity. Aracha are the type of tea made by dried and rolled leaves and finally roasted that cut into the final product for the market.

4. **Chemicals Present in Tea**

   Since the ancient time, tea is the most likeable drink but the search of chemicals in tea has been started in the modern time. Tea is made by unique components, for example theanine (an amino acid) found in tea and other amino acids. Catechins are the most prominent bioactive compounds present in tea along with vitamin C. During 1927-1935, Tsujimura identified epicatechin gallate, epicatechin and epigallocatechin.
Table 1: Polyphenols present in *Camellia* species.

<table>
<thead>
<tr>
<th><em>Camellia</em> species</th>
<th>Polyphenols</th>
<th>(+)-C</th>
<th>EC</th>
<th>EGC</th>
<th>ECg</th>
<th>EGCg</th>
<th>Theanine</th>
<th>Caffeine</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>C. sinensis</em></td>
<td></td>
<td>0.07</td>
<td>1.13</td>
<td>2.38</td>
<td>1.35</td>
<td>8.59</td>
<td>1.21</td>
<td>2.78</td>
</tr>
<tr>
<td><em>C. assamica</em></td>
<td></td>
<td>0.02</td>
<td>1.44</td>
<td>0.35</td>
<td>3.356</td>
<td>12.10</td>
<td>1.43</td>
<td>2.44</td>
</tr>
</tbody>
</table>

(+)-C = catenin, EC = epicatechin, EGC = epigallocatechin, ECg = epicatechin gallate, EGCg = epigallocatechin gallate

Green tea contains natural components such as polyphenols, vitamins, theanine, caffeine. The tea polyphenols include epigallocatechin (EGC), epicatechin (EC), epicatechin-gallate (ECg), epigallocatechin-gallate (EGCG), catechins and their derivatives. Theanine is the most common amino acid found in green tea that play a significant role for human health. Metabolites are found in green tea that are affected from various biological activities as well as geographical factors such as climatic conditions, genetic strain of tea, rainfall, soil, temperature, growth altitude, soil and plucking time.

Table 2: Seasonal changes in contents of polyphenols depending on tea species (g/100g dried leaves).

<table>
<thead>
<tr>
<th>Polyphenols</th>
<th><em>C. sinensis</em></th>
<th><em>C. assamica</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)-Catechin(C)</td>
<td>Tr*</td>
<td>0.07</td>
</tr>
<tr>
<td>(+)-Gallocatechin (GC)</td>
<td>Tr*</td>
<td>Tr*</td>
</tr>
<tr>
<td>(-)-Epicatechin</td>
<td>1.50</td>
<td>1.50</td>
</tr>
<tr>
<td>(-)-Epicatechin gallate</td>
<td>2.80</td>
<td>4.10</td>
</tr>
<tr>
<td>(-)-Epigallocatechin</td>
<td>4.00</td>
<td>3.70</td>
</tr>
<tr>
<td>(-)-Epigallocatechin gallate</td>
<td>8.80</td>
<td>12.20</td>
</tr>
</tbody>
</table>

Tr* = trace

5. **Tea as a Wonder Drug**

Being a most preferable beverage all over the world, tea is used as panacea to cure many diseases. Since ancient times, Chinese used to take tea as a source of nutrients to improve their health, to cure headache, stomach problems, fever and to improve digestion. Some of the studies on the effect of green tea used to cure several ailments. Tea contains a curative power that is consumed in all over the world. In earlier time, Chinese literature mentioned its uses as a remedy for a wide range of illness. The great significance of tea for nomadic or for Tibetans in peripheral China is something special even today. These people seem to consume much of their vital elements from tea. The Buddhist priests not only found the beverage useful for keeping them awake during their meditation, but also found that it impart them of their physical
tiredness. Tea drinking gradually spread from being popular not only among the priests and religious people but also among the common people.18

A. Effect on intestinal microflora

Intestinal flora has its own importance because it affects many factors pertaining to human health. These factors include immune response, age factors, cancer and infection.

Our diet affects the intestinal microflora. Well-balanced diet promotes beneficial bacteria and removes the harmful ones. However, tea polyphenols (especially black tea polyphenols and green tea catechins) show antimicrobial effects against harmful microorganisms and enhance the growth of useful microorganisms. The tea polyphenols present in the intestine before being excreted in the feces and reduce the fecal odour. The antimicrobial action has not been observed against lactic acid bacteria (LAB). Experimentally proved that 5-6 cups/day of tea surpass the bowel condition in animals as well as in humans.

Fig 1. Effect of intestinal flora on the host.

