

Partial Effect of EGCG, Theanine and Tea Polysaccharide

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Abstract: It is widely acknowledged that numerous benefits of green tea have been shown to the public. This article aims to show the utilization of three tea compounds: epigallocatechin-3-gallate, L-theanine, and tea polysaccharide. To demonstrate this, the article collects studies demonstrating the use of three compounds respectively. Firstly, by controlling the serotonin and serotonin synthesis in the brain or the nerve system, theanine can regulate blood pressure and protect brain cells. Theanine, by inhibiting the excitation of the coffee, can help to relax and relieve stress. Theanine can eliminate cancer in an indirect way by enhancing the effect of anti-tumor medicine to promote apoptosis and cut the proliferation of cancer cells. Secondly, tea polysaccharide has been proved to restore oxidative damage in vitro and vivo. Moreover, suppressed A-amylase activity made by Tea Polysaccharide can control glucose. The tea polysaccharide can control the Zn/Cu ratio in the liver, which is relevant to lipid metabolism. Immunity was enhanced by an increase in anti-inflammatory cytokines, a decrease in pro-inflammatory cytokines, and the production of immune regulatory molecules. Thirdly, EGCG goes against oxidants by scavenging free radicals and inhibiting cholesterol oxidation. By way of inducing apoptosis of cancer cells, causing cell cycle arrest for anti-cancer decreased proliferation of transformed fibroblasts, enhancing the cytotoxic sensitization of some cells. The EGCG shows its vitality to health. EGCG keeps the mouth clean by absorption of certain gases so as to deodorize, which has been applied to daily use. Last but not least, EGCG will reduce UVB-induced malondialdehyde deposition by improving antioxidant enzyme activity to protect ourselves from the ultraviolet.

1. Introduction

It is widely acknowledged that numerous benefits of green tea have been shown to the crowd. The clinical effects on a variety of diseases such as cancer, diabetes, cardiovascular disease including acute coronary disease, and obesity have been spread among the public. There are still use of antioxidant, deodorization effect and so on. Tea can serve as functions to fight cancer and oxidization with three of its main compounds: epigallocatechin-3-gallate, L-theanine, and tea polysaccharide (Figure 1). Through the previous cellular, animal, and human experiments over the years, green tea and its main components have demonstrated a variety of activities such as anti-tumor and anti-oxidization, deodorization, ultraviolet protection, and so on, which can be achieved by inhibiting the proliferation of cancer cells, enhancing the effect of anti-tumor medicine, scavenging oxygen free radicals, eliminating smelly sulfur compounds and reducing UVB-induced malondialdehyde deposition, etc. In brief, this paper describes the function of tea through three of its main compounds so as to provide further application of tea to human health.

