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Bioavailability and Efficiency of Tea Catechins as an Antioxidant

– Review –

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Abstract

Tea is a pleasant, popular and safe beverage in the world. During the past decade, epidemiological studies have shown that tea catechins intake is associated with lower risk of cardiovascular disease. Tea provides a dietary source of health-promoting components to help humans reduce a wide variety of cancer risks and chronic diseases. The antioxidative activity of tea-derived catchins has been extensively studied. The antioxidant effect is a synergistic action between catechins e.g. EGCG, EGC, ECG, EC, pheophytins *a* and *b*, and other components in tea leaves, which are more bioavailable for human body. Green tea has a higher content of catechins than other kinds of tea. Green tea extract with hot water has high potential and more efficiency to reduce cancer risk than any other tea products or pure EGCG. Protein, iron, and other food components may interfere with the bioavailability of tea catechins. Interaction of catechins with drug affects the cancer-preventive activity of some cancer-fighting medication. Further studies are required to determine the bioavailability of tea catechins and cancer-preventive functionality.

Key words: bioavailability, cancer, catechins, polyphenol, tea

INTRODUCTION

Tea is consumed as one of the most popular beverages throughout the world. An estimated 2.5 million metric tons of dried teas are manufactured annually. Its extracts have been prepared in a variety of physical forms such as soft extracts and powders. It is widely available in a range of foods and beverages. The majority of tea beverage is prepared from three types of manufactured tea: green tea, oolong tea and black tea. Green tea is prepared when the fresh leaves are processed rapidly to prevent "fermentation". Oolong tea is partially fermented tea products and has a unique flavor. Black tea is made by crushing and drying fresh tea leaves to cause "fermentation" prior to final processing. Of all the tea consumed in the world, 78% is black tea which is usually consumed in the USA, Europe, Africa and India; 20% is green tea which is commonly consumed in Asian countries, especially in China and Japan; and 2% is Oolong tea which is produced in Southern China. Extracted from black tea, iced tea accounts for 85% of tea consumption in the USA. Tea is usually prepared from tea bags infused in hot water in a proportion of 1 g dried leaves to 100 mL water. The resulting tea extract has a solid concentration of 0.35%. Green tea infusion contains approximately 30% catechins and 2% flavonols. Black tea infusion contains approximately 9% catetins, 4% theaflavins, 3% flavonols.

The possible cancer-preventive activity of tea is receiving a great deal of attention. The anticarcinogenic and antimutagenic properties of tea were first elucidated two decades ago. Some epidemiological studies suggest that regular tea consumption reduces cancer risk in humans (1). Studies in mice have shown that the oral consumption or topical application of catechins constituents from tea affords protection against carcinogenesis induced by chemicals or ultraviolet radiation (2). Other animal studies also showed that tea affords prevention against chemically induced carcinogen-induced malignancies in lung, forestomach, esophagus, duodenum, pancreas, liver, breast, and colon (3). Although tea leaves contain more than 2000 components, most attention has been paid to the tea catechins. Catechins are the major components of tea polyphenols, and constitute about 30~42% of the dry weight of green tea, and 9% of the dry weight of black tea. The major catechins in fresh teal leaves are epigallocatechin gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG) and epicatechin (EC). The composition varies depending on the location of cultivation of tea plant, variety of plant, season of harvest, and manufacturing process. Catechins are colorless, water soluble compounds which impart bitterness and astringency to tea infusion. Almost all of the characteristics of tea such as taste, color, aroma are associated with modification to the catechins. The usual composition is 10~15% EGCG, 6~10% EGC, 2~3% ECG,

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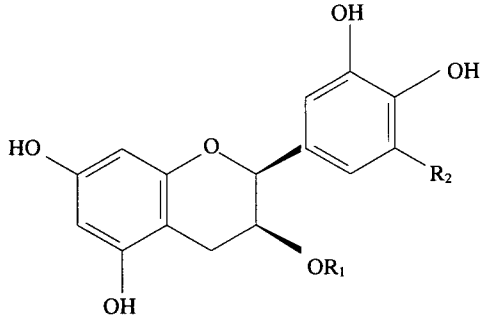
and 2% EC. The structures of the major catechins are shown in Fig. 1. EGCG is the most abundant catechins and has received by far the most attention in clinical study. Flavonols such as quercetin and their glycosides exist at lower levels. In addition, caffeine, theobromine, theophylline, and phenolic acids such as gallic acid, are also present as minor constitutes. Caffeine usually accounts for 3~6% of the dry weight of brewed tea.