B. Tea as a Immunomodulator

Tea acts as immunomodulator, helps to regulate the immune system of the normal individual but it also helps to maintain normal physiological function in altered conditions. Immunomodulation is the process by which the immune system is enhanced through certain substance known as immunomodulators. According to the Ayurveda, the concept of ‘Rasayana’ is based on modulation of immune system to control the diseases. The word ‘Rasayana’ defines the property of the plant that rejuvenate the immune system. Many plants are used as a ‘Rasayana’ to manage the neurogenerative disease and used as rejuvenators 25. The therapeutic effects of natural constituents are beneficial for human health.

(i) Antimicrobial effect

The antimicrobial activity of tea is due to its polyphenols which inhibit the growth of a large number of food borne pathogens such as Vibrio parahaemolyticus, Clostridium perfringens, Bacillus cereus, Staphylococcus aureus, etc. The methicillin-resistant Staphylococcus aureus (MRSA) is a most common pathogen causing disease in human where patients have depressed
immune system. It is commonly present in the environment and create problems related to the health such as inflammation, nose, pharynx and intestinal tract (food poisoning), septicemia.  

Tea polyphenols are very effective antibacterial compounds that act against MRSA. The EGCg polyphenol has been reported to show bactericidal activity on MRSA.

**(ii) Antioxidant property of tea**

Antioxidants are present in various kind of food such as vegetables, fruits, etc. and are made up of polyphenols. Oxidative reactions not only occur in our body, but some compounds also help to enhance the oxidation reaction in the body. Different antioxidants are derived from natural and artificial sources. Catechins also have antioxidant property derived from tea leaves are safe. Catechins and other four components of tea such as (-)-epicatechin (EC), (-)-epigallocatechin (EGC), (-)-epicatechin gallate (ECg) and (-) - epigallocatechin gallate (EGCg) revealed their antioxidative activity. The order of antioxidative property of compounds are EGC >EGCg> EC >ECg. The antioxidative property of compounds increases when hydroxyl group is present in 5’ position. Green tea leaf extract containing catechins showed superoxide radical activity and hydrogen peroxide. The EGCG, EGC and ECG compounds present in tea have ability for good lipid oxidation-inhibition and lipoxygenase inhibition ability. Tea leaves containing theaflavins (TF-2 and TF-1) showed weak activity of lipid oxidation but strong ability to inhibit lipoxygenase. Consuming green tea is the effective way to use the antioxidant to reduce the undesirable compounds and off-flavors of food.

**(iii) Anti-cancerous**

Tea polyphenols reduce and inhibit the growth of cancer by making strong bonds between aminoacids but at the low concentration it inactivates the activity of harmful enzymes and inactivates the viruses. Kadaet al., 1986 have reported bioantimutagens activity in tea leaves. Tea polyphenols have ability to prevent cancer. The most active component is (-)-epigallocatechin gallate (EGCg). Theaflavins present in black tea act to inhibit the action of cancerous cells.

C. Epidemiological Effects

Tea polyphenols inhibit the action of tumour development both in vitro and in vivo experiments. It also shows good results against the cancer patients and enhances their immune system. A reduction in the rate of cancer by drinking over 10 cups of green tea by patients has been reported by Kono et al., 1988.

*Heliohacter pylori* is a causal agent of stomach cancer. It affects in the epidermal layer of stomach damaging the membrane and causing peptic ulcers. *H. pylori* metabolizes urea and produces ammonia that make the environment acidic in the stomach and thereby enables the survival of bacteria. Meanwhile, natural compounds like tea catechins are used in place of antibiotics to cure the diseases.
D. Revitalization of antibiotics with tea polyphenols

Due to continuous use of antibiotics, several human pathogens have developed multidrug resistance. But, in-vitro tests have proved the revitalization with the addition of tea catechins. The antibiotic oxacillin enhances its antimicrobial property against MRSA and gave effective results.\textsuperscript{32}

It has been reported that clinical MRSA strain showed resistance upto 2000 µg/ml oxacillin but research showed that addition of green tea catechins (GTC) reduces the number of resist MRSA. Therefore, oxacillin regained its antibacterial property with green tea at 10 µ/ml. The addition of tea polyphenols effectively revitalized antibiotics against resistant bacteria. Some antibiotics show neither synergistic activity nor antimicrobial activity such as kanamycin against MRSA.\textsuperscript{32}

E. Induction of apoptosis

Apoptosis is a process of cell death that occurs naturally in multicellular organisms. Hence, it is also known as programmed cell death. Changes occurs in cell morphology including cell shrinkage, nuclear fragmentation, blebbing, chromatin condensation while in necrosis, the cells and tissue undergo inflammation, rupture and bloating. Isemura \textit{et al.}, 1997\textsuperscript{10} reported the occurrence of apoptosis in metastatic mouse Lewis lung carcinoma cell, LL2, LL3 (1×10^6). Thereafter, tea infusions (2g/ml) given to the mice suffering from tumour inhibited the growth and number of the tumours developed in lungs almost half as compared to control group of animals.\textsuperscript{38}