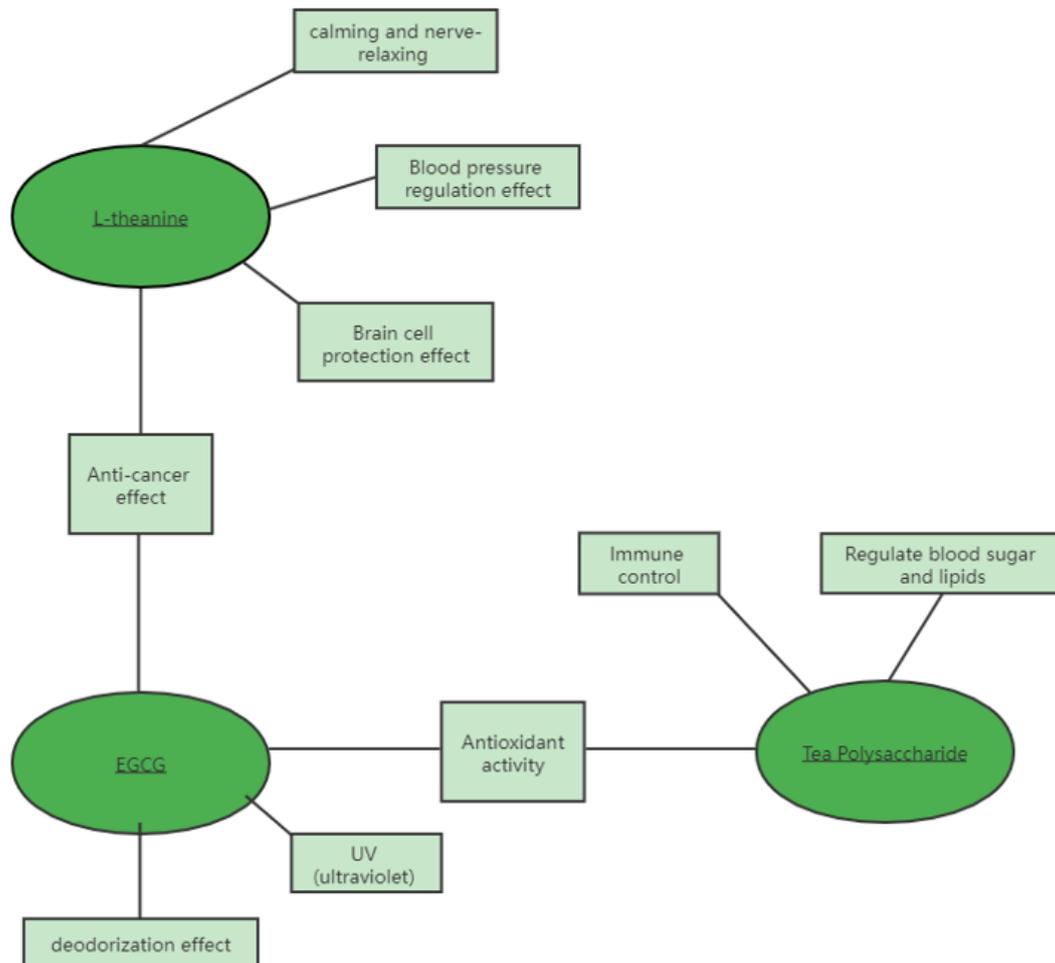


Figure 1. Functions of L-theanine, EGCG and tea polysaccharide.

2. Theanine

2.1 Blood pressure regulation

The central and peripheral nerve systems regulate blood pressure primarily via increasing or decreasing serotonin levels. According to research, murine treatment reduces serotonin concentration, limits serotonin synthesis in the brain, and increases serotonin breakdown in the brain. When spontaneously hypertensive rats (SHR) were given different doses of theanine, blood pressure dropped, and the fact that blood pressure was reduced suggested a dose-reflective relationship [1]. Also, blood pressure drops significantly in the higher dose group. However, even the largest dose of theanine has no effect on the blood pressure of healthy rats, and even glutamate, which has a similar structure to theanine, has not been found to have a blood pressure-lowering effect [2].

2.2 Brain cell protection effect

The brain has been discovered to be the major receptor for theanine. Theanine boosts the intramitochondrial neurotransmitter dopamine in brain cells after it passes across the blood-brain barrier. Adrenaline and norepinephrine are made up of dopamine. It's a crucial chemical that transmits the excitation of nerve cells in the brain. The loss of dopamine will have a significant impact on people's emotions. 5-hydroxytryptamine (serotonin), a neurotransmitter, can certainly influence the brain cells with excessive amounts. Furthermore, the use of serotonin metabolism inhibitors has shown that theanine can impact the synthesis and decomposition of serotonin in the brain. The content of tryptophan in the brain increased significantly or had a propensity to rise after consuming theanine, but the quantity of serotonin dropped. Theanine can either diminish serotonin production or promote its breakdown, or it can inhibit serotonin release.

2.3 calming and nerve-relaxing effect

Caffeine has a revitalizing and rejuvenating effect on the body. Tea leaves also have a high caffeine content. Caffeine used on its own has side effects on the human body. However, it will not create the same level of caffeine excitatory impact after drinking tea. Theanine has an antagonistic impact on caffeine excitation [3]. According to the research, it was found that the amount of central nervous system spontaneous exercise generated by caffeine, and the results revealed that when caffeine and theanine were given together, they had a strong inhibitory influence on excitation. Some researchers have recently employed EEG assessment methods to confirm that theanine and caffeine, at about the same molar concentration, can counteract caffeine activation [4]. These findings strongly suggest that theanine is a caffeine antagonist with calming, tension-relieving, and nerve-relaxing properties.

