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Tea and Health: Studies in Humans

Naghma Khan and **Hasan Mukhtar***
Department of Dermatology, University of Wisconsin, Madison, WI 53706, USA

Abstract

Tea, next to water is the cheapest beverage humans consume. Drinking the beverage tea has been considered a health-promoting habit since ancient times. The modern medicinal research is providing a scientific basis for this belief. The evidence supporting the health benefits of tea drinking grows stronger with each new study that is published in the scientific literature. Tea plant *Camellia sinensis* has been cultivated for thousands of years and its leaves have been used for medicinal purposes. Tea is used as a popular beverage worldwide and its ingredients are now finding medicinal benefits. Encouraging data showing cancer-preventive effects of green tea from cell-culture, animal and human studies have emerged. Evidence is accumulating that black tea may have similar beneficial effects. Tea consumption has also been shown to be useful for prevention of many debilitating human diseases that include maintenance of cardiovascular and metabolic health. Various studies suggest that polyphenolic compounds present in green and black tea are associated with beneficial effects in prevention of cardiovascular diseases, particularly of atherosclerosis and coronary heart disease. In addition, anti-aging, antidiabetic and many other health beneficial effects associated with tea consumption are described. Evidence is accumulating that catechins and theaflavins, which are the main polyphenolic compounds of green and black tea, respectively, are responsible for most of the physiological effects of tea. This article describes the evidences from clinical and epidemiological studies in the prevention of chronic diseases like cancer and cardiovascular diseases and general health promotion associated with tea consumption.

Keywords

Tea polyphenols; cancer prevention; cardiovascular diseases; health effects

INTRODUCTION

Tea, the most popular beverage consumed by two-thirds of the world's population is made from the processed leaf of *Camellia sinensis*. Tea types, based on processing or harvested leaf development are black (fermented), green (non-fermented) and oolong (semi-fermented). These major tea types differ in how tea is produced and processed according to

*Address correspondence to this author at the Helfaer Professor of Cancer Research, Director and Vice Chair for Research, Department of Dermatology, University of Wisconsin-Madison, 4385, Medical Sciences Center, 1300 University Avenue, Madison, WI, 53706; Tel: 608-263-3927; Fax: 608-263-5223; hmukhtar@wisc.edu.

CONFLICT OF INTEREST

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the different processes of drying and fermentation that determine its chemical composition. Green tea is produced by using young tea leaves and sold for consumption without fermentation after withering, steaming or pan firing, drying and grading. Pan firing is required to prevent the tea leaves from fermenting by the natural enzyme activities. Tea leaves are allowed to ferment for several hours before being either smoke fired, flame fired or steamed to make black tea. Oolong tea is produced by a partial oxidation of the leaf, intermediate between the process for green and black tea [1]. Black tea is made by first exposing the tea leaves to air, causing them to oxidize. This oxidation process turns leaves into a deep brown color and during this process, the flavor is intensified. The leaves are then left as such or are heated, dried and crushed. Green tea is best studied for its health benefits, including cancer chemopreventive and chemotherapeutic effects [2, 3], but emerging data is showing that black tea may possess similar health promoting attributes.

Green tea contains characteristic polyphenolic compounds, (−)-epigallocatechin-3-gallate (EGCG), (−)-epigallocatechin (EGC), (−)-epicatechin-3-gallate (ECG) and (−)-epicatechin (EC). Flavonols, including quercetin, kaempferol, myricitin and their glycosides are also present in tea.

A typical cup of green tea usually contains 250–350 mg tea solids, of which 30–42% are catechins and 3–6% caffeine [4]. The major active constituents of tea are catechins, and among them, EGCG is the most potent and much of the anticarcinogenic effect of green tea is predominantly credited to it. Some catechins are oxidized or condensed to theaflavins (theaflavin, theaflavin-3-gallate, theaflavin-3′-gallate and theaflavin-3-3′-digallate) (3–6%) and thearubigins (12–18%) during fermentation of fresh tea leaves and are responsible for the bitter taste and dark color of black tea. Black tea contains mainly thearubigins, theaflavins, flavonols and catechins. The total polyphenol content of green and black teas is similar, but with different types of flavonoids present due to the degree of oxidation during processing [5].

