



Beneficial Effect of Tea on Human Health

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Abstract

Tea, with its 5,000-year history, is one of the most popular beverages in the world. According to various estimates, over 4 billion people consume tea. This number has increased in recent years due to the widespread marketing of cold tea-based beverages. During the first millennium tea was primarily considered to be medicine rather than an ordinary drink. Over the last few years a large number of epidemiological studies have conclusively proven that tea is beneficial for people with cardiovascular and neurodegenerative diseases, and cancers. Tea catechins are included in numerous dietary supplements and medicinal products. This review summarizes scientific information related to the effects of tea on human health which have been published in the last decade.

Keywords: green tea; polyphenols; catechins, free radicals, activity, human health.

1. Introduction

In ancient China, tea was used as a medicine for many centuries before it was eventually used as a beverage. In recent decades, numerous studies conducted in several countries of Eastern Europe, Africa, and America have shown that tea—especially green tea—has potent health-improving effects.

Tea is a health beneficial nutraceutical. This is confirmed by millions of people who have been

consuming tea for five thousand years in China and for over 400 years for the rest of the world. Today, more than 4 billion people in the world drink tea. Many research articles, reviews and books describe the effects of tea on human health [1-37]. In the past 20 years, clinical laboratory research and epidemiological review of data for both animals and humans have convincingly shown that green tea catechins reduce the risk of cardiovascular diseases and cancers. The positive effect of catechins is associated with their high antioxidant activity. Catechins can inhibit cell

proliferation, regulate carcinogen-metabolizing enzymes, and induce apoptosis [30].

2. Radical Capturing Activities

It has been experimentally shown that the beneficial effects of green tea polyphenols are associated with the capturing (neutralization) of free radicals. One study explored the ability of green tea catechins to capture free radicals, such as hydroxyl radicals, superoxide radical, lipid free radicals, and singlet oxygen [38]. The concentration of free radicals was determined by electron spin resonance, a direct and reliable method.

Free radicals were generated by established techniques, in particular hydroxyl radicals generated by Fenton reaction ($0.1\% \text{H}_2\text{O}_2 + \text{Fe}^{2+} \rightarrow \text{Fe}^{3+} + \text{OH}^\cdot + \text{RH}$).

Epicatechin gallate (ECG) at concentrations of $0.75 \mu\text{M}$ decreased the amount of hydroxyl radicals by 46.5%. Epicatechin (EC) at low concentrations reduced the amount of hydroxyl radicals by 19.1%. At these very low concentrations, epigallocatechin gallate (EGCG) and epigallocatechin (EGC) did not neutralize hydroxyl radicals at all. But when the concentration of EGCG was increased to 1.5, 3.75, and $7.5 \mu\text{M}$, the amount of hydroxyl radicals decreased by 61.1%, 83.9%, and 87.9% respectively [38].

Efficiency in neutralizing hydroxyl radicals by various green tea catechins follows this order: $\text{ECG} > \text{EC} > \text{EGCG} > \text{EGC}$.

Superoxide radical was shown to be neutralized by green tea catechins, vitamin E, rosemary extract, curcumin, and vitamin C. In contact with these, superoxide radical in solution decreased by $72 \pm 7.4\%$, $23 \pm 6.1\%$ and $23 \pm 5.1\%$, $17 \pm 5.5\%$ respectively. Green tea catechins in this case were shown to be stronger than vitamin E, rosemary, curcumin, and also vitamin C.

The difference in capturing superoxide radicals by catechins and their epimers was specifically investigated.

Neutralization activity increased in the following order: $\text{EC} < (+)\text{C} < \text{EGC} < \text{GC} < \text{EGCG} < \text{GCG}$.

The difference in the activity of EGCG, EGC, EG and their respective epimers, GCG, GC, (+)C, at low concentrations was further studied. The lower the concentration, the greater the difference in their capturing activity [36].

The neutralization activity of catechins relative to lipid free radicals was in the following sequence: $\text{EGCG} > \text{ECG} > \text{EGC} > \text{EC}$.

Free radicals generated by AAPH, were captured as follows, in ascending order of catechin activity: $\text{ECG} < (+)\text{C} < \text{EGC} < \text{GC} < \text{EGCG} < \text{GCG}$.

The neutralization activity relative to free radicals generated by DPPH (1,1-biphenyl-2-picrylhydrazyl), at concentrations of 12.5-25 μM , was in the following sequence: $\text{EC} < (+)\text{C} < \text{EGC} < \text{GC} < \text{EGCG} < \text{GCG}$ [38].