Animals and humans, in general, create extremely faint pulses on the surface of the brain, which are referred to as brain waves. The brain produces brain waves with varied current frequencies depending on the mental state. According to frequency, brain waves are classified as α , β , δ , and θ waves. δ Waves are in a deep state of sleep, θ waves are in a state of beating, α waves are in a calm state (relaxed state), and β waves appear in a condition of excitement. Human trials were undertaken to confirm theanine's mental effects. After 60 minutes, the individuals were instructed to drink water and an aqueous solution of theanine, and their EEG was recorded; the results showed that the EEG altered after drinking water, but not after drinking theanine. After that, significant alpha waves are produced. As a result, theanine promotes the creation of second waves, resulting in a sensation of relaxation and pleasure. In addition, theanine did not increase the quantity of theta waves in the sleep state, indicating that it stabilizes emotions while simultaneously increasing attention. After 60 minutes, the individuals were instructed to drink water and an aqueous solution of theanine, and their EEG was recorded; the results showed that the EEG altered after drinking water, but not after drinking theanine. After that, significant alpha waves are produced. As a result, theanine promotes the creation of second waves, resulting in a sensation of relaxation and pleasure. In addition, theanine did not increase the quantity of theta waves in the sleep state, indicating that it stabilizes emotions while simultaneously increasing attention.

2.4 Anti-cancer effect

Although theanine doesn't have a direct anti-tumor effect, studies have shown that it can boost the efficacy of a range of anti-tumor medications, aiding in the fight against cancer. Adriamycin, for example, has an inhibiting effect on various cancers in the human body. Theanine, on the other hand, can protect adriamycin concentrations in tumor tissues and inhibit adriamycin exudation from Ehrlich ascites tumor cells [5]. As a result, when theanine and THP-doxorubicin (THP) are used together, they can boost the growth inhibition of living tumors by 1.3 times and the curative impact in tumor tissues by 1.7 times when used together. Also, scientists have looked into how theanine improves adriamycin's anti-cancer activity and discovered that theanine increases adriamycin concentration in tumor cells by blocking glutamate transmission in tumor cells, resulting in an increase in resistance. When the anti-cancer medicine doxorubicin combines with theanine, it can prevent M5076 ovarian sarcoma from spreading to the liver. Furthermore, theanine inhibited the EGFR, VEGFR, JAK2/STAT3, Met, Akt/mTOR, and ERK/NFKB pathways, as well as triggering the intrinsic apoptosis pathway and caspase-independent programmed cell death. In this case, theanine exerts its anti-cancer effect on melanoma cells by inhibiting the proliferation and promoting apoptosis, which relies on the regulation of the clock gene *Bmal1* in melanoma cells [6, 7]. The results indicated moderate apoptotic, antimetastatic, antimigration, and anti-invasion effects, along with the mild antiproliferative influence of theanine on cancer. Further studies are necessary to ascertain the effectiveness of theanine on the prevention and suppression of cancer and shed light upon the attributable mechanisms in the *in vivo* condition. All in all, it not only enhances the effects of certain anti-tumor treatments, but it also improves the quality of life of cancer patients by relaxing nerves, releasing stress, and encouraging relaxation, among other things. To conclude, theanine is particularly helpful in cancer patients' clinical treatment [8].

3. Tea Polysaccharide

3.1 Antioxidant activity

A vast number of researchers have been drawn to the antioxidant properties of tea polysaccharides. Oxidative stress is defined as an increase in the production of reactive oxygen species (ROS) relative to the body's overall antioxidant capacity, resulting in damage to the normal functions of lipids, proteins, and DNA in the human body while also influencing the onset and progression of many chronic diseases. In order to examine its antioxidant activity, a great number of scientists reported the effects of tea polysaccharides with varied tea raw materials, extraction processes, and purity on various antioxidant indexes *in vivo* and *in vitro*. The antioxidant activity of tea polysaccharides was previously established mostly using chemical or biological enzymology, or by utilizing animal models such as mice and rabbits, or by combining these approaches with *in vitro* cell culture methods. *In vitro*, the effect of tea polysaccharide on scavenging oxygen free radicals has been experimented with. TPS was also studied using mouse models to indicate that it may reduce oxidative damage. To assess the effect of selenium-containing TPS (Se-TPS) from Ziyang green tea on hepatic oxidative stress, healthy male Kunming mice fed with 20% fructose water were given 200, 400, or 800 mg/kg of Se-TPS for 8 weeks. The results showed that after Se-TPS administration, liver steatosis and oxidative stress damage in mice were significantly reduced, and antioxidants and hepatic lipid levels rose again to normal levels [9]. These studies also showed that TPS can alleviate oxidative damage.