These catechins have been proved to have a variety of physiological functions. It is found that the catechins have *in vitro* and *in vivo* antioxidative activity which may be closely related to their preventive effects on various diseases including liver injury, arteriosclerosis and inflammation caused by lipid peroxidation and excessive free radical production. Tea catechins have been paid attention to function as cancer chemopreventive agents in clinic trial and animal models. Although there is increasing interest in the potential health effect of tea catechins as cancer-preventive agent, the bioavailability and pharmacokinetics of tea catechins as well as their interaction with other food and medical components are largely unknown. There is a big gap in our knowledge on the absorption, metabolism, and tissue distribution as well as the biological activities of the condensed catechins from tea beverage. A good understanding of the association of tea consumption with the cancer prevention requires quantitative data on the bioavailability of tea catechins and other components. Information on the bioavailability and disposition of tea catechins such as EGCG, EGC, and EC is important for understanding the biological effects of tea.

INHIBITION OF HUMAN CANCERS AND SYNERGISTIC EFFECTS OF TEA CATECHINS

The most widely recognized properties of tea catechins are the antioxidant properties that result from the ability of scavenge reactive oxygen and nitrogen species and to sequester metal ions to reduce their damage in lipid membranes, protein and nucleic acids (4). Many epidemiological studies have been conducted to investigate the effects of tea consumption on human cancer incidence. Some studies have focused on the different functionality of green tea and black tea in cancer-prevention, because of the difference of component content and variety between green tea and black tea. The results have shown that the cancer prevention activity of green tea is stronger than that of black tea. In the studies on the inhibition of cancer formation by tea in animal models, the effective components are catechins, but black tea contains much lower catechins than green tea. On the basis of some recent studies, cancer chemopreventive effects of green tea are mediated by EGCG, which is the major catechin constituent of green tea. Catechins are reduced by 85% during black tea manufacturing, only 10% can be accounted for as theaflavins and theaflavic acids. Tea catechins are orally bioavailable, but the degree of absorption, retention is still under investigation. Data reports on plasma concentrations after ingestion vary enormously. The catechins undergo several chemical modifications after absorption. These include condensation reactions, methylation, glycosylation and sulfation (5). The reduction of cancer risks and chronic diseases by catechins as the most active component depends on the content, the composition of catechins, their bioavailability and bioactivity.



		R_1	R_2
Epigallocatechin gallate	EGCG	Gallate	OH
Epigallocatechin	EGC	H	OH
Epicatechin gallate	ECG	Gallate	H
Epicatechin	EC	H	H

Fig. 1. Major tea catechins in tea.

Synergistic effects of EGCG, ECG, EGC, and EC

Although there are similarities in their chemical structure, EGCG, EGC, and EC display different pharmacokinetics. According to Chen et al. (6), EGC and EC seemed to be absorbed faster than EGCG, and EGCG had much lower bioavailability in terms of fraction of absorption. The low bioavailability of EGCG is found when given either in decaffeinated green tea or pure EGCG. It seems that EGCG is better absorbed when given through tea infusion rather than in pure form. All catechins components are not equal active. Galloyl esters of catechins are more active than non-galloylated catechins, because they have lower redox potentials (7). Some catechins such as EC show synergistic effects with other catechins and caffeine (8). So unfractionated tea extract has synergistic, stronger effects than single individual tea catechin. Most studies focus on EGCG as health-promoting components of green tea because EGCG is the most abundant catechins in the tea leaves. However, other components should be considered on the basis of their biological activities and bioavailability. EGCG has synergistic potential for cancer-preventive activity with EC. According to the study of Suganuma et al. (8), EC can significantly enhance EGCG's potential cancer-

preventive activity, but ECG, EGC have slight effect to inhibited EGCG's incorporation. These result indicated that EC has no galloyl moiety to enhance incorporation of EGCG. In one study of bioavalability where decaffeinated green tea and pure EGCG were administered to rats intravenously, the results showed that other components in decaffeinated tea also affected the plasma concentration of EGCG (9). Synergistic effects on cancer-preventive activity in tea catechins-rich extract show great potential.