I. METABOLISM AND BIOAVAILABILITY

For all catechins, the metabolic pathways of methylation, glucuronidation and sulfation have been observed. Methylation, a major metabolic pathway, forms the metabolites 3′ and 4′-*O*-methyl-(−)-EC and *O*-methyl-(−)-EC-glucuronide, 4″-*O*-methyl-ECG, 4′-*O*-methyl-EGC, 4″-*O*-methyl-EGCG and 4′,4″-di-*O*-methyl-EGCG, and 4″-*O*-methyl-EGCG-3′-*O*-glucuronide and 3′,4′- or 3′,5′-di-*O*-methyl-EGCG-4″-*O*-glucuronide [6]. In human liver cytosol, (−)-EC was efficiently sulfated mainly through SULT1A1 while in the intestine, both SULT1A1 and SULT1A3 also contributed to the sulfation. (−)-EC was not glucuronidated by human liver and small intestinal microsomes. It has also been reported that there was no confirmation of glucuronidation by human colon microsomes or by recombinant UDP-glucuronosyltransferase-1A7 (UGT1A7), which is present in stomach and esophagus, but not in liver. (−)-EC was efficiently glucuronidated with the formation of two glucuronides in rat liver microsomes. Sulfation of (−)-EC was a major pathway in human liver and intestine without glucuronidation [7]. The absorption of green tea catechins in the small intestine is quite small. Flavanols are absorbed without deconjugation or hydrolysis and pass through biological membranes. The greater part of ingested green tea catechins

reaches the large intestine and encounters the colonic microflora, with further hydrolysis of glycosides into aglycones and extensive transformation into various aromatic acids like phenylvalerolactones and hydroxyphenylpropionic acids [8]. In humans, plasma bioavailability of green tea catechins is very low. After the administration of either 697 mg of green tea or 547 mg of black tea to healthy volunteers, plasma EGC and EC content was 0.26–0.75% compared with EGCG and ECG with 0.07–0.20% with similar observations in urine [9]. With a single catechin, plasma concentration was found to be 1.53 M at a dose of 1050 mg for (−)-EC, 3.1 μM at a dose of 664 mg for ECG, 5 μM at a dose of 459 mg for EGC and 6.35 μM at a dose of 1600 mg for EGCG [6]. Six metabolites were identified in human urine: (−)-EC-glucuronide, three (−)-EC-sulfates, two *O*-methyl-(−)-EC-sulfates. Microbial metabolites (−)-5-(3′,4′-dihydroxyphenyl)-γ-valerolactone, and their glucuronide conjugates were also present. The major pathway for the elimination of EGCG is the biliary excretion. The total amount of metabolites excreted in urine is associated with maximum plasma concentrations. Urinary recovery was 0.5–6% for some tea catechins [10]. The half-lives of flavanols are 2–3 h in plasma, except EGCG, which is eliminated more slowly probably due to higher biliary excretion and greater complexing with plasma proteins [11].

II. CANCER PREVENTIVE EFFECTS OF TEA IN HUMANS

Earliest documented cancer preventive effect of tea is our study in 1988 [12]. Currently, there are 1000 scientific publications in the scientific literature found on PubMed documenting cancer preventive ability of tea. Several studies initiated in our laboratory and subsequently verified from many other laboratories have suggested that catechins and theaflavins found in tea may reduce the risk of various types of cancers in humans. Various reports have shown an inverse association of tea consumption with the development of certain types of cancer [2, 13, 14]. The reported effects of tea on skin, prostate, lung and breast cancer in humans are shown in Table 1.

This review article describes the major epidemiological and clinical studies on tea consumption and the risk of cancer at different organ sites in humans. We also present the evidences for the association of tea drinking and its effects on diabetes, arthritis and neurological system in humans.