The chemotheraphies of breast cancer of animals is a cost-effective approach. Interestingly the chemopreventive efficacy of black tea polyphenols Polyphenon-B has been found to inhibit its effect in prophase of 7,12-dimethylbenz[a]anthracene (DMBA) that induced mammary cancer by employing the xenobiotic-metabolizing enzymes, apoptosis, angiogenesis, proliferation of cell, cellular redox status used as biomarkers of chemoprevention. Polyphenon-B recommended as dietary that effectively decreased the level of mammary tumours as revealed by the alteration of xenobiotic-metabolizing enzymes and oxidant–antioxidant status, cell proliferation inhibition, angiogenesis and induced apoptosis. Polyphenon-B also employs multifunctional inhibitory effects on DMBA-induced mammary carcinogenesis and act as a potential chemopreventive agent.\textsuperscript{20}

The black tea theaflavins and green tea catechins have potential to inhibit the anti-apoptotic Bcl-2 family proteins. The tea polyphenols show anticancer activity and play a crucial role in antiapoptotic pathway, which is known as the inducer of many human malignancies.\textsuperscript{26} Tea is a good source of compounds with antimicrobial, antioxidant, antimutagenic and anticarcinogenic activity. Most of the populations in the world are suffering from lung infection. The black tea and their polyphenols used as chemopreventive intervention may also be used to reduce death from lung cancer. The compounds of tea such as
theaflavin, theasinensin and theaflavin-3-gallate (TF-1 and TF-2a,b) showed strong inhibitory effects against human histolytic lymphoma U937, but less effective against human acute T-cell leukemia Jurkat, EGCG and TF-3\textsuperscript{15}. The polyphenols affect the mechanism inducing apoptosis, caspase activation and DNA fragmentation. Tea polyphenol treatment helps to induce the activity of caspase-3, enhanced proteolytic cleavage of poly (ADP-ribose)-polymerase (PARP), but did not show activity for caspase-1. Tea theasinensin A promotes the loss of mitochondrial cytochrome C into the cytosol and induce the activity of caspase-9. Theasinensin A has also been found effective in degradation of DFF-45 (an inhibitor binding to DNase) that allow the entry of caspase-activated DNase to enter in the nucleus and to degrade chromosomal DNA. Theasinensin A and tea polyphenols provide a significant mechanism for the chemopreventive measures of cancer. Blockage of mitotic signal transduction through tea polyphenols desperately is explained by Lin et al., 2005\textsuperscript{22}.

**Fig 2.** Mechanism of anticarcinogenesis by tea polyphenols.

### E. Suppression of LDL oxidation by tea polyphenols

Low-density lipoprotein (LDL) is responsible for antherogenicity\textsuperscript{14}. It is reported that vitamin E contains antioxidant property which enhances resistance to antherogeneity. It included in dietary habit lowers the occurrence of coronary artery disease where mortality occurs due to intake of flavonoids in dietary \textsuperscript{7}. Its low mortality rate in French is due to intake of high-fat diet red wine (Paradox) on regular basis. The mortality rate of coronary artery disease in Japan and China is low as
compared to West where people use tea as beverage. Ishikawa et al 1997\textsuperscript{11} explained the potential of tea polyphenols \textit{in vitro} and \textit{in vivo} in suppression of LDL as follow:

\textbf{In vitro experiment}

\textit{In vitro} experiment shows that tea polyphenols play a significant role to suppress the LDL level in the blood. Blood plasma was treated with polyphenols present in tea in order to decrease and adsorb LDL particles and then measure the oxidation capacity. Healthy male blood was centrifuged to obtain serum, which in turn was treated with tea components such as tea catechins and theaflavins. The results showed that tea catechins and theaflavins significantly suppressed the TBARS and lipid peroxides formation in the LDL sample\textsuperscript{6}.

\textbf{In vivo experiment}

Healthy male having normolipidemic volunteers were divided into two groups. First group consumed tea about (11g/750 ml/day) and the other group consumed the same amount of water. Samples of blood were collected at the start and at the end of the experiment. After four weeks, the lag time of tea consumption group increased before LDL oxidation but no significant changes were observed in second group in terms of HDL cholesterol, plasma total cholesterol, triglycerides, apolipoprotein B. ECGg component of tea are responsible to suppress the LDL oxidation\textsuperscript{4,6}.

