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The Beneficial Effects of Tea on Bodily Systems: Good or Bad?

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Abstract

Objectives: Using food to prevent diseases has become the focus of different researchers in recent years. Tea is a natural source of caffeine, flavonoids, ascorbate, theanine, and antioxidants. The purpose of this study was to provide a review of the benefits and harms of tea for different body systems.

Methods and Materials: The present review study was conducted by searching through the websites and assessing the results in the literature using a library research method. The data were collected for publications during 2000-2018.

Results: Various epidemiological studies concluded that tea and its polyphenolic contents have beneficial effects on different bodily systems including the cardiovascular system, diabetes control, and different types of cancer. However, some studies argue that tea may have harmful effects on the bodily systems.

Conclusions: Overall, tea is considered beneficial to human health. It can also be recommended as a healing beverage. Nevertheless, conflicting findings are reported about the risks of tea as well. Therefore, more studies are needed to further explore the benefits and possible harms of different types of tea.

Keywords: Tea, Tea compounds, Health, Benefits, Risks

Introduction

Tea is regarded as a popular beverage in different cultures. Apart from its flavor and stimulant effect, tea compounds may be highlighted for human health. For example, antioxidant, anti-inflammatory, and antitumor effects of tea contents, among others, can be beneficial for preventing all kinds of cancer, coronary artery, and inflammatory diseases.

Similarly, tea is the most globally used beverage after water and makes up 78% of all drinks (1-3). Its history goes back to 500 years ago in China and the north of India (4). In addition, tea, which is scientifically known as camellia sinensis from the Aceae family, is a large shrub plant with evergreen leaves and is native to East Asia where it is cultivated widely. Further, this beverage has dark green, leathery leaves, and white aromatic flowers and its plant (Figure 1) can be as high as 10 meters but its shrubs are kept at a 1-1.5-meter height for easy harvest (5).

Tea is currently cultivated in more than 30 countries with approximately three billion kilograms of production and consumption worldwide. Furthermore, it is classified into 3 categories based on the production method. Out of the total global produced tea, 78% is black tea, mainly produced in India and Sri Lanka, and 20% is green tea which is mostly cultivated in China, Japan, the Middle East, and America while only 2% is oolong which is mainly produced in China through partial fermentation (6-9).

Caffeine, ascorbate, flavonoids, and anti-inflammatories are the effective compounds of tea that are appreciated for their positive effects on human health (4).

The chemical compound of tea is complex because of numerous contents which are produced through the curing process, namely, the conversion of green tea to black tea and drying. Moreover, tea leaves contain varying amounts of polyphenol and catechin compounds. The main polyphenols (PPs) are flavonoids like catechin, epigallocatechin gallate, and proanthocyanidin (Figure 2). Other contents (Figure 3) include tannins, caffeine (0.4-1% or 10-50 mg), low amounts of xanthine, protein (15%-20%), fiber, sugar (5%), vitamins B, ascorbic acid (exists in fresh leaves but it is destroyed during the processing for black tea), amino acid, and fat (10).

Both green and black teas are produced from a single plant while they are different in terms of processing. For black and white tea, fresh leaves are oxidized to lose 55% of their weight. During the oxidation, the existing enzymes turn the simple PPs into more complex ones with less effective compounds and these complex PPs give a specific color and taste to black and white tea. Additionally, high fermentation reduces PPs while increasing the caffeine content. Black tea has 2-3 times more caffeine than green tea as well (11).

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Figure 1. Flowered *Camellia sinensis* Plant.

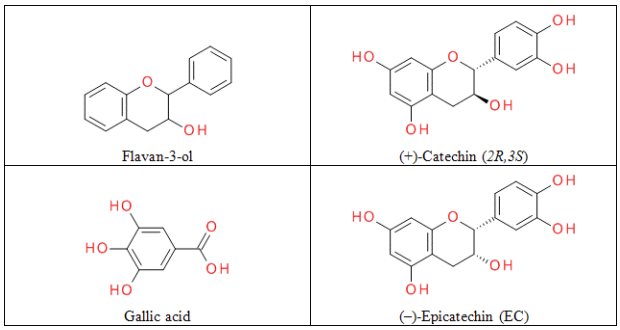

Figure 2. Chemical Compounds of Tea.

Likewise, green tea is prepared through gradual and gentle withering of the fresh leaves and its chemistry varies depending on the season, variety, farming operations, geography, as well as the age of the leaf, growth conditions, and production process (12, 13). Catechin constitutes more than 70% of the flavonoids in the green tea. Fresh leaves are steamed which leads to the deactivation of enzyme polyphenol oxidase. In addition, oolong tea is prepared by firing the leaves shortly after rolling to terminate the oxidation and dry the leaves. The difference between black and green tea and the processing stages of various types of tea are illustrated in Figures 3 and 4, respectively.

Tea is of special importance in the market basket of families. Many animal and in vivo studies have confirmed the benefits of tea in recent years which are related to PPs. In addition, although different studies have approved the role of tea in preventing coronary artery diseases (CADs), cancers, neurological diseases, depression, and other diseases, few studies have addressed the harms and risks of tea. Accordingly, the present study aimed to review the benefits of this beverage and inform about the rare but yet important risks of tea.

Methods

This review study was conducted by means of library research method and searching for various texts and scientific publications in Google Scholar, PubMed, and

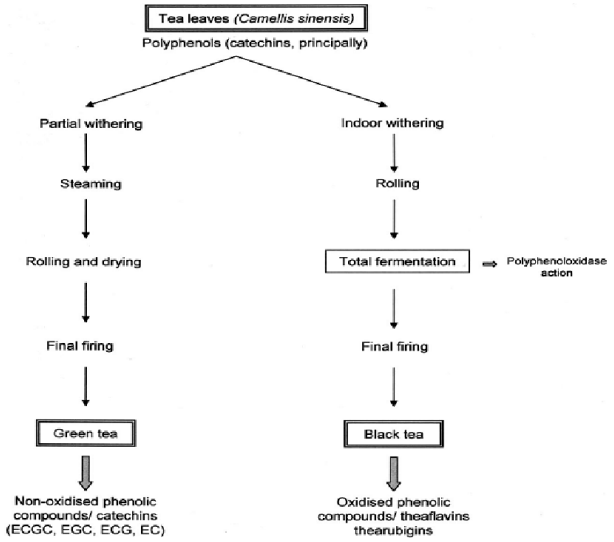

Figure 3. Principal Differences Between Green and Black Tea Processing and its Influence on the Final Polyphenol Content.

Cochrane databases using several keywords such as tea, the type of tea, benefits, and harms.