i. Tea and Skin Cancer

Various studies have reported beneficial effects of regular tea consumption against squamous cell carcinoma of the skin. In a population-based case-control study, adjusting for brewing time, the association between squamous cell carcinoma and hot black tea consumption suggests a significantly lower risk in consumers of hot tea compared to non-consumers. It was suggested that tea concentration, brewing time and beverage temperature have major influences on the potential protective effects of hot black tea in relation to squamous cell carcinoma of the skin [15]. A population-based case-control study was conducted to evaluate the relationships between citrus peel use and black tea intake and squamous cell carcinoma of the skin. The independent and interactive effects of citrus peel and black tea in the development of squamous cell carcinoma were also assessed. Subjects who reported consumption of both hot black tea and citrus peel had a significant marked decrease risk of skin squamous cell carcinoma suggesting that both citrus peel use and

strong black tea had protective effects in relation to squamous cell carcinoma of the skin [16]. In a case-control study conducted in Italy, a significant inverse association between vitamin A intake and cutaneous malignant melanoma risk was found. There was no appreciable association of cutaneous malignant melanoma risk with selected food items, including fish, meat, vegetables, fruit, dairy products, whole meal bread, alcohol, coffee and tea drinking. Consumption of tea had a protective effect on cutaneous malignant melanoma risk [17]. The effect of Polyphenon E ointment was investigated for efficacy and safety in the treatment of anogenital warts in immunocompetent men and women. Polyphenon E 15% or 10% ointment or matching vehicle was self-applied by 530 patients three times daily to all warts. The assessment of response and of adverse events was performed biweekly until complete clearance or for up to 16 weeks. Treatment with 10 and 15% Polyphenon E ointment showed complete clearance of all baseline and new anogenital warts in 51 and 53% of patients, respectively. It was also noted that 78% of all patients treated with either 10 or 15% Polyphenon E ointment showed wart clearance rates of 50% or better. There were only mild or moderate adverse effects as demonstrated by the safety profile of Polyphenon E ointments [18].

ii. Tea and Prostate Cancer

Among many dietary agents investigated for chemopreventive properties against prostate cancer (PCa), green tea and its constituent polyphenols (GTP) have received much attention. A Phase II trial was conducted in patients with androgen independent prostate carcinoma to investigate the explored the antineoplastic effects of green tea. Forty two patients asymptomatic who had manifested, progressive prostate specific antigen (PSA) elevation with hormone therapy were evaluated. Six grams of green tea per day orally in 6 divided doses were given to patients and each dose contained 100 calories and 46 mg of caffeine. A decline in more than or equal to 50% in the baseline PSA value occurred in a single patient and it was not continued beyond 2 months. Median change in the PSA value increased by 43% at the end of the first month. Grade 1 or 2 green tea toxicity occurred in 69% of patients, along with Grade 3 toxicity and one episode of Grade 4 toxicity [19]. In Hangzhou, southeast China, a case-control study was conducted in 130 incident patients with histologically confirmed adenocarcinoma of the prostate. The risk of PCa declined with increasing frequency, duration and quantity of green tea consumption and there were significant dose-response relationships, suggesting preventive effects of green tea [20]. The efficacy of green tea capsules was tested on patients with hormone refractory prostate cancer (HRPCa) by Choan *et al.* [21]. Efficacy of green tea, prescribed as an alternative complementary formulation was tested on HRPCa. PSA was the primary endpoint and estimates after a minimum of 2 months of therapy. It was found that 12 patients reported at least one side effect among 19 patients enrolled into the study. The minimum 2 months of therapy was not completed by 4 patients and 15 patients completed at least 2 months of therapy. Within 2 months of starting therapy, progressive disease was noted in 9 of these patients and 6 patients developed it after additional 1 to 4 months of therapy. Therefore, based on the results of this study, it was concluded that green tea had minimal clinical activity against HRPCa [21]. In high-grade prostate intraepithelial neoplasia volunteers, a clinical trial was conducted to assess the safety and efficacy of green tea catechins for the chemoprevention of PCa. Daily treatment consisted of three green tea catechins capsules