3.2 Regulate blood sugar and lipids

The tea polysaccharides found in various types of tea were shown to reduce blood sugar and blood lipid levels, according to the findings. The author has claimed that tea polysaccharides can lower fasting and postprandial blood glucose in alloxan-induced diabetic mice, and that the hypoglycemic mechanism may be related to the suppression of A-amylase activity, thereby delaying carbohydrate absorption in the small intestine [10]. The therapeutic efficacy of Oolong tea polysaccharide on alloxan diabetic mice was further confirmed by scientists utilizing cellulase to aid extraction and a membrane filtering technology to purify oolong tea polysaccharide." The tea polysaccharides had a certain impact on decreasing blood cholesterol in rats, had a good antioxidant effect *in vivo*, and could control the concentrations of Zn, Cu, Mg, and the Zn/Cu ratio in the liver linked to lipid metabolism to a normal level," according to the scientists [11].

3.3 Immune control effect

Tea polysaccharide immune regulation research is also extensive, with numerous studies on tea polysaccharide immune regulation detailed in the tea polysaccharides review. The following sections investigate the immune-regulatory role and mechanism of tea polysaccharide in depth. Tea polysaccharide can activate macrophages and increase the quantity and phagocytic activity of peritoneal macrophages in mice. An *in vivo* test on Kunming mice revealed that oral administration of tea polysaccharide reduced the levels of pro-inflammatory cytokines like TNF- α but increased the levels of anti-inflammatory cytokines like serum immunoglobulin A (IgA), IgG, IgM, IL-2, IL-4, IL-10, as well as IL-6, which is involved in T cell activation [12]. Tea polysaccharides can also increase T cell proliferation, stimulate T cell-mediated immunological responses, and cause the production of immune-regulatory molecules, such as interleukin ("L"), enhancing the body's immune regulatory abilities. B lymphocytes are activated by tea polysaccharides. Natural killer cells are boosted by tea polysaccharides. In the membrane phase of gonorrhoea, tea polysaccharide can activate the complement system and increase the activity of the complement acceptor.

4. EGCG

4.1 Antioxidant effect

By scavenging free radicals, preventing peroxidation, and boosting the efficacy of other antioxidants, EGCG, however, plays a more significant part in these functions. They can scavenge

free radicals and inhibit cholesterol oxidation, which is accompanied by the oxidation of low-density lipoprotein in vitro.

Firstly, the researcher used ESR and chemiluminescence technology to investigate the scavenging effect of four catechins on superoxide radicals. The results revealed that EGCG has the greatest potential to scavenge free radicals. The capacity of catechins to resist copper and induce oxidation was shown to be EGCG =epicatechin (ECG) > C > EGC [13]. Through comparing the capacity of tea monomers to activate metabolic detoxification enzyme activity via NAD (P) h-quinone reductase (QR) activity in hepG2 liver tumor cells cultivated in vitro via the activity of NAD (P) h-quinone reductase (QR), the findings indicated that EGCG had a considerable impact [14,15]. Even in catechins, EGCG has shown strong ability on anti-oxidation.

4.2 anti-cancer effect

Unlike theanine itself, which has no anti-tumor activity, EGCG is a popular topic among the anti-tumor fields. The fact that EGCG can serve as the function of antitumor has been widely acknowledged by researchers in that field all around the world, and because of this, the antitumor product made of EGCG has been studied in many countries such as China and the United States. Researchers are studying the aspects below. The mechanism of EGCG on various tumors was researched and experimented upon. EGCG had the strongest anti-cancer effect among catechin monomers.

EGCG can induce apoptosis of cancer cells. EGCG suppressed the proliferation of human MCF-7 breast cancer cells and promoted apoptosis of cancer cells. Through using the RT-PCR and western blot analysis, scientists test the apoptosis effect of three groups: si-P53, EGCG, and EGCG-combined si-P53 groups. To estimate the apoptosis rate of MCF-7 breast cancer cells so as to find out that EGCG has better apoptosis than the other two [16]. Moreover, it was found that catechin monomer had obvious inhibitory and apoptotic effects on prostate cancer cells, and the effect order was EGCG > epicatechin gallate (ECG) > epicatechin (EGC).

EGCG causes cell cycle arrest for anti-cancer. EGCG treatment has been shown to stop the cell division cycle in the G₀, G₁, G₂, and S stages in some research. EGCG has an anti-proliferative action via indirectly downregulating pro-proliferative factors and effectors such as cyclin D1, cyclin E, cyclin A, cyclin B, CDK4, CDK6, CDK2, and CDK1, as well as upregulating anti-proliferative effectors such as CDK inhibitors p27, p21, p16, and p18. Furthermore, EGCG has been discovered to affect cytokinesis through interacting with the 67LR receptor. Causing the division of a mother cell into two daughter cells. The formation of an actomyosin ring, also known as a contractile ring, is necessary early in the process to allow the formation of the cleavage furrow at the equator of mitotic cells. The furrow's formation allows for the equal division of genetic material between the two developing cells, as well as their later separation.