Results

Tea and Coronary Artery Diseases

CADs are the most common diseases across the world and are highly increasing in developing countries as the number one cause of deaths (14). Further, this disease occurs when a patient has multiple symptoms, signs, or complications from insufficient blood flow to the myocardium. The obstruction of coronary arteries is due to atherosclerosis (15). CAD is also the main cause of mortality in industrialized countries (16,17) and accounts for around one-third of all mortalities or higher in above 35-year-old individuals (18).

American Heart Association classifies the risk factors for developing CADs as high cholesterol, high homocysteine level, atherosclerosis, artery calcification, diabetes, hypertension, overweight, and smoking (19).

The results of some studies on humans and animals show that epigallocatechin-3-gallate (EGCG) is the most active compound, which is known as the main source of green tea benefits and makes up 65% of all the catechin content in the green tea. Meanwhile, green tea has a wide range of positive effects on arteries and endothelium (12,20).

There is a body of research on drinking tea and the risk of a heart attack. Green tea is believed to have antioxidant, anti-inflammatory, anticancer, antivirus, antimicrobial, antiparasitic, probiotic, anti-cell surface adhesion, and neuron protection effects (12,21,22). For example, Negishi et al concluded that the proteins in both black and green tea reduced hypertension through antioxidant properties in mice with high blood pressure and stroke (23). The

consumption of green tea may also have some protection against hypertension.

In a cross-sectional study, Yang et al also found that the consumption of 120 mL/d or more of medium strength green or oolong tea for a year may significantly reduce the risk of hypertension (24). Flavonoids reduce the accumulation of platelets and prevent the oxidation of low-density lipoproteins because of their antioxidant effects (25, 26).

Similarly, the results of a study in Rotterdam showed that drinking tea prevents cardiac ischemic diseases due to its flavonoid contents. Based on the findings of another study on a group of German men and women, the daily consumption of three to six cups of tea led to lower risks of mortality from CADs (27). Furthermore, one meta-analysis of 10 intervention and seven control groups indicated that increased tea consumption up to three cups a day reduced the incidence rate of myocardial infarction by 1% (28).

Another meta-analysis demonstrated that ischemic stroke was 21% less in individuals who drank more than three cups of tea (green or black) per day compared to those who had less than one cup (29). Overall, these results suggest that tea may have beneficial effects on heart diseases through the mechanisms which are associated with enhanced endothelial performance and the inhibition of platelet activation (30-32). However, the results of a similar meta-analysis of randomized controlled trials revealed that drinking tea has no impact on hypertension, low-density lipoprotein, or high-density lipoprotein. On the contrary, drinking high amounts of black tea was found to improve endothelial performance (33). In general, the daily consumption of one liter of tea reduces 4-10% of the platelet activation (32).

Tea and Atherosclerosis

Likewise, a limited number of studies are available regarding the relationship between drinking tea and atherosclerosis. For instance, Debette et al assessed the relationship between tea, flavonoids, and atherosclerosis and reported lower carotid plaques with higher tea consumption in women (34). Moreover, Mursu et al found a relationship between reduced carotid atherosclerosis and flavonoid consumption in Finnish middle-aged men (35). The compounds in tea prevent vascular inflammation and atherosclerosis through antihypertensive, antilipidemic, anti-inflammatory, antiproliferative, and antithrombogenic activities (36, 37) although further human research is required to explain the effect of tea on atherosclerosis.

Tea and Antioxidant Effects

According to previous experimental research, green tea PPs are regarded as strong antioxidant compounds that have greater traces of vitamins C and E. The strong antioxidant activity of tea extracts generally originates catechin, epicatechin, epigallocatechin, epigallocatechin gallate, and epicatechin gallate (38). Catechins are considered as nonvolatile flavor compounds and constitute 8-15% of the dried tea leaves weight (39,40). Regarding the antioxidant activity and phenolic contents of different tea extracts, Liebert et al found that in all cases, the antioxidant activity and total phenolic content would rise by the increased brewing time (41). Su et al also examined the total phenolic profile and antioxidant activity of oolong tea in different conditions and recorded the highest antioxidant activity at minute three (42). Additionally, investigating the effect of different brewing methods on antioxidant properties of the green tea, Lin et al concluded that hot water extracts have higher antioxidant activity compared to cold water extracts (43). Nevertheless, determining the antioxidant effect of tea is subject to further research.

Tea and Anti-gastrointestinal Tract Cancer Effects

Gastric cancer (GC) is one of the main causes of mortality around the world. The research confirmed the likelihood of reduced risk for gastrointestinal cancers in green tea drinkers (44,45). Various studies sought to find the protective chemical compounds that may reduce the risk, among which, green tea has a protective effect against GC. The findings of a previous study show that green tea decreases the risk of developing GC (46). In other words, green tea activates intracellular antioxidants, inhibits procarcinogen formation, suppresses angiogenesis, and proliferates cancer cells in the gastrointestinal tract.

However, studies respecting the preventive effects of green tea on esophageal cancer yielded unfavorable results and reverse relations are yet reported between drinking tea and gastric and colon cancers. Green tea extract is found to inhibit the gastric tumors of rats up to 88%. The catechol in the green tea combines with nitro compounds, thus reducing their carcinogenic effects. In addition, green tea and its catechin contents prevent gastrointestinal carcinoma in mice and have esophageal cancer-inhibiting effect in rats. The theaflavin in this type of tea also reduces tumor development in the rat model of esophageal cancer (47).

Further, drinking green tea has a preventive effect on lowering the risk of developing GC, especially if consumed for a long time. However, it is noteworthy that drinking high-temperature green tea may increase the risk of GC but it is still unclear whether this issue is a risk factor for GC. Therefore, more studies are required to gather evidence about the relation between green tea and GC and to achieve more accurate results regarding other risk factors of GC such as smoking, alcohol use, and the dosage of effective molecules in the green tea (48). There is insufficient evidence respecting the protective role of tea in developing colorectal, pancreatic, and urinary tract cancers, as well as glioma, lymphoma, and leukemia. Thus, further research should be conducted to provide definitive evidence for the positive effect of drinking tea on cancer

development in humans (49).

Peptic Ulcer

A peptic ulcer caused by nonsteroidal anti-inflammatory drugs is a significant complication that is the fourth cause of morbidity and mortality (50). Numerous herbs are used in traditional medicine for gastrointestinal disorders. The regular drinking of black tea may lower the risk of developing a peptic ulcer (51).

Tea and Analgesic and Anti-inflammatory Effects

Pain is often a sign of injury to or its progress in the body and is known as a discomforting situation that may not be tolerated by an individual. Thus, he or she seeks a way to alleviate the pain. It is a protective response to a threat or immediate injury as well (52, 53).

Inflammation is also a vital biological process and the response of the immune system to maintain body hemostasis through which complicated events and various mediators are involved in inducing, maintaining, or exacerbating the inflammatory reaction. Inflammation, especially the chronic type, is a common side-effect of many diseases that weakens the immune system, leads to infectious complications while delaying the improvement of related diseases (54, 55).

Chemical analgesics and anti-inflammatory drugs are divided into opioid analgesics (e.g., enkephalin, endorphin, morphine, methadone, and the like), as well as nonsteroidal analgesics and anti-inflammatory drugs (e.g., aspirin, acetaminophen, and the like). The side-effects of a number of opioid drugs might threaten a patient's life. Herbal drugs create a biological balance due to natural effective contents and other compounds that prevent the toxic accumulation of opioids (56).

Although the use of chemical drugs is now influential in reducing the pain and inflammation, their severe complications are well-known and inevitable. Therefore, research suggests herbal therapy as a low-cost and minimally complicated treatment. Herbal drugs including tea have antioxidant and flavonoid contents that can be utilized for decreasing pain and inflammatory symptoms (57, 58).

Ahmadian et al, examining the hydroalcoholic extract of green tea in mice, concluded that it has analgesic effects and thus can be an appropriate alternative to chemical analgesics (59). Nasiri et al also reported that the hydroalcoholic extract of *Stachys lavandulifolia* Vahl has analgesic and anti-inflammatory effects and might be a good alternative to analgesic and anti-inflammatory drugs. This plant is used in traditional medicine as an analgesic and anti-inflammatory herb owing to its flavonoid, iridoid, and saponin compounds (60). Furthermore, Singal et al found that green tea extract enhances the analgesic effect of morphine on the neuropathic pain of diabetic patients by inhibiting nitric oxide (NO) production (61).

Previous research shows that the protective agents of tea flavonoid compounds can exert anti-inflammatory effects (62) and thus alleviate pain and inflammation. The direct effect of flavonoids on prostaglandin biosynthesis is firmly proved as well (63).

Many of the beneficial effects of green tea are now attributed to the most common type of catechin, namely, EGCG (64, 65). It is the most essential catechin in the green tea and has antioxidant activities against NO by eliminating free radicals, chelating metal ions, and inducing androgenic antioxidant enzymes. NO and nitric oxide synthase (NOS) have a significant role in the pain process. Choi et al. found that ECGC reduces the pain from a pressured spinal nerve in rats, and therefore, has an analgesic effect on neuropathic pains caused by the pressure on the spinal nerve through stopping the NOS expression and inhibiting the pro-nociceptive effect of No (66). Endothelial exocytose is the early stage of leukocyte migration and vascular minor inflammation and ECGC decreases the endothelial exocytose in a concentration-dependent pattern (67). Another anti-inflammatory aspect of ECGC may be attributed to its ability to decrease the migration of inflammatory cells, stop metalloproteinase (MMP-9) and free radical production, and regulate NOS activity thus slowing down the inflammation (68).

Considering the findings of the above-mentioned studies, the compounds of different types of tea have analgesic and anti-inflammatory properties and that tea can be a good replacement for chemical drugs. Nevertheless, more studies are required on analgesic and anti-inflammatory effects, as well as various fractions of different tea extracts and the interference of the extracts with agonists and antagonists which are effective on pain and inflammation.

Tea and Anti-skin Cancer Effects

Green tea protects the skin from carcinogenic chemicals and is also useful against inflammatory reactions in skin cancers caused by chemicals or rays. Moreover, this type of tea and its PP extracts have a protective effect against mouse skin papilloma and inhibit skin tumors, UV ray-induced skin cancer in human and animal models, and photocarcinogens in mice. Skin tumor growth is significantly inhibited, or in some cases, decreased by the oral prescription of green or black tea or EGCG in mice with papilloma (69).

In a previous study, feeding tumorous mice with black tea accelerated the growth of indefinite tumors, squamous cell carcinoma, and the tumor volume. In addition, DNA synthesis was inhibited while apoptosis showed an increase (70). In another study, the oral infusion of black tea (for 11 weeks) to female mice exposed to UVB light decreased the number and volume of nonpolar and malignant tumors (54-84%). The findings of another study indicated that the oral consumption of black tea (for 11-15 weeks) increased the growth of papilloma (35-48%) which was developed in mice (70). Based on the results of one case-control study in

Italy, tea consumption had a protective effect on malignant melanoma and a significant decrease was reported in squamous cell carcinoma progression in individuals who drank black tea (71). Like many other practical methods, the EGCG extract of the green tea protects the skin against skin cancer (71).

Tea and Diabetes

Diabetes is the most prevalent endocrine disease that causes long-term ocular, vascular, and neurological complications and metabolic disorders in carbohydrate, lipid, and protein metabolism (72). Although insulin and sugar-reducing drugs are considered as the most common treatment for type 1 and type 2 diabetes, respectively, nutritional approaches and the use of herbal drugs are very widespread in many countries (73,74). The effect of green tea on blood sugar reduction is reported in very few studies (75,76). Green tea, which is rich in PPs, contributes to the treatment of diabetes-induced retinopathy (77,78). Epidemiological research also showed that green tea consumption prevents type 2 diabetes (79).

Additionally, there are specific serum proteins in green tea that might contribute to its antihyperglycemic effects (75). Decreased glucose level is reported in diabetic rats after receiving the green tea. Likewise, some of the green tea extracts increase the uptake of base and insulin-stimulated glucose in rat adipocytes (80). In addition, this type of tea is confirmed to have no effect on glucose and lipid levels (81). Generally speaking, tea is effective in reducing blood sugar level and protecting pancreatic beta cells in diabetic mice while human epidemiological studies show contradictory results about the relation between consuming tea and the risk of developing type 2 diabetes. Nonetheless, daily tea consumption (≥3 cups/day) may lead to a lower risk of type 2 diabetes (82).

In a laboratory study, the researchers found that the compounds of black tea are more effective than those of green and oolong tea respecting reducing blood sugar uptake. Further, 1040 elderly people who received long-term black tea had a lower incidence of diabetes (88).

The reports regarding the effect of green tea extract on blood sugar are contradictory. According to one study, green tea has no significant effect on glycemia but inhibits hyperlipidemia and enhances retinal superoxide formation (77) while another research argues that some of the green tea extracts raise the uptake of base and insulin-stimulated glucose in rat adipocytes (80).