200 mg each. Only one tumor was diagnosed among the 30 green tea catechins-treated men with an incidence of 3%, whereas nine cancers were found among the 30 placebo-treated men with an incidence of 30% after 1 year. There was no significant change in total PSA between the two arms, but green tea catechins-treated men showed values constantly lower with respect to placebo-treated ones. International Prostate Symptom Score and quality of life scores of green tea catechins-treated men with coexistent benign prostate hyperplasia, a condition prevalent in older men were also improved. There were no reports of significant side effects and administration of green tea catechins also reduced lower urinary tract symptoms [22]. Green tea consumption habit of 49,920 men aged 40–69 years was investigated in the Japan Public Health Center-based prospective study. During that time, 404 men were newly diagnosed with PCa, of which 114 had advanced cases, 271 were localized, and 19 were of an undetermined stage. It was established that localized PCa was not affected by the consumption of green tea, there was a dose-dependent decrease in the risk of advanced PCa by intake of green tea [23]. It has been reported that there was a significant reduction in serum levels of PSA, hepatocyte growth factor and vascular endothelial growth factor in men with prostate cancer after brief treatment with green tea extract containing EGCG (Polyphenon E), with no elevation of liver enzymes [24]. In PCa patients scheduled to undergo radical prostatectomy, a randomized, double-blind, placebo-controlled trial of Polyphenon E was conducted to determine the bioavailability of GTP in prostate tissue and to measure its effects on systemic and tissue biomarkers of PCa. Polyphenon E or placebo daily was given to patients for 3 to 6 weeks before surgery. Treatment with Polyphenon E caused promising but not statistically significant changes in the levels of serum PSA, serum insulin-like growth factor (IGF) axis, and oxidative DNA damage in blood leukocytes. In the prostatectomy tissue, tissue biomarkers of cell proliferation, apoptosis, and angiogenesis did not differ between the treatments. Patients receiving Polyphenon E had a decrease in Gleason score between biopsy and surgical specimens but it was not statistically significant [25].

iii. Tea and Lung Cancer

Various studies have demonstrated the relationship between tea consumption and threat of lung cancer. Tea drinking was associated with reduced risk of lung cancer in male cigarette smokers in a case control study in Uruguay [26]. In a population-based case-control study in Shanghai, China, consumption of green tea was associated with a reduced risk of lung cancer among non-smoking women and the risk decreased with increasing consumption [27]. There was a significant decrease in urinary 8-hydroxydeoxyguanosine after drinking decaffeinated green tea among smokers over a 4 month-period in a randomized controlled tea intervention phase II trial [28]. In a case control study, a protective effect of frequent, daily or several times/week black tea drinking appeared among non-smoking women [29]. The maximum tolerated dose of green tea extract (GTE) in patients with advanced lung cancer was determined by Laurie *et al.* Seventeen patients with advanced lung cancer were given oral doses of GTE once daily, starting with a dose of 0.5 g/m^2/day with increasing doses. The maximum tolerated dose of GTE was found to be 3 g/m^2/day without grade 3 or 4 toxicity [30]. A case-control study was conducted on 241 lung cancer patients in Taiwan and the effects of smoking, green tea consumption, IGF1, IGF2, and IGFBP3 polymorphisms were evaluated on lung cancer risk. It was found that lung cancer cases had

a higher proportion of smoking, green tea consumption of <1 cup/day, exposure to cooking fumes and family history of lung cancer than controls. There was higher risk of lung cancer in smokers who never drank green tea, as compared to smokers who drank green tea >1 cup/day [31].