The proliferation of transformed fibroblasts was decreased by EGCG, but not that of normal fibroblasts. The effect of EGCG on growth-promoting factors was investigated to find out how it conducts its preferential inhibitory function. EGCG significantly inhibited proliferation activity of breast cancer cell MDA MB 435, and p21 mRNA and protein expression could be detected after being treated by EGCG for 24 hours, indicating that EGCG could inhibit the proliferation of breast cancer cells, suggesting that the mechanism may be related to the induction of p21 expression and thus the inhibition of cell cycle transition [17]. The effect of EGCG on the growth of thyroid cancer FRO cells was measured by MTT assay. It was found that EGCG significantly inhibited the proliferation of FRO cells, and the telomerase activity of FRO cells gradually decreased with the increase of EGCG concentration, which provided a theoretical basis for the application of EGCG in the clinical treatment of thyroid cancer. Moreover, it has been shown that EGCG inhibits the growth of transformed but not of normal fibroblasts. In an attempt to elucidate the mode of the preferential inhibitory activity of EGCG, its effect on growth-promoting factors has been examined. The level of ornithine decarboxylase (ODC, EC 4.1.1.17), which is a signal for cellular proliferation, was reduced by EGCG in the transformed but not in the normal cells [18]. EGCG also showed strong inhibition of tyrosine kinase and mitogen-activated protein kinase (MAPK) activities, without affecting the kinases in the

normal cells. Similarly, EGCG also preferentially decreased the levels of the oncogenes Ras and Jun in the transformed cell. EGCG preferentially induced apoptosis in the transformed fibroblasts. In the test of vitro chemo sensitivity, it was demonstrated that EGCG inhibited the proliferation of leukemic cells.

EGCG can also improve the cytotoxic sensitization of some cells. The cytotoxic sensitization of catechin components ECG and EGCG on human drug-resistant hepatoma cell BEL-7404 / A and drug-resistant oral cell KBv200 is found that the combination of these two catechin components and antitumor drugs can reduce the expression of P-glycoprotein (P-gp) and increase the amount of rhodamine-123 (Rh-123) in cells. It has been proved that EGCG, ECG and Adriamycin (ADM) or vincristine (VCR) can enhance the cytotoxicity of the drug on tumor cell BEL-7404 / A and drug-resistant oral cell KBv200. It is speculated that the mechanism may be related to reducing the expression of MDRT mRNA, down regulating the expression of P-gp and inhibiting the function of P-gp. It provides an experimental basis for the discovery of new multidrug resistance reversal agents and possible targets.

In brief, the role of EGCG plays in the curing or prevention on cancer has been shown in Table 1

Table 1. Based on vitro study, the utilization of EGCG in cancer

Cancer	EGCG functions and brief mechanisms
Urinary bladder cancer	Inhibition of cell proliferation via induction of apoptosis and inhibited cancer cell migration [19]
Prostate Cancer	Induction of apoptosis [20]
Renal Cell Carcinoma	Inhibition of the proliferation, and induction of apoptosis via upregulation of Cx32 in cancer cells [21,22]
Gastric cancer	Inhibited proliferation and increased apoptosis of cancer cells [23,24]
Cervix cancer	Greatly inhibition on the cellular proliferation [25]
Leukemia	Induced growth inhibition and apoptosis in a time- and dose-dependent manner Increased levels of Bax protein expression [26-28]
Esophagus cancer	Decreased proliferation of cancer cells and induction of apoptosis [29]
Liver cancer	Reduced expression of MMP-9, syndecan-1, and FGF-2, decreased hypoxia- incited apoptosis in HepG2 cells as well as enhanced cell survival [30,31]
Thyroid cancer	Suppressed proliferation in anaplastic cancer cells [32]
Lung cancer	Decreased expression of both Axl and Tyro 3 receptor tyrosine kinases [33]
Lymphoma	Induction of growth inhibition and apoptosis in a time- and dose-dependent manner, inhibited growth of malignancy cell lines [34,35]