Furthermore, the prescription of green tea powder for lab animals with high blood sugar would improve their insulin resistance (84). A study on human showed that the consumption of 1.5 g/d dry green tea powder could improve sugar resistance and metabolism in diabetic patients (75).

Decreased serum glucose is reported in Alloxan diabetic rats fed with green tea. The PPs in green tea improves sugar metabolism in lab animals as well (85) and the extract of this tea prevents diabetes-induced weight loss (81). However, the findings of another study indicated that the tea extract had no effect on the prevention of blood sugar and weight loss but it was effective on reduced food intake (77).

Likewise, Mehdizadeh et al evaluated the effect of three different dosages of green tea hydroalcoholic extract on blood sugar reduction in rats. The extracts at 50, 100, and 200 mg/kg dosages could reduce blood sugar in diabetic rats. The results further showed that the 100 mg/kg dosage was the most appropriate one at the end of week six while higher dosages had no significant effect on lowering the blood sugar (86). Mohammadi et al also concluded that green tea extracts could contribute to controlling the complications of type 2 diabetes by raising the serum level of adiponectin, weight, and body mass index control, along with the HbA1C level (87). However, more studies should be conducted to confirm these findings, particularly in relation to different types of tea.

Tea and Antibacterial, Antivirus, and Probiotic Effects

The screening effect of green tea methanolic extract for antimicrobial properties against 111 bacteria, including two genera of Gram-positive and seven genera of Gram-negative bacteria, led to further inhibition of these species. Moreover, the protection of Swiss white mice by varying dosages of Salmonella Typhimurium proved the in vitro antibacterial effects of the tea extract (88). EGCG was also found to be effective in inhibiting HIV infections and *Staphylococcus aureus* infections (89). Drinking tea not only reduces bacteria, that produce ammoniac and other harmful amines, but also results in significantly increased amounts of *Lactobacillus* and *Bifidobacterium* (organic acid production) and decreased intestine pH (90). Nonetheless, the effect of tea on viral infections should not be ignored either. Meanwhile, tea PP is confirmed to have an inhibitory effect on rotavirus in the cultured cells of the monkeys, as well as influenza A virus in animal cells as well (70). Several flavonoids including EGCG and epicatechin-3-gallate (ECG) prevent the spread of human immunodeficiency virus (rhinovirus) by restricting the enzyme which is responsible for virus production in the host cells (91). Therefore, tea may be considered a complementary treatment for HIV but further research is needed since many of the chemicals, proved to be effective on HIV in mice, cannot produce similar in vivo results. Thus, tea may be used along with common drugs (92).

Tea and the Risk of Preeclampsia

Although tea helps the prevention of vascular diseases, its contribution to pregnancy vascular diseases such as preeclampsia increases some concerns. Pregnant women, who frequently drink tea, are at the risk of preeclampsia which may be caused by different tea compounds through possible mechanisms including oxidative stress or the modulation of angiogenic factors (93).

Tea and Alzheimer's Disease

Alzheimer's disease (AD) is an important concern since it is increasing among the elderly. Tea is proposed as a traditional complementary treatment for neurological diseases (94). Additionally, its consumption is found to be related to the decreased risk of developing AD-related neurological diseases or improved cognitive functions in older populations across the world. There are various mechanisms through which the bioactive compounds of tea (i.e., EGCG, ECG, EGC, EC, L-theanine, and rutin) have anti-amyloid effects and protect against AD. The anti-amyloid mechanisms of these bioactive compounds that fight AD are as follows (Figure 4).

- Inhibiting amyloid precursor protein cleavage by regulating relevant enzyme activities;
- Preventing protein concentration and Aβ-induced membrane damage;
- Reducing Aβ-caused oxidative stress;
- Suppressing Aβ oligomers accumulation;
- Regulating signaling paths including Aβ production;
- Reducing Aβ-induced mitochondria dysfunction;
- Inhibiting the hyperphosphorylation of T protein (95).

Further research on these agents is needed to fill the gap between in vitro studies and the applied clinical programs.

Tea and Parkinson's Disease

Tea PPs might play an important role in the onset, delay, or progression of Parkinson's disease (PD) and black and green tea are rich in PPs many of which are EGCG and thioflavin. Some information is available about the neuroprotein and neuroregenerative effects of tea PP which shows that they not only have antioxidant effects but also, in vitro and animal models of EGCG may be involved in the accumulation of αS protein and thus modulate the intracellular signaling paths. Future studies should address the effects of other black tea PPs including thioflavin. Contrarily, although there is significant evidence regarding the protective effects against neuroprotein, clinical research is still limited and it is only EGCG that has made it to phase II trials (96).

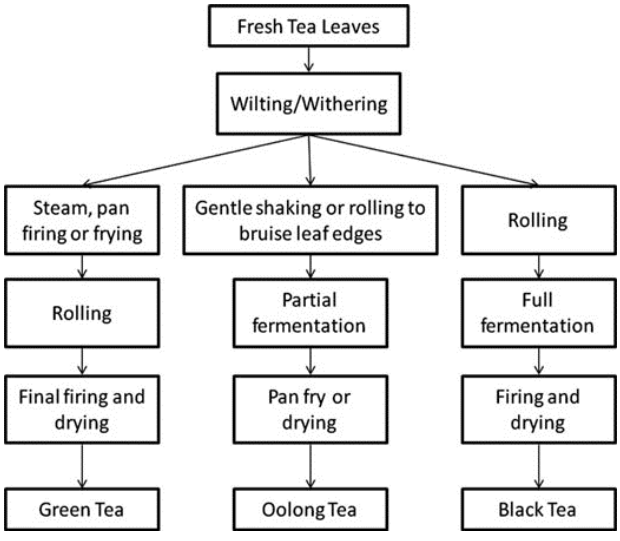

Figure 4. Production and Processing of Three Different Types of Tea.

Several epidemiological and interventional studies on humans demonstrated the positive effects of green and black tea on neurogenic disorders including cognitive disability and memory loss. In addition, the positive effects of tea on PD have already been confirmed with regard to specific cerebral disorders. Tea, along with drugs such as L-DOPA has a synergic effect for maximizing its effect at specific levels in the path of canonical diseases induced by the phenotype of PD (97).

On the other hand, other studies rejected these effects on PD. The discrepancy may depend on various factors including brewing methods, the beverage temperature, smoking, alcohol use, as well as genetic and environmental differences including race, gender, age, and lifestyle (98,99). Intestinal microbiota and genetic polymorphism may also be influential on the results (100,101). Therefore, more accurate human studies seem to be necessary to confirm the neuroprotective effects of tea.

Tea and its Side-Effects

Green tea might be associated with several side-effects or toxicity (102). Evidence indicates that catechin complex tannins accelerate esophageal cancer development in areas where people drink strong tea. Adding milk could mitigate this effect by attaching to tannins. Further, the daily consumption of 250 cc of tea in children leads to iron metabolism deficiency, and consequently, anemia. Like other caffeinated beverages, excessive drinking of green tea may cause stimulatory effects such as nervousness, anxiety, insomnia, sensitivity, and the like (103).

Previous evidence also shows that caffeine in animals may be teratogenic. Although its precise mechanism is still unknown in both humans and animals and safe dosages are not yet recommended, the Food and Drug Administration recommends that pregnant women should avoid using caffeinated products. Therefore, more studies should be conducted on the long-term outcomes of consuming caffeine during pregnancy since different variables including fetal, maternal, and placental morphological outcomes should also be taken into account in future research (104).

Conclusions

For centuries, people consumed tea as practical food and different studies have currently identified the chemical performance and bioavailability of tea contents. Given that both internal and external factors contribute to the incidence and prevalence of chronic diseases, the results showed that tea is a herbal drug which is absorbed and metabolized by the body and the effects of its contents may be observed at cellular levels.

Epidemiological studies and investigation of the

interferences can probably determine whether regular drinking of tea is effective against different cancers, cardiovascular diseases, diabetes mellitus, and other diseases and if tea can be recommended as a healing beverage. On the other hand, several cases of hepatotoxicity, neurogenic disorders, and other side-effects are also reported regarding tea consumption. Accordingly, future studies should focus on the side-effects and harms of tea as well.

Conflict of Interests

None to be dclared.

Ethical Issues

Not applicable.

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References

1. Wang H, Provan GJ, Helliwell K. Tea flavonoids: their functions, utilisation and analysis. Trends Food Sci Technol. 2000;11(4-5):152-160. doi:10.1016/S0924-2244(00)00061-3
2. Perva-Uzunalić A, Škerget M, Knez Ž, Weinreich B, Otto F, Grüner S. Extraction of active ingredients from green tea (Camellia sinensis): Extraction efficiency of major catechins and caffeine. Food Chem. 2006;96(4):597-605. doi:10.1016/j.foodchem.2005.03.015
3. Li S, Lo CY, Pan MH, Lai CS, Ho CT. Black tea: chemical analysis and stability. Food Funct. 2013;4(1):10-18. doi:10.1039/c2fo30093a
4. Blumberg JB, Bolling BW, Chen C, Xiao H. Review and perspective on the composition and safety of green tea extracts. European J Nutr Food Saf. 2015;5(1):1-31. doi:10.9734/EJNFS/2015/12712
5. Owuor PO, Wachira FN, Ng'etich WK. Influence of region of production on relative clonal plain tea quality parameters in Kenya. Food Chem. 2010;119(3):1168-1174. doi:10.1016/j.foodchem.2009.08.032
6. Ahmad N, Gupta S, Mukhtar H. Green tea polyphenol epigallocatechin-3-gallate differentially modulates nuclear factor kappaB in cancer cells versus normal cells. Arch Biochem Biophys. 2000;376(2):338-346. doi:10.1006/abbi.2000.1742
7. Cabrera C, Artacho R, Gimenez R. Beneficial effects of green tea--a review. J Am Coll Nutr. 2006;25(2):79-99.
8. Khan N, Mukhtar H. Tea polyphenols for health promotion. Life Sci. 2007;81(7):519-533. doi:10.1016/j.lfs.2007.06.011
9. Butt MS, Sultan MT. Green tea: nature's defense against malignancies. Crit Rev Food Sci Nutr. 2009;49(5):463-473. doi:10.1080/10408390802145310
10. Pan X, Niu G, Liu H. Microwave-assisted extraction of tea polyphenols and tea caffeine from green tea leaves. Chem Eng Process. 2003;42(2):129-133. doi:10.1016/S0255-2701(02)00037-5
11. Adak M, Gabar M. Green tea as a functional food for better health: A brief review. Res J Pharm Biol Chem Sci. 2011;2(2):645-664.
12. Sherwani SK, Bashir A, Haider SS, Shah MA, Kazmi SU. Thrombolytic potential of aqueous and methanolic crude extracts of Camellia sinensis (Green tea): In vitro study. J Pharmacogn Phytochem. 2013;2(1):125-129.
13. Mbata TI, Debiao LU, Saikia A. Antibacterial activity of the crude extract of Chinese green tea (Camellia sinensis) on Listeria monocytogenes. Afr J Biotechnol. 2008;7(10):1571-1573.
14. Mendonça MI, Palma dos Reis R, Brehm A. Prediction of Coronary Heart Disease Risk in a South European Population: a case-control study. In: Coronary Artery Diseases. InTech; 2012.
15. Sayols-Baixeras S, Lluis-Ganella C, Lucas G, Elosua R. Pathogenesis of coronary artery disease: focus on genetic risk factors and identification of genetic variants. Appl Clin Genet. 2014;7:15-32. doi:10.2147/tacg.s35301
16. Islam MA. Cardiovascular effects of green tea catechins: progress and promise. Recent Pat Cardiovasc Drug Discov. 2012;7(2):88-99.
17. Mendis S, Puska P, Norrving B, Organization WH. Global atlas on cardiovascular disease prevention and control. Geneva: WHO; 2011.
18. Masoumi M, Saeidi M, Piri F, Abdoli G. Epidemiological evaluation of coronary artery diseases (CAD) in patients referred to cardiovascular centers of Kermanshah (2001-2002). Behbood. 2004;8(2):37-46.
19. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med. 2016;4(13):256. doi:10.21037/atm.2016.06.33
20. Moore RJ, Jackson KG, Minihane AM. Green tea (Camellia sinensis) catechins and vascular function. Br J Nutr. 2009;102(12):1790-1802. doi:10.1017/s0007114509991218
21. Hassanain E, Silverberg JI, Norowitz KB, et al. Green tea (Camelia sinensis) suppresses B cell production of IgE without inducing apoptosis. Ann Clin Lab Sci. 2010;40(2):135-143.
22. Choi YB, Kim YI, Lee KS, Kim BS, Kim DJ. Protective effect of epigallocatechin gallate on brain damage after transient middle cerebral artery occlusion in rats. Brain Res. 2004;1019(1-2):47-54. doi:10.1016/j.brainres.2004.05.079
23. Negishi H, Xu JW, Ikeda K, Njelekela M, Nara Y, Yamori Y. Black and green tea polyphenols attenuate blood pressure increases in stroke-prone spontaneously hypertensive rats. J Nutr. 2004;134(1):38-42. doi:10.1093/jn/134.1.38
24. Yang YC, Lu FH, Wu JS, Wu CH, Chang CJ. The protective effect of habitual tea consumption on hypertension. Arch Intern Med. 2004;164(14):1534-1540. doi:10.1001/archinte.164.14.1534
25. Nègre-Salvayre A, Salvayre R. Quercetin prevents the cytotoxicity of oxidized LDL on lymphoid cell lines. Free Radic Biol Med. 1992;12(2):101-106.
26. Gresele P, Cerletti C, Guglielmini G, Pignatelli P, de Gaetano G, Violi F. Effects of resveratrol and other wine polyphenols on vascular function: an update. J Nutr Biochem. 2011;22(3):201-211. doi:10.1016/j.jnutbio.2010.07.004
27. de Koning Gans JM, Uiterwaal CS, van der Schouw YT, et al. Tea and coffee consumption and cardiovascular morbidity and mortality. Arterioscler Thromb Vasc Biol. 2010;30(8):1665-1671. doi:10.1161/atvbaha.109.201939
28. Peters U, Poole C, Arab L. Does tea affect cardiovascular