Methyl free radicals were trapped by green tea catechins at a much higher rate than by vitamin C.

GCG captured more singlet oxygen (excited-state oxygen molecules, not a free radical) compared to EGCG.

Therefore, the existing data provides direct evidence that tea catechins capture reactive oxygen compounds (including free radicals).

The range of beneficial health effects from tea is exceptionally broad.

Table 1 shows only some of the biological and health-improving properties of tea extracts.

Table 1. Biological and health-improving properties of tea

No.	Biological Properties of Tea	References
1.	Antioxidant action	[7,12]
2.	Antisclerotic action	[16,20,22]
3.	Anticarcinogenic action	[14,15,25,27,29-35]
4.	Antimutagenic action	[26]
5.	Anti-allergic action	[35]
6.	Antibacterial action	[39,40]
7.	Antimicrobial action	[41,42]
8.	Anti-inflammatory action	[35]
9.	Antiviral action	[43]
10.	Antidiabetic action	[44-48]

Table 2 shows a partial list, far from complete, of diseases upon which consumption of tea has a beneficial effect.

Table 2. Beneficial effect of tea consumption on some human diseases

No.	Diseases	References
1	Different types of cancer	[14,15,25,27,29-34,37]
2	Cardiovascular diseases	[16,19,22]
3	Stroke	[27]
4	Diabetes	[27,35,36]
5	Parkinson's Disease	[49,50]
6	Alzheimer's disease	[27,50]
7	Microbial and viral diseases	
	– dental caries	[51]
	– HIV	[52]
8	Aging	[53]
9	Obesity	[54-56]

3. Tea and Cardiovascular Diseases

Cardiovascular disease (CVD) is the main cause of mortality in many countries. CVD accounts for 40% of all deaths, and mortality from CVD is growing worldwide [57]. In the United States, about 70 million people suffer from CVD.

The useful effects of green tea on CVD have been repeatedly well tested [58-61]; extensive data are provided in numerous reviews [59-63]. Epidemiological studies show a positive causality between tea consumption and reduced risk of CVD [5,64-83].

There are many known causes of CVDs [16]. These include: oxidative stress, impaired lipid metabolism, impaired cardiovascular tone, platelet aggregation, inflammatory processes, growth of cardiovascular cells, etc.

It has been experimentally proven that catechins contribute to the improvement of processes associated with cardiovascular dysfunctions, particularly those related to lipoprotein oxidation, blood aggregation, changes in lipid profile, inflammatory disorders, etc.

In an 11-year study (1995-2005) conducted among 40,000 middle-aged Japanese individuals, it was found that the risk of mortality is 22-33% lower for those who drank more than two cups of green tea a day, than for those who drank only half a cup [5].

Consumption of about 120-600 ml of green tea a day for one year reduces the risk of developing hypertension by 46%. In those who consumed more than 600 ml of green tea, the risk of developing hypertension was reduced by 65% compared with those who drank only 120 ml [70].

Some attempts were also made to establish the relationship between tea consumption and risk of death from cardiovascular diseases [13,16]. Among men aged from 65 to 84, annual mortality among those who consumed 0-250 ml of tea a day was 17 per 1,000 people, and among those who consumed 250-500 ml a day, this rate dropped to 8 per 1,000.

Studies conducted in Holland (Zutphen Elderly Study) demonstrated that among elderly individuals who regularly drank black tea for 5 years, the mortality was by 50 percent lower than among those who did not consume black tea [71,72]. According to a multicenter study (Onset Study), mortality from myocardial infarction is lower among people who regularly drink tea than among non-drinkers.

Epidemiological studies in the U. S. have also shown an inverse correlation between tea consumption and risk of CVD [57]. The same relationship was established during the Rotterdam Study in Holland among 3454 adults over 35 years of age [76].

In Japan, the impact of tea consumption on mortality from CVDs was studied on 8552 volunteers. It turned out that daily consumption of 10 cups of tea decreased mortality from CVDs for men by 40%. The striking result was that the same effect was not observed in women [77].

In Norway, a large study was conducted on healthy volunteers (no CVDs or diabetes) with the participation of 9,856 men and 10,223 women. Those that consumed black tea had reduced total cholesterol [21,75].

The first blind placebo-controlled clinical trials of catechins were conducted among patients with moderate hypercholesterolemia in 2003. Total cholesterol decreased by 11%, and low-density lipoproteins by 16% [40]. Intake of catechins in 224 mg and 674 mg doses resulted in

lower triglyceride levels by 15% and 29% respectively.