Anti-oxidative activity associated with pheophytins *a* and *b*

Pheophytins *a* and *b* as anti-genotoxic substances in the non-polyphenolic fraction of tea have been identified. Pheophytins *a* and *b* exhibited considerable suppressive activities against the autoxidation of linoleic acid at concentration of 0.2 mg per mL (Table 1). In addition, as a control experiment, the same amounts of EGCG showed relatively low activities compared with those of non-polyphenotic fraction and pheophytins *a* and *b*. The result showed that non-polyphenolic fraction of tea leaves has potential antioxidative activity which might be associated with pheophytins *a* and *b*.

INTERACTION OF CATECHINS WITH FOODS AND MEDICAL COMPOENETS

Catechin intake associated with dietary factors

Catechins are the major components of tea, but they are present in many other fruits and vegetables as well. Catechins are quantitatively important health-promoting components of the daily diet, which should be considered for the relation between diet and chronic diseases. Tea is the main catechin source for most people, whereas chocolate is second in children, and apples and pears are the second source in adults and elderly. Catechin intake is only moderately associated with the intake of other nutrients.

Some positive associations between intake of catechins and intake of fiber, vitamin C and β-carotene is shown in Table 2. In children dietary, fiber has strong association with catechin absorption. Catechin intake is not associated with intake of vitamin E, saturated fatty acids, polyunsaturated fatty acids, but was inversely associated with intake of alcohol in elderly. Catechins also limit consumption of α-tocopherol and allow it to act as a scavenged aqueous peroxyl radicals near the membrane surface (12).

Table 1. Antioxidative effects of non-polyphenolic fraction and non-polyphenolic pheophytins *a* and *b* on autioxidation of linoleic acid (0.2 mg/mL) (10)

Treatment	Absorbance at 500 nm
Negative control (-linoleic acid)	0.06±0.01
Positive control (+linoleic acid)	1.79±0.13
α-Tocopherol	0.56±0.005
EGCG	0.61±0.08
Non-Polyphenolic fraction	0.33±0.02
Pheophytin *a*	0.22±0.01
Pheophytin *b*	0.31±0.04

Table 2. Partial rank-order correlation coefficients between total catechin intake and other dietary factors (11)

	Children (1~18) (n = 1539)	Adults (19~64) (n = 3954)	Elderly (>65) (n = 707)
Alcohol	-0.01	-0.08	-0.015
Saturated fatty acids	0.5	-0.03	0.02
Polyunsaturated fatty acids	-0.02	-0.02	0.01
Fiber	0.21	0.20	0.13
Vitamin C	0.07	0.17	0.11
Vitamin E	0.01	0.05	0.07
β-carotene	0.06	0.10	0.11

Interaction of tea catechins and medication

Sulindac is a popular agent used for suppression of colon adenoma formation in familial adenomatous polyposis patients. Some cancer-fighting medication such as Sulindac and Tamoxifen, are significantly enhanced by EGCG (8). Sulindac, Tamoxifen and EGCG synergistically inhibited cell growth of mouse colon cancer more strongly than Sulindac, Tamoxifen alone, respectively (Fig. 2). There is a distinct possibility that high consumption of tea catechins (more than 10 cups of green tea a day) will enhance the preventive activity of Tamoxifen against breast cancer development. It is advised that patients may drink green tea to enhance the preventive effects of Sulindac or Tamoxifen while reducing its toxicity when they take this medication. From these results, catechins from green tea appear to be a natural synergistic agents to enhance the cancer-preventive effect and reduce adverse effects of some medication. It may be advisable to recommend that patients take some medication with tea rather than water alone. Tea may be used together with a variety of other foods and drinks as part of a healthy diet to promote healthy living.

It has been reported that long term supplementation of β-carotene decreased endogenous α-tocopherol level in

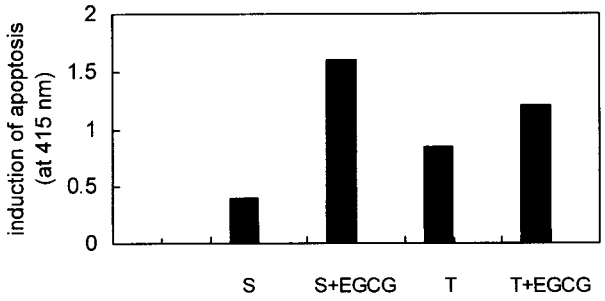


Fig. 2. Synergistic effects of EGCG (75 μm) with Sulindac (S) and Tamoxifen (T) on induction of apoptosis (absorbance at 415 nm) (8).

plasma (13). Tea catechins supplementation caused no change in the levels of β-carotene, lycopene, and α-tocopherol in human plasma. This suggests that tea catechins affect other nutrients absorption.

Tea catechins and protein

Tea catechins have strong affinities for proteins with a high proline content such as caseins in milk, gelatin, and salivary proline-rich protein. The strong binding of catechins to proteins derive from the fact that catechins bind protein via various phenolic groups at more than one point to the proline rich protein due to their open extended structure on the one hand, and the high content of proline residues on the other. Hydrophobic interactions and hydrogen bonding result in the formation of protein-catechins complexes, that affect certain enzymes, and membrane activities (14). Such interactions will reduce the absorption of tea catechins and digestibility of dietary protein. As a habit in the West, milk is often added into tea infusion, which is likely to reduce the content of bioactive catechins and the functionality of cancer-prevention.

Tea catechins and iron absorption

Tea catechins have strong affinity for Fe^{2+}, Fe^{3+} to form insoluble complexes. Tea catechins are considered to interfere with iron absorption, thereby lowering the bioavailability of iron. Green tea decreased nonheme-iron absorption by 28%. This interaction makes the tea catechins and transition metal irons both less available for absorption (15). The inhibitory effect is more pronounced when there are galloyl group (3-hydroxyl groups) on the phenolic structure than when there are 2-phdroxyl groups. The green tea extract was composed of EGCG, EGC, ECG, EC, which consist primarily of galloyl groups. The reduction of nonheme-iron absorption in the presence of tea suggests that the chelation of iron may be one of the mechanisms of antioxidant action in the human digestive system (16). However, tea consumption will not affect iron absorption as long as tea is not consumed together with iron-containing food (17). People should not drink tea with meals because the iron in the foods is chelated by tea catechins. Alternatively, it is advised to drink tea between meals.

CONCLUSION

The major tea catechins have a strong prevention effect on human cancer risk. The prevention effect is a synergistic action between EGCG, EGC, ECG, EC, pheophytins *a* and *b*, and other components in tea leaves, which are directly related to the bioactivity potency of tea catechins for health benefit of humans. Green tea has a higher content of catechins than black tea. Green tea extract has a higher potential, more effective, and practical to prevent cancer risks than any other tea products or pure EGCG. Protein, iron, and other food components may interfere with the bioavailability of tea catechins. Tea extract by hot water is a mixture of anti-oxidants from tea leaves. Drinking tea (or catechins-rich tea extract) enhances the cancer-preventive activity of some cancer-fighting medication such as Sulindac and Tamoxifen, resulting in the need for smaller doses of these drugs and fewer adverse effects. Tea is relatively inexpensive, simple to use, non-toxic, and has strong cancer-preventive effects. Isolation of EGCG in its pure form as a cancer-preventative agent is expensive through complex purification processes. Green tea extract contains components similar to tea leaves, which is better bioavailable for human body. Further studies are required to determine the best dosage for tea consumption. Pure components in capsules may not be the best way to deliver the active catechin components effectively, comparing to drinking of tea which is more practical for cancer prevention in human health.

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