disease? A meta-analysis. Am J Epidemiol. 2001;154(6):495-503. doi:10.1093/aje/154.6.495
29. Arab L, Liu W, Elashoff D. Green and black tea consumption and risk of stroke: a meta-analysis. Stroke. 2009;40(5):1786-1792. doi:10.1161/strokeaha.108.538470
30. Gardner EJ, Ruxton CH, Leeds AR. Black tea--helpful or harmful? A review of the evidence. Eur J Clin Nutr. 2007;61(1):3-18. doi:10.1038/sj.ejcn.1602489
31. Wang ZM, Zhou B, Wang YS, et al. Black and green tea consumption and the risk of coronary artery disease: a meta-analysis. Am J Clin Nutr. 2011;93(3):506-515. doi:10.3945/ajcn.110.005363
32. Ostertag LM, O'Kennedy N, Kroon PA, Duthie GG, de Roos B. Impact of dietary polyphenols on human platelet function--a critical review of controlled dietary intervention studies. Mol Nutr Food Res. 2010;54(1):60-81. doi:10.1002/mnfr.200900172
33. Hooper L, Kroon PA, Rimm EB, et al. Flavonoids, flavonoid-rich foods, and cardiovascular risk: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2008;88(1):38-50. doi:10.1093/ajcn/88.1.38
34. Debette S, Courbon D, Leone N, et al. Tea consumption is inversely associated with carotid plaques in women. Arterioscler Thromb Vasc Biol. 2008;28(2):353-359. doi:10.1161/atvbaha.107.151928
35. Mursu J, Nurmi T, Tuomainen TP, Ruusunen A, Salonen JT, Voutilainen S. The intake of flavonoids and carotid atherosclerosis: the Kuopio Ischaemic Heart Disease Risk Factor Study. Br J Nutr. 2007;98(4):814-818. doi:10.1017/s0007114507744410
36. Babu PV, Liu D. Green tea catechins and cardiovascular health: an update. Curr Med Chem. 2008;15(18):1840-1850. doi:10.2174/092986708785132979
37. Naito Y, Yoshikawa T. Green tea and heart health. J Cardiovasc Pharmacol. 2009;54(5):385-390. doi:10.1097/FJC.0b013e3181b6e7a1
38. Lee KW, Lee HJ, Lee CY. Antioxidant activity of black tea vs. green tea. J Nutr. 2002;132(4):785; author reply 786. doi:10.1093/jn/132.4.785
39. Bankova V. Chemical diversity of propolis and the problem of standardization. J Ethnopharmacol. 2005;100(1-2):114-117. doi:10.1016/j.jep.2005.05.004
40. Nwuha V, Nakajima M, Tong J, Ichikawa S. Solubility study of green tea extracts in pure solvents and edible oils. J Food Eng. 1999;40(3):161-165.
41. Liebert M, Licht U, Böhm V, Bitsch R. Antioxidant properties and total phenolics content of green and black tea under different brewing conditions. Zeitschrift für Lebensmitteluntersuchung und -Forschung A. 1999;208(3):217-220. doi:10.1007/s002170050406
42. Su X, Duan J, Jiang Y, Duan X, Chen F. Polyphenolic profile and antioxidant activities of oolong tea infusion under various steeping conditions. Int J Mol Sci. 2007;8(12):1196-1205.
43. Lin SD, Liu EH, Mau JL. Effect of different brewing methods on antioxidant properties of steaming green tea. LWT-Food Sci Technol. 2008;41(9):1616-1623. doi:10.1016/j.lwt.2007.10.009
44. Mu LN, Lu QY, Yu SZ, et al. Green tea drinking and multigenetic index on the risk of stomach cancer in a Chinese population. Int J Cancer. 2005;116(6):972-983. doi:10.1002/ijc.21137
45. Zhou Y, Li N, Zhuang W, et al. Green tea and gastric cancer risk: meta-analysis of epidemiologic studies. Asia Pac J Clin Nutr. 2008;17(1):159-165.
46. Hou IC, Amarnani S, Chong MT, Bishayee A. Green tea and the risk of gastric cancer: epidemiological evidence. World J Gastroenterol. 2013;19(24):3713-3722. doi:10.3748/wjg.v19.i24.3713
47. Koo MW, Cho CH. Pharmacological effects of green tea on the gastrointestinal system. Eur J Pharmacol. 2004;500(1-3):177-185. doi:10.1016/j.ejphar.2004.07.023
48. Huang Y, Chen H, Zhou L, et al. Association between green tea intake and risk of gastric cancer: a systematic review and dose-response meta-analysis of observational studies. Public Health Nutr. 2017;20(17):3183-3192. doi:10.1017/s1368980017002208
49. Yuan JM. Green tea and prevention of esophageal and lung cancers. Mol Nutr Food Res. 2011;55(6):886-904. doi:10.1002/mnfr.201000637
50. Hawkey CJ. Non-steroidal anti-inflammatory drugs and peptic ulcers. BMJ. 1990;300(6720):278-284. doi:10.1136/bmj.300.6720.278
51. Adhikary B, Yadav SK, Roy K, Bandyopadhyay SK, Chattopadhyay S. Black tea and theaflavins assist healing of indomethacin-induced gastric ulceration in mice by antioxidative action. Evid Based Complement Alternat Med. 2011;2011. doi:10.1155/2011/546560
52. Bruckenthal P. Integrating nonpharmacologic and alternative strategies into a comprehensive management approach for older adults with pain. Pain Manag Nurs. 2010;11(2 Suppl):S23-31. doi:10.1016/j.pmn.2010.03.004
53. Guyton AC, Hall J. Textbook of Medical Physiology. Philadelphia: Elsevier Saunders; 2006:748-760.
54. Ricciotti E, FitzGerald GA. Prostaglandins and inflammation. Arterioscler Thromb Vasc Biol. 2011;31(5):986-1000. doi:10.1161/atvbaha.110.207449
55. Kotas ME, Medzhitov R. Homeostasis, inflammation, and disease susceptibility. Cell. 2015;160(5):816-827. doi:10.1016/j.cell.2015.02.010
56. Nasri S, SalehiSourmaghi MH, Amin G, Mohebali S, Sharifi A. Major essential oil components, antinociceptive and anti-inflammatory effects of hexane extract of Vitexagnus-castus L. fruits and possible mechanism in male mice. J Paramed Sci. 2013;4(3):1-16.
57. Nishimoto N, Kishimoto T. Interleukin 6: from bench to bedside. Nat Clin Pract Rheumatol. 2006;2(11):619-626. doi:10.1038/ncprheum0338
58. Hajhashemi V, Ghannadi A, Hajiloo M. Analgesic and anti-inflammatory effects of Rosa damascena hydroalcoholic extract and its essential oil in animal models. Iran J Pharm Res. 2010;9(2):163-168.
59. Ahmadian-Baghbadorani N, Azhdari-Zarmehri H, Puzesh S, Mousavi FS, Rajaei F. Antinociceptive effect of hydroalcoholic extract of green tea in male mice. Feyz Journal of Kashan University of Medical Sciences. 2014;17(6):528-536. [Persian].
60. Nasri S, Ramezanghorbani A, Kamalinejad M. Analgesic and anti-inflammatory effects of hydroalcoholic extract of Stachys lavandulifolia vahl S, aerial parts in male mice. Armaghane Danesh. 2011;16(2):161-171. [Persian].
61. Singal A, Anjaneyulu M, Chopra K. Modulatory role of