Other studies show that long-term consumption of green or black tea reduces the risk of cardiovascular diseases, as well as the risk of death related to coronary atherosclerosis. So far, no relationship was identified between the quantity of tea consumption and atherosclerosis, according to a few small epidemiological studies carried out in Australia, Scotland and Wales [81], this may be due to inadequate experiment design—tea type and catechin content were not specified. Different tea varieties are known to have various catechin contents. This is well illustrated in some publications. In addition, the experimental subjects may have included those who smoked, drank alcohol, consumed fatty foods, or had other diseases. There may have been some other factors which affected the results of the experiment. This clearly shows that in such epidemiological studies the content of tea catechins should be accurately specified, tea consumption should be standardized, and subjects should be carefully selected. An excellent review was prepared by L.N.Maslov on the prospects of utilizing the flavonoids in tea and red wine for prevention of atherosclerosis and atherothrombosis [11]

L.N.Maslov suggested that tea catechins "prevent coronary thrombosis rather than atherosclerosis." This is confirmed by many publications in which consumption of green tea was shown to inhibit platelet aggregation. This finding is supported by numerous studies on animals (mice, rats, hamsters, rabbits, monkeys, etc.).

Free-radical oxidation, particularly of low-density lipoproteins, is one of the causes of CVD. Oxidized LDL begins to be deposited more rapidly on blood vessel walls, which leads to the development of atherosclerosis. In dozens of studies, green tea catechins have been shown to reduce LDL oxidation.

In the last 10-15 years, many epidemiological studies have been conducted to determine the relationship between tea consumption and incidence of cardiovascular disease.

Japanese researchers established a direct link between consumption of green tea EGCG and the

level of coronary artery stenosis. When consumption of green tea was increased from one to four cups a day, the level of stenosis decreased by 65% [64].

With increased consumption of flavonoids, mortality from cardiovascular diseases in different countries decreased by 65% (Finland > USA > Greece > Italy > Netherlands > Japan) (V.A. Tutelyan, private lectures).

It is commonly believed that green tea prevents cardiovascular diseases better than black tea. This is based on the low level of cardiovascular disease and cancer in Asian countries where primarily green tea is consumed. However, in recent years, research conducted on hamsters has shown that the effect of green and black teas is equivalent. Both types of tea effectively inhibited atherosclerosis. Atherosclerosis is inhibited by three mechanisms: hypolipemic, antioxidant, and antifibrinolytic. In animal studies, it was shown that tea consumption reduces plasma content of LDL, the LDL/HDL ratio, triglycerides content, lipid peroxides, and fibrinogen.

Studies in Korea have shown that tea consumption lowers LDL ratio and the LDL/HDL ratio.

In a large Chinese study, it was found that consumption of one capsule of concentrated tea extract (equivalent to 7 cups of black tea per day) reduced LDL by 16% in patients with high cholesterol on a low-fat diet.

Among American subjects with moderate cholesterol, the intake of 5 cups of black tea reduced cholesterol and LDL. Epidemiological studies in the United States have shown that consumption of 2 or more cups of tea a day can reduce by half the number of deaths from heart attacks.

4. Tea and Cancer

Cancer is the second cause of deaths both in the United States and in Russia—each year five hundred thousand people die from cancer. Conventional treatment of oncological diseases includes surgery and chemotherapy. Many studies have shown that consumption of natural

antioxidants can reduce the risk of cancer. Green tea is especially effective in this regard.

General issues related to oncological diseases and tea are discussed in numerous publications [14,25,34,84-122].

Research on cancer cell lines in animals and humans has shown that catechins and other tea constituents inhibit or block the development of cancer. Some types of cancer, for which beneficial effects via green tea and its components may be facilitated, are provided in Table 3.

Table 3. Types of Cancer; Beneficial Effects Facilitated by Green Tea and Its Components

No.	Types of Cancer	References
1.	Breast cancer in women	[103,122-125]
2.	Lung cancer	[109,114,126-129]
3.	Stomach cancer	[99,102,118,122,130-132]
4.	Prostate cancer in men	[108,110,113,133-135]
5.	Rectal cancer	[136,137]
6.	Colon cancer	[101,107,119,120,138]
7.	Esophageal cancer	[131,139]
8.	Skin cancer	[140]
9.	Kidney cancer	[141]
10.	Bladder cancer	[141]
11.	Pancreatic cancer	[35,115,117]
12.	Oral cancer	[111]
13.	Adenocarcinoma	[112]
14.	Leukemia	[121]

Green Tea for Cancer Prevention. One of the anti-carcinogenic mechanisms of action of green tea catechins was identified. EGCG increases synthesis of glutathione-S-transferase enzymes which neutralize various toxins, some of which cause cancer through DNA damage. People in China and Japan who regularly consume large amounts of green tea, are less prone to cancer than people in other countries where green tea is consumed in smaller quantities or not consumed at all.