\textbf{G. Effect of tea polyphenols on hypoglycemic}

Diabetes and obesity are the most serious problems in recent years due to uncontrolled dietary habit. In diabetes, ingested sugars are not fully utilized as energy source due to lack of insulin. Therefore, it remains in the bloodstream in the form of glucose. The concentration of glucose increases in blood rendering the vein walls fragile and renal failure, heart attacks stroke and high blood pressure. If diabetes is not carefully controlled it can also damage eyes, kidneys and lungs. The control of diabetes, requires the control the obesity and intake of less carbohydrates. Insulin injections are recommended for diabetic patients. Exercise may also include to control diabetes. The primary aim to follow various dietary plans is to reduce absorption of sucrose and starch in case of obesity and diabetes. In any case, intake of tea polyphenols or tea can achieve to reduce the risk of diabetes and obesity. Tea polyphenols make a balance in the activity in the body and inhibit the digestive enzymes such as $\alpha$-amylase or sucrase by tea polyphenols\textsuperscript{4,6}.

\textbf{In vitro enzyme inhibition}

Green tea contains many active compounds such as polyphenols and catechins (EC, EGC, ECg, EGCg) but black tea contains theaflavins (TF1, TF2A, TF2B, TF3). These compounds were tested for the enzyme inhibition activity of $\alpha$-amylase of human saliva. $\alpha$-amylase activity was determined to separate the amount of maltose. Crude sucrase was obtained by scraping the small intestinal mucosal brush border in rats. Sucrase activity is determined by measuring the amount of glucose separated from sucrose\textsuperscript{4}. The inhibition of enzymes by tea polyphenols plays a significant role in suppression of plasma glucose levels. Green tea increases insulin secretion or the prevention of glucose absorption from the bloodstream into the body. Tea polyphenols are very effective against the hypoglycemic activity occurring in humans\textsuperscript{6}.

\textbf{H. Toxicology}
Tea catechins present in green tea play a major role in daily tea drinkers. About 2 g of green tea present in an ordinary amount of tea bag is brewed by hot water. An average of 80 mg of catechins are extracted in a brew. The heavy tea drinkers consume more than 10 cups per day consuming about 1 g of tea catechins per day. Consequently, the heavy tea drinkers had decreased serum concentration of total cholesterol, LDL cholesterol, triglycerides, and an increased proportion of good cholesterol (HDL cholesterol) as compared with the less eagerly drinkers.\(^{16}\)

**Acute toxicity test**

Tea catechins were applied by orally or intraperitoneally to determine the lethal dose of tea polyphenol samples. Polyphenon 60 (EGCg) are widely used because it contains about 60% catechins, therefore its LD50 is 2,856 mg/kg. It can be interpreted that there is no lethal acute toxicity of tea catechins after administering the same dose (143g/50 kg body weight, which is equal to 1,000 cups of catechins in tea at single time) as given to humans (Matsumoto., 1999).

**Chronic toxicity test**

To determine the safety measures of tea catechins consumption on whole life, experiment done on rats proved that tea catechins did not show harmful effect on human health. Tea catechins were consumed by the groups of five weeks old rats were fed in concentration of 0.5%, 1.0% and 2.0% of Polyphenon 70STM capsules. About 2.0% concentration fed for a period equivalent to 100 cups consumed every day. After six months, consumption of tea catechins, rat group increases digestion capacity of food and balances body weight as compared with control.\(^{24}\)

The consumption of huge amount of catechins does not have side effects on human health. Polyphenon (catechin capsules) has been given to patients suffering from *H. pylori* and Hepatitis C virus during hundreds of years under the administration of doctors, without any harmful effects. Tea catechin (900-1200 mg) taken in a daily routine does not pose toxic effect on human health.\(^{38}\)

**6. Storage**

Green tea, black tea and oolong tea get deteriorated by heat and moisture. But green tea are more sensitive than black or oolong tea. Therefore, it is necessary to reduce the moisture content by 2-3% during refining process. Nitrogen gas is used to protect the tea from deterioration through oxidation. The finished product should be stored in dark condition at 5°C, usually in refrigerator.\(^{38}\)

**CONCLUSION**

Beneficial effects of tea are being increasingly recognize day by day, it could be recommended that consumption of tea on regular basis. Now-a-days, tea is one of the more consuming beverage for the cure and treatment of many diseases such as cancer, gastrointestinal and skin diseases etc. and subsequently, it is being studied the beneficial properties of tea all over the world. Number of studies demonstrated animal models proved that it contains many health benefits such as antiviral, antioxidant, antibacterial, anti-inflammatory properties. It is inexpensive beverage are more energetic and contain very less amount of caffeine. Bioactive compounds present in tea play a significant role to decrease the risk factors that induce cancer. It is a natural and herbal component that has no side-effects on human health.
REFERENCES:


[38] Yukihiko Hara (Tokyo Food Techo Co. Ltd), Tokyo, Japan CRS press, 2001- Technology and engineering pp-280.

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