green tea extract on antinociceptive effect of morphine in diabetic mice. J Med Food. 2005;8(3):386-391. doi:10.1089/jmf.2005.8.386
62. Albrecht DS, Clubbs EA, Ferruzzi M, Bomser JA. Epigallocatechin-3-gallate (EGCG) inhibits PC-3 prostate cancer cell proliferation via MEK-independent ERK1/2 activation. Chem Biol Interact. 2008;171(1):89-95. doi:10.1016/j.cbi.2007.09.001
63. Alcaraz MJ, Hoult JR. Actions of flavonoids and the novel anti-inflammatory flavone, hypolaetin-8-glucoside, on prostaglandin biosynthesis and inactivation. Biochem Pharmacol. 1985;34(14):2477-2482. doi:10.1016/0006-2952(85)90529-5
64. Park OJ, Surh YJ. Chemopreventive potential of epigallocatechin gallate and genistein: evidence from epidemiological and laboratory studies. Toxicol Lett. 2004;150(1):43-56. doi:10.1016/j.toxlet.2003.06.001
65. Mandel S, Weinreb O, Amit T, Youdim MB. Cell signaling pathways in the neuroprotective actions of the green tea polyphenol (-)-epigallocatechin-3-gallate: implications for neurodegenerative diseases. J Neurochem. 2004;88(6):1555-1569. doi:10.1046/j.1471-4159.2003.02291.x
66. Choi JI, Kim WM, Lee HG, Kim YO, Yoon MH. Role of neuronal nitric oxide synthase in the antiallodynic effects of intrathecal EGCG in a neuropathic pain rat model. Neurosci Lett. 2012;510(1):53-57. doi:10.1016/j.neulet.2011.12.070
67. Yamakuchi M, Bao C, Ferlito M, Lowenstein CJ. Epigallocatechin gallate inhibits endothelial exocytosis. Biol Chem. 2008;389(7):935-941. doi:10.1515/bc.2008.095
68. Kim SH, Park HJ, Lee CM, et al. Epigallocatechin-3-gallate protects toluene diisocyanate-induced airway inflammation in a murine model of asthma. FEBS Lett. 2006;580(7):1883-1890. doi:10.1016/j.febslet.2006.02.052
69. Conney AH, Lu Y, Lou Y, Xie J, Huang M. Inhibitory effect of green and black tea on tumor growth. Proc Soc Exp Biol Med. 1999;220(4):229-233. doi:10.1046/j.1525-1373.1999.d01-39.x
70. Khan N, Mukhtar H. Tea polyphenols for health promotion. Life Sci. 2007;81(7):519-533. doi:10.1016/j.lfs.2007.06.011
71. Naldi L, Gallus S, Tavani A, Imberti GL, La Vecchia C. Risk of melanoma and vitamin A, coffee and alcohol: a case-control study from Italy. Eur J Cancer Prev. 2004;13(6):503-508.
72. Imperatore G, Boyle JP, Thompson TJ, et al. Projections of type 1 and type 2 diabetes burden in the U.S. population aged <20 years through 2050: dynamic modeling of incidence, mortality, and population growth. Diabetes Care. 2012;35(12):2515-2520. doi:10.2337/dc12-0669
73. Grover JK, Yadav S, Vats V. Medicinal plants of India with anti-diabetic potential. J Ethnopharmacol. 2002;81(1):81-100.
74. Khan A, Anderson RA. Insulin potentiating factor (IPF) present in foods, species and natural products. Pak J Nutr. 2003;2(4):254-257. doi:10.3923/pjn.2003.254.257
75. Tsuneki H, Ishizuka M, Terasawa M, Wu JB, Sasaoka T, Kimura I. Effect of green tea on blood glucose levels and serum proteomic patterns in diabetic (db/db) mice and on glucose metabolism in healthy humans. BMC Pharmacol. 2004;4:18. doi:10.1186/1471-2210-4-18
76. Lind L. Circulating markers of inflammation and atherosclerosis. Atherosclerosis. 2003;169(2):203-214. doi:10.1016/s0021-9150(03)00012-1
77. Mustata GT, Rosca M, Biemel KM, et al. Paradoxical effects of green tea (Camellia sinensis) and antioxidant vitamins in diabetic rats: improved retinopathy and renal mitochondrial defects but deterioration of collagen matrix glycoxidation and cross-linking. Diabetes. 2005;54(2):517-526. doi:10.2337/diabetes.54.2.517
78. Kowluru RA, Odenbach S. Role of interleukin-1beta in the pathogenesis of diabetic retinopathy. Br J Ophthalmol. 2004;88(10):1343-1347. doi:10.1136/bjo.2003.038133
79. Shankar S, Ganapathy S, Srivastava RK. Green tea polyphenols: biology and therapeutic implications in cancer. Front Biosci. 2007;12:4881-4899.
80. Wu LY, Juan CC, Ho LT, Hsu YP, Hwang LS. Effect of green tea supplementation on insulin sensitivity in Sprague-Dawley rats. J Agric Food Chem. 2004;52(3):643-648. doi:10.1021/jf030365d
81. Ryu OH, Lee J, Lee KW, et al. Effects of green tea consumption on inflammation, insulin resistance and pulse wave velocity in type 2 diabetes patients. Diabetes Res Clin Pract. 2006;71(3):356-358. doi:10.1016/j.diabres.2005.08.001
82. Yang J, Mao QX, Xu HX, Ma X, Zeng CY. Tea consumption and risk of type 2 diabetes mellitus: a systematic review and meta-analysis update. BMJ Open. 2014;4(7):e005632. doi:10.1136/bmjopen-2014-005632
83. Panagiotakos DB, Lionis C, Zeimbekis A, et al. Long-term tea intake is associated with reduced prevalence of (type 2) diabetes mellitus among elderly people from Mediterranean islands: MEDIS epidemiological study. Yonsei Med J. 2009;50(1):31-38. doi:10.3349/ymj.2009.50.1.31
84. Sun CL, Yuan JM, Koh WP, Yu MC. Green tea, black tea and breast cancer risk: a meta-analysis of epidemiological studies. Carcinogenesis. 2006;27(7):1310-1315. doi:10.1093/carcin/bgi276
85. Sabu MC, Smitha K, Kuttan R. Anti-diabetic activity of green tea polyphenols and their role in reducing oxidative stress in experimental diabetes. J Ethnopharmacol. 2002;83(1-2):109-116.
86. Mehdizadeh M HTA, Ebrahimniya F and et al. The effect of green tea extract hydroalcoholic extract Blood Glucose and Streptozotocin-Induced Diabetic Male Hair Weight. Journal of Gorgan University of Medical Sciences. 2010;11(29):8-11. [Persian].
87. Mohammadi S, Hasseinzadeh Attar M, Karimi M, et al. The effects of green tea extract on serum adiponectin concentration and insulin resistance in patients with type 2 diabetes mellitus. J Adv Med Biomed Res. 2010;18(70):44-57. [Persian].
88. Bandyopadhyay D, Chatterjee TK, Dasgupta A, Lourduraja J, Dastidar SG. In vitro and in vivo antimicrobial action of tea: the commonest beverage of Asia. Biol Pharm Bull. 2005;28(11):2125-2127. doi:10.1248/bpb.28.2125
89. Nance CL, Shearer WT. Is green tea good for HIV-1 infection? J Allergy Clin Immunol. 2003;112(5):851-853. doi:10.1016/j.jaci.2003.08.048
90. Weisburger JH. Tea and health: the underlying mechanisms. Proc Soc Exp Biol Med. 1999;220(4):271-275. doi:10.1046/j.1525-1373.1999.d01-46.x
91. Yamamoto T, Juneja LR, Chu DC, Kim M. Chemistry and applications of green tea. CRC Press; 1997.
92. Williamson MP, McCormick TG, Nance CL, Shearer WT.