iv. Tea and Breast Cancer

Epidemiological studies have demonstrated inconsistent results of the relation between green tea intake and risk of breast cancer. Stages I and II breast cancer patients showed a lower recurrence rate and a longer disease-free period when consuming more than 5 cups of green tea/day compared to those consuming less than 4 cups/day [32]. A significant inverse relationship between intake of green tea and risk of breast cancer was reported in a case-control study conducted among Asian-American women in Los Angeles County. In a meta-analysis published by Sun *et al.,* 13 studies were examined and data on consumption of either green tea or black tea, or both in relation to breast cancer risk was provided [33]. The combined results from the four studies indicated a reduced risk of breast cancer for highest versus non/lowest intake for green tea. Contradictory results were observed in case-control as compared to cohort studies for black tea. There was a minor inverse association between black tea consumption and risk of breast cancer by the combined results from the eight case-control studies. Modest increase in risk was found to be associated with black tea intake in five cohort studies. Therefore, the meta-analysis concluded that there was a lower risk for breast cancer with green tea consumption and a possible late-stage, promotional effect of black tea on breast cancer [33]. The consumption of green tea was associated with a reduced risk of developed breast cancer in a case-control study with breast cancer confirmed patients [34]. Ogunleye *et al.,* performed a meta-analysis of studies of breast cancer risk and recurrence including 5,617 cases of breast cancer. They identified two studies of breast cancer recurrence and seven studies of breast cancer incidence. The results of the analysis indicated that the increased green tea consumption of >3 cups a day was inversely associated with breast cancer recurrence. There was an inverse association with green tea consumption following analysis of case-control studies of breast cancer incidence while no association was found among cohort studies of breast cancer incidence [35]. From the baseline survey in 1990–94, 581 cases of breast cancer were newly diagnosed in 53,793 women during 13.6 years follow-up in a Japan Public Health Center-based Prospective Study. In 1995–98, after the 5-year follow-up survey, 350 cases were newly diagnosed in 43,639 women. The frequency of total green tea drinking was assessed by the baseline questionnaire, while two types of green tea, Sencha and Bancha/Genmaich were assessed by 5-year follow-up questionnaire. The adjusted hazard ratio [HR] for women who drank >/= 5 cups/day was 1.12 in the baseline data as compared with women who drank <1 cup of green tea/week. The adjusted HR for women who drank >/=10 cups/day were 1.02 for Sencha and 0.86 for Bancha/Genmaicha as compared with women who drank <1 cup of Sencha or Bancha/Genmaicha/week. This study found no association between green tea drinking and risk of breast cancer [36]. A phase I dose escalation trial in women with a history of stage I to III hormone receptor-negative breast cancer was conducted. Polyphenon E was given at different doses twice daily or matching placebo for 6 months. The primary endpoint of the study was to establish the maximum tolerated dose (that causes 25% dose-limiting toxicity). At baseline and 6 months, a mammogram and random core biopsy of the contralateral breast

were obtained along with serial blood/urine collections every 2 months for biomarker analyses. After treatment with 400 mg of Polyphenon E, there was one dose-limiting toxicity, three dose-limiting toxicities at 600 mg and one dose-limiting toxicity at 800 mg. At 600 mg of Polyphenon E, the dose-limiting toxicity rate was 27% and the maximum tolerated dose for Polyphenon E was found to be 600 mg twice daily [37].

v. Tea and other Cancers

Tea consumption has been reported to have beneficial effects against several types of cancers. Consumption of green tea was associated with a lower risk of esophageal cancer in a case-control study of esophageal cancer patients in Shanghai [38]. In a prospective cohort study in Yoshimi town in Saitama Prefecture, respondents were divided into three groups according to daily consumption of green tea: less than 3 cups, from 4 to 9 cups, and more than 10 cups. Individuals who consumed more than 10 cups of green tea/day showed remarkable reduction of relative risk for lung, colon, and liver cancers [39]. It has been reported in a study that consumption of black tea reduces colon cancer risk in both men and women [40]. The association between green tea consumption and colorectal cancer risk was evaluated in a population-based prospective cohort stud which included 60,567 Chinese men aged 40–74 years at baseline. The subjects were followed up for 5 years and 243 incident cases of colorectal cancer were identified. Regular green tea consumption of at least three times/week for more than six consecutive months was related with reduced risk of colorectal cancer in non-smokers and the risk decreased with the increased amount of green tea consumption. Each 2 g rise of intake of dry green tea leaves/day was associated with a 12% reduction in risk of colorectal cancer. However, there was no significant association of green tea consumption with the risk of colorectal cancer among smokers suggesting that regular consumption of green tea may reduce colorectal cancer risk among non-smokers [41]. A total of 13 epidemiological studies consisting of six case-control and seven prospective cohort studies were included in a meta-analysis to evaluate the association between tea consumption and the risk of primary liver cancer. An inverse association with a borderline significance was found between tea consumption and primary liver cancer with demonstrated preventive effects of tea intake on the development of primary liver cancer in both men and women. It was concluded that green tea consumption was associated with a moderate reduction in risk for primary liver cancer [42]. The association between green tea drinking and the risk of pancreatic cancer was investigated in a population-based case-control study in urban Shanghai with recruitment of 908 patients of pancreatic cancer and 1067 healthy controls. Interview questionnaire was filled by the subjects to give information on tea drinking, type of tea, amount of tea consumption, temperature of tea, and the duration of regular tea drinking. Regular green tea drinking was associated with 32% reduction of pancreatic cancer risk as compared to those who did not drink tea regularly in women with increased consumption and longer duration of tea drinking associated with reduced pancreatic cancer risk. Lower temperature of tea was associated with reduced risk of pancreatic cancer in both men and women, irrespective of the amount or duration of tea drinking among regular tea drinkers [43]. In case control studies on the relationship between gastric cancer and tea consumption conducted in China and Japan, a significant inverse relationship was found in four studies and an insignificant inverse relationship was found in two studies [44].