4.3 Deodorization effect

EGCG provides deodorizing and caries-prevention properties. With the effect of inhibiting the volatile sulfur compounds, the company uses the tea compounds as the ingredients of the toothpaste for deodorization. In the contrast conducted in the experiment, green tea showed the biggest decrease in the centralization of both H (2) S and CH (3) SH gases, particularly CH (3) SH, which likewise exhibited a preferred connection with scent strength over H (2) S. Other conventional objects for deodorizing such as chewing gum, mints, and parsley-seed oil items didn't lessen the centralization of VSCs in the mouth air. Chewing gum, mints, and parsley-seed oil products did not reduce the concentration of VSCs in mouth air at any time through using gas chromatography to investigate how catechin eliminates the odors of trimethylamine, hydrogen sulfide, and indole [36]. As table 2 shows, green tea also displayed considerable deodorant action in vitro, but no significant deodorant activity was found in mints, chewing gum, or a parsley-seed oil product. We concluded that green tea was particularly beneficial in temporarily lowering oral malodor due to its antibacterial and deodorant actions, but other foods were not.

Table 2. Comparison of deodorization effects of different products.

Deodorization group	In vitro	In vivo
tea	effective	effective
mint	ineffective	effective
parsley-seed oil	ineffective	effective
chewing gum	ineffective	effective

4.4 UV (ultraviolet) protection effect

The protective mechanism of EGCG against oxidative damage caused by ultraviolet radiation was discovered to be that it can reduce UVB-induced malondialdehyde deposition by improving antioxidant enzyme activity, as well as inhibit UVB-induced MMPL mRNA expression and reduce collagen degradation, indicating that EGCG can protect cultured fibroblasts damaged by UVB radiation.

In the experiment, HSFs (human skin fibroblasts) were isolated from the baby foreskin, cultured, and separated into six groups: control group, EGCG group (treated by 25 microg/ml EGCG), UVA group (lighted by 10 J/cm (2) UVA for a considerable length of time), UVB group (illuminated by 30 mJ /cm (2) UVB for a very long time), UVA + EGCG group and UVB + EGCG group. Beta-galactosidase (beta-GAL), an organic marker related to senescence, was distinguished by histochemical staining. The HPRT quality transformation recurrence was identified by the HPRT mutagenesis measure.

The HSFs of the control and EGCG groups just demonstrated a couple of beta-GAL positive cells, and the beta-GAL positive cell proportions of the other 4 gatherings were higher and could be orchestrated from high to low as to succession: EGCG + UVA group > EGCG + UVB group > UVA group > UVB group. The transformation paces of the control and EGCG groups were extremely low. The transformation pace of the UVB and UVA bunches was at least 72 times that of the benchmark group. The transformation pace of the UVB + EGCG and UVA + EGCG bunches was fundamentally lower than those of the UVB and UVA groups [37].

5. Conclusions

This article discusses the proven biological effects of theanine, tea polysaccharide, and EGCG, which have shown that theanine can regulate blood pressure and protect brain cells by controlling serotonin and serotonin synthesis in the brain or nervous system. Theanine, by inhibiting the excitation of the coffee, can help to relax and relieve stress. Instead of having a direct anti-tumor effect, theanine can eliminate cancer in an indirect method by enhancing the effectiveness of anti-tumor medicine to induce apoptosis and reduce tumor growth.

In vitro and in vivo, tea polysaccharide can repair oxidative damage. Furthermore, Tea Polysaccharide's decreased A-amylase activity can manage glucose levels. The Tea Polysaccharide can regulate the Zn/Cu ratio in the liver, which is crucial for lipid metabolism. Anti-inflammatory cytokines were increased, pro-inflammatory cytokines were decreased, and immune regulatory molecules were produced, which improved immunity. EGCG inhibits oxidants by scavenging free radicals and inhibiting cholesterol oxidation. By inducing apoptosis in cancer cells, producing cell cycle arrest for anti-cancer lowered proliferation of altered fibroblasts, and increasing the cytotoxic sensitization of some cancer cells. EGCG demonstrates its importance to health. EGCG keeps the mouth clean by absorbing specific gases that deodorize when used on a daily basis. Last but not least, EGCG improves antioxidant enzymes to minimize UVB-induced malondialdehyde accumulation to protect us from UV damage. Although we have collected many of the data and explained how these compounds work, some mechanisms of the three compounds are still unknown while some functions cannot be utilized properly. We should pay more attention to the three compounds in daily and clinical use.

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