Studies conducted on people with low enzyme activity showed that the use of green tea concentrates (Polyphenon E) by 800 mg (4 capsules) in the morning for four weeks,

increased the activity of enzymes of the glutathione-S-transferase family by 80%. Polyphenon does not affect people with initially high or moderate activity level of these enzymes. Therefore, according to the author of this publication (S. Chow, Arizona Cancer Center), green tea extract can be used to prevent cancer in people with low activity of glutathione-S-transferase enzymes.

Chemoprevention of prostate cancer using green tea catechins. The incidence of prostate cancer is growing both in European countries and the United States. Currently, of all cancer-related deaths, prostate cancer is the second highest cause of death among men.

Clinical trials were carried out to assess the efficacy and safety of green tea catechins to prevent prostate cancer in patients with high-grade prostatic intraepithelial neoplasia (PIN) [110].

The green tea preparation consisted of a catechin mixture isolated by HPLC: EGC – 5.5%, EC – 12.24%, EGCG – 51.88%, ECG – 6.12% (total catechins 75.7%). This preparation contained less than 1% of caffeine. The daily dose was 600 mg—three 200 mg capsules.

In the group of 30 patients receiving the capsules for one year, only one tumor was diagnosed (the probability of disease is 3%). In the group of similar patients receiving placebo, nine cancer tumors were detected (probability is 30%).

The values of PSA (prostate-specific antigen) were lower in patients treated with catechins.

No side effects were detected in patients taking catechins.

Only positive effects were noted, such as reduction of lower urinary tract symptoms.

Low incidence of cancer in Asian countries compared to the Western countries is associated with regular consumption of green tea [133].

Interestingly, the Asian immigrants in the USA who do not drink green tea are at the same risk of developing cancer as the national average level.

Antitumor effect of tea catechins, especially of epigallocatechin gallate, has been shown in experiments on animals in vitro and in vivo [134,135].

The efficacy of treatment can be as high as 90% in men at risk when green tea catechins are administered orally [110]. These same studies also showed that green tea catechins are safe for humans.

Impact of green tea catechins on leukemia. EGCG consumption shows a positive impact on leukemia at an early stage. Lymphocyte content is reduced in 30% of patients. Patients with chronic lymphocytic leukemia are tolerant to high doses of EGCG. 33 patients received different amounts of Polyphenon E (60% EGCG) ranging from 200 mg to 2,000 mg twice a day. The maximum allowable norm was not reached. This type of leukemia is the most common type in the USA; 50% of patients have an aggressive form of the disease and die early.

Remission of chronic lymphocytic leukemia was observed at high doses of EGCG. Researchers hope that EGCG may stabilize the disease at an early stage and enhance the effectiveness of treatment in combination with other therapies [121].

5. Other Health-Beneficial Properties of Tea

Green tea improves bone condition. According to Zhonglan Bin from Hong Kong University (published in *J. Agric. Food Chem.*), green tea may improve bone condition—it stimulates the growth of bone tissue and prevents osteoporosis. The most active catechins for this purpose is epigallocatechin (EGC)—it increases the activity of key enzymes, promotes bone growth by 79% while also increasing the level of mineralization of bone tissue. High concentrations of EGC block the activity of osteoclasts—cells that destroy bone tissue. Green tea catechins do not have a toxic effect on cells. Experiments were conducted on the cells of rats.

Tea helps with stress. M. Cross, psychologist from the University of London, has shown that tea has a calming effect in stressful situations [142-145].

According to surveys, 70% of the British drink tea before making critical decisions.

Tea lowers blood pressure. Studies conducted by the University of Florida, Harvard Medical School and Food Research Institute in Boston

have shown that extracts of green tea administered for three weeks reduced systolic/diastolic blood pressure and reduced LDL levels down to 9 mg/dL. At the same time, the concentration of malondialdehyde, a marker of oxidative stress, was reduced. During oxidative stress, the levels of free radicals in the body exceed the norm, which can lead to dangerous diseases and premature aging.