III. TEA AND CARDIOVASCULAR DISEASES

Consumption of tea is increasingly being shown to be associated with enhanced cardiovascular and metabolic health. Green tea caused an increase in the activity of enzymes implicated in cellular protection against reactive oxygen species: superoxide dismutase in serum and the expression of catalase in the aorta. This action is combined with direct action on oxygen species by a decrease in the nitric oxide plasma concentration [45]. Green tea catechins affect lipid metabolism by different pathways and prevent the appearance of atherosclerotic plaque. Its intake decreases the absorption of triglycerides and cholesterol and these findings are in accordance with the fact that it increases excretion of fat [46]. In patients, who underwent coronary arteriography for the first time in China, green tea consumption was associated with a reduced risk of coronary artery disease in male patients, with an adjusted odds ratio of 0.62 compared with those who did not drink green tea. Compared to non-tea drinkers, the adjusted odds ratios were 1.09 in male patients consuming less than 125 g of dried green tea leaves per month, 0.36 for 125–249 g per month and 0.36 for more than or equal to 250 g per month. There were similar dose-response relationships for frequency, duration, concentration and starting age of green tea drinking in male patients, while no inverse association was found between green tea consumption and coronary artery disease in female patients [47]. In a matched case-control analysis including 518 myocardial infarction, 333 hemorrhagic stroke, and 1927 ischemic stroke cases, the associations of these lifestyle factors with myocardial infarction and stroke were evaluated. Alcohol consumption was inversely associated with myocardial infarction, tea consumption was inversely associated with hemorrhagic and ischemic stroke and weight increase from age 20 to 40 was positively associated with myocardial infarction and stroke in a dose-response manner [48]. In a case-control study in southern China, a significant decrease in ischemic stroke risk was observed for drinking at least one cup of tea weekly when compared with infrequent or non-drinkers, the risk reduction being largest by drinking one to 2 cups of green or oolong tea daily. Significant inverse dose-response relationships were also found for years of drinking and the amount of dried tea leaves brewed [49]. In a meta-analysis, data from 9 studies involving 4378 strokes among 194,965 individuals was pooled. Individuals consuming more than or equal to 3 cups of tea/day had a 21% lower risk of stroke than those consuming less than 1 cup/day regardless of their country of origin with the proportion of heterogeneity not explained by chance alone being 23.8% [50].

IV. TEA AND DIABETES

Various studies have shown that tea may affect glucose metabolism and insulin signaling, causing interest in the health effects of tea consumption on diabetes. In a large cohort of U.S. middle-aged and older women from the Women’s Health Study, women who consumed more than or equal to 4 cups/day of tea had a 30% lower risk of developing type 2 diabetes than did those who did not consume tea [51]. In a retrospective cohort study among Japanese adults, adults who consumed more than or equal to 6 cups/day of green tea lowered their risk of diabetes by 33%, while no association with diabetes risk was found for oolong or black teas. Consumption of more than or equal to 3 cups/day of coffee lowered the risk of diabetes by 42% and high caffeine intake was also associated with a 33% reduction in risk of diabetes. A lowered diabetes risk was also observed in women after green tea and

caffeine consumption [52]. The effects of continuous ingestion of a catechin-rich beverage in patients with type 2 diabetes who were not receiving insulin therapy in a double-blind controlled study were investigated. The patients were given green tea containing either 582.8 mg of catechins or 96.3 mg of catechins/day for 12 weeks. Waist circumference decreased in the catechin group than in the control group at 12 weeks. There was increase in insulin and the decrease in hemoglobin A(1c) levels in the catechin group than in the control group in patients treated with insulinotropic agent [53]. The possible effects of different daily doses of black tea intake on certain oxidative stress, inflammatory and metabolic biomarkers in patients with type 2 diabetes mellitus. Patients were given 150, 300, 450 and 600 ml of black tea extract (BTE) during the weeks 1, 2, 3 and 4, respectively, while the control group received 150 ml BTE throughout the intervention period. It was found that serum total antioxidant capacity was enhanced similarly in both test and control groups, but a suppressing effect on serum malondialdehyde was observed with daily intake of 2 cups of BTE. After ingesting 4 cups (600 ml) of BTE a day, there was decrease in the level of serum C-reactive protein and increase in the glutathione levels. It was concluded that regular consumption of BTE had anti-oxidative and anti-inflammatory effects in patients with type 2 diabetes mellitus [54].