Epigallocatechin gallate, the main polyphenol in green tea, binds to the T-cell receptor, CD4: Potential for HIV-1 therapy. J Allergy Clin Immunol. 2006;118(6):1369-1374. doi:10.1016/j.jaci.2006.08.016
93. Wei SQ, Xu H, Xiong X, Luo ZC, Audibert F, Fraser WD. Tea consumption during pregnancy and the risk of pre-eclampsia. Int J Gynaecol Obstet. 2009;105(2):123-126. doi:10.1016/j.ijgo.2008.12.003
94. Pervin M, Unno K, Ohishi T, Tanabe H, Miyoshi N, Nakamura Y. Beneficial effects of green tea catechins on neurodegenerative diseases. Molecules. 2018;23(6). doi:10.3390/molecules23061297
95. Polito CA, Cai ZY, Shi YL, et al. Association of Tea Consumption with Risk of Alzheimer's Disease and Anti-Beta-Amyloid Effects of Tea. Nutrients. 2018;10(5). doi:10.3390/nu10050655
96. Caruana M, Vassallo N. Tea polyphenols in Parkinson's disease. In: Vassallo N, ed. Natural Compounds as Therapeutic Agents for Amyloidogenic Diseases. Springer; 2015. p. 117-137.
97. Dutta D, Mohanakumar KP. Tea and Parkinson's disease: Constituents of tea synergize with antiparkinsonian drugs to provide better therapeutic benefits. Neurochem Int. 2015;89:181-190. doi:10.1016/j.neuint.2015.08.005
98. Jurado-Coronel JC, Avila-Rodriguez M, Echeverria V, et al. Implication of green tea as a possible therapeutic approach for Parkinson disease. CNS Neurol Disord Drug Targets. 2016;15(3):292-300.
99. Li FJ, Ji HF, Shen L. A meta-analysis of tea drinking and risk of Parkinson's disease. ScientificWorldJournal. 2012;2012:923464. doi:10.1100/2012/923464
100. Suzuki T, Pervin M, Goto S, Isemura M, Nakamura Y. Beneficial Effects of Tea and the Green Tea Catechin Epigallocatechin-3-gallate on Obesity. Molecules. 2016;21(10). doi:10.3390/molecules21101305
101. Yang CS, Wang X, Lu G, Picinich SC. Cancer prevention by tea: animal studies, molecular mechanisms and human relevance. Nat Rev Cancer. 2009;9(6):429-439. doi:10.1038/nrc2641
102. Palacio Sánchez E, Ribero Vargas ME, Restrepo Gutiérrez JC. Toxicidad hepática por té verde (*Camellia sinensis*): Revisión de tema. [Hepatotoxicity due to green tea consumption (*Camellia sinensis*): A review]. Rev Colomb Gastroenterol. 2013;28(1):46-52.
103. Toolsee NA, Aruoma OI, Gunness TK, et al. Effectiveness of green tea in a randomized human cohort: relevance to diabetes and its complications. Biomed Res Int. 2013;2013:412379. doi:10.1155/2013/412379
104. e Paula TMD, Shang FLT, Chiarini-Garcia H, de Almeida FRCL. Caffeine Intake during Pregnancy: What Are the Real Evidences? J Pharm Pharmacol. 2017;5:249-260. doi:10.17265/2328-2150/2017.05.004