Epigallocatechin gallate (EGCG) in green tea increases the shelf life of platelets. When stored, the platelets undergo biochemical changes which make their cell membranes lose their functional characteristics and hemostatic properties. When EGCG is added to platelets, their active functions are preserved for longer periods (1.5-2 times). Chinese University Professor S-K. Chion who conducted relevant studies suggested that EGCG prevents activation of platelet cells and protects their membrane lipids from oxidation. These findings open up new possibilities for storing platelets.

HIV prevention with green tea. Dr. Williamson, M. P. from the University of Sheffield, England, demonstrated that epigallocatechin gallate (EGCG) from green tea enters into the human immune system faster than the immunodeficiency virus [145a]. Thus, the spread of HIV in the body is slowed down. However, the author believes that EGCG cannot protect against the infection, but, in combination with conventional therapy, may improve the quality of life of HIV-infected patients. Studies on the role of EGCG continue

Green tea is effective against sepsis. Sepsis (blood poisoning) is an infectious disease that develops when various microorganisms that produce toxins enter in human blood in conditions of reduced body resistance. In the Russian Federation, sepsis is the third cause of deaths of women in childbirth and of newborn babies. Scientists from the Michigan University showed that consumption of EGCG increased the survival of mice with sepsis by three times.

Consumption of EGCG is also effective for rheumatoid arthritis, an autoimmune disease.

Consumption of green tea improves cognitive abilities and memory [146].

GABA and Gabaron teas contain elevated levels of gamma-aminobutyric acid (γ -aminobutyric acid, GABA). Gamma-aminobutyric acid (GABA) is a universal inhibitory neurotransmitter which reduces the overall activity of the brain, especially during sleep. GABA was first found in the brain by Roberts et al. in 1950.

GABA tea was first developed in 1987 in Japan [146]. GABA content in this tea was 150 mg per 100 g. The amount of GABA in plant tissues typically ranges from 0.3 to 32 μ mol/g.

When tea leaves (oolong tea, black tea) undergo anaerobic treatment for more than 10 hours, the content of GABA and alanine rises 8 and 5 times, respectively, while the content of glutamic and aspartic acid is reduced by 80-90%. Specialized GABA tea is considered to have a therapeutic effect as it shows many beneficial biological actions.

The primary biological functions of GABA tea include: it produces a reduction in blood pressure in humans [147]; it plays an important role in cardiovascular regulation [148]; counteracts low GABA levels in plasma which may affect Parkinson's disease, epilepsy [149,150], alcoholism [151,152], depression [149,150], and menopause [149,150]; it helps cure stress-related insomnia as well as insomnia in elderly people, and improves sleep quality [149,150,153]; helps cure alcoholism—alcoholics have decreased GABA content in the blood [154,155]; alleviates depression (WHO estimates that by 2020 depression will be the second most common disease after cardiovascular diseases [154]; GABA helps in the treatment of diabetes [155], Alzheimer's disease [149,150], and prevents premature aging [155].¹⁷⁶

Clinical trials have been conducted to assess the effect of GABA tea [156] and compare the biological activity of GABA tea and green tea.¹⁷⁸

GABA is produced in inert carbon dioxide more effectively than in nitrogen, yet nitrogen is recommended due to its cost-effectiveness and safety. Anaerobic treatment of tea does not alter the content of tannins, caffeine, and theanine.

6. Conclusion

This brief review clearly demonstrates that tea—especially green tea—is beneficial to human health. In addition, several publications in recent years also show consumption of black tea to be as beneficial as that of green tea. Some companies have begun to sell mechanical mixtures of green and black tea. Special attention should be paid to the oolong or wulong tea (fermented by 50%), which are the most popular tea varieties in China and Taiwan (80% of the population consume wulong tea). Some scientists suggested that these teas may have even greater potential for improving human health. Unfortunately, they are not sufficiently studied yet. The effects of Pu-erh tea on health also need extensive research.

For the sake of fair-mindedness, it should be noted that despite the thousands of articles on the benefits of tea, there are a few publications on the harm of tea consumption. For example, one publication presents some cases of hepatotoxicity related to consumption of green tea [157]. Yet, another publication demonstrates on a large number of volunteers that green tea does not alter liver functions in any way [158]. The most recent publications have examined the biochemical and pharmaceutical properties of tea catechins and their impact on human health [159-164]. We would like to conclude this review with an appeal, 'Drink tea for the benefits to your health!'

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