V. TEA AND ARTHRITIS

Few studies have reported the beneficial effects of tea against arthritic disease in humans. In a study in Britain, it was found that those who drank tea had greater bone mineral density than those who did not drink tea [55]. Coffee, tea, and caffeine consumption were evaluated as risk factors for rheumatoid arthritis onset among older women in a prospective cohort study. Compared with those reporting no use, subjects drinking more than or equal to 4 cups/day of decaffeinated coffee were at increased risk of rheumatoid arthritis. In contrast, women consuming more than or equal to 3 cups/day of tea displayed a decreased risk of rheumatoid arthritis compared with women who never drank tea, while caffeinated coffee and daily caffeine intake were not associated with the development of rheumatoid arthritis. The associations of rheumatoid arthritis onset with the highest categories of decaffeinated coffee and tea consumption were stronger in women with seropositive disease compared with those with seronegative disease [56].

VI. TEA AND NEUROLOGICAL EFFECTS

Due to lack of well-controlled clinical trials, the effect of tea in the progression of neurodegenerative disorders has not been studied on a large scale. The protective effect of EGCG against neuronal diseases may involve its radical scavenging and iron chelating activity and/or regulation of antioxidant protective enzymes. Reduced risk for Parkinson’s disease was observed for more than or equal to 2 cups/day of tea consumption and two or more cola drinks/day. The associations for tea and cola drinks were not affected by smoking or coffee consumption [57]. A case control study was conducted in China to examine the relationship between coffee and tea drinking, cigarette smoking, and other environmental factors and risk of Parkinson’s disease. It was found that one unit of coffee and tea (3 cups/day for 10 years) would lead to 22% and 28% risk reduction, respectively, of Parkinson’s disease demonstrating a dose-dependent protective effect of coffee and tea in an

ethnic Chinese population [58]. The association of coffee and tea consumption with the risk of incident Parkinson's disease among 29,335 Finnish subjects aged 25 to 74 years without a history of Parkinson's disease at baseline was investigated. There were followed up for 12.9 years and during this time, 102 men and 98 women developed an incident Parkinson's disease. It was noted that subjects who habitually drank ≥ 3 cups of tea/day had a reduced risk of incident Parkinson's disease [59]. In the Singapore Chinese Health Study, a prospective cohort of 63,257 Chinese men and women, all 157 incident Parkinson's disease cases were identified. There was an inverse relationship of black tea with Parkinson's disease risk that was not confounded by total caffeine intake or tobacco smoking, while green tea was unrelated to Parkinson's disease risk [60].

VII. CONCLUSION

Tea is the most widely consumed beverage in the world, next only to water. There is often a misconception, essentially a marketing gimmick, that herbal tea is also tea. However, herbal tea is not made from the plant *Camellia sinensis*. Due to the popularity of tea, generally on a common trip to the grocery store, at least in US markets, one can find many types of tea preparations sold which are supplemented with various extracts of mango, strawberry, pomegranate, lemon, etc. These marketing strategies have boosted the sale of tea products to a non-tea drinking population. Similarly, tea constituents supplemented cosmetics and other products are sold to consumers.

It is increasingly appreciated that tea contains polyphenols and other components that may reduce the risk of developing chronic diseases such as cancer, cardiovascular diseases, arthritis and diabetes. More recently, the beneficial properties associated with daily consumption of green tea are getting better recognized. Particularly interesting are the studies which report that green tea reduces the risk of cancer, which is the major cause of mortality throughout the world. It has become increasingly clear that tea acts as a chemopreventive agent against a wide range of cancers. To evaluate the efficacy of tea against cancer, clinical trials are being conducted. Encouraging data from many trials are available and from many ongoing trials are awaited. However, results from human studies are not always positive, may be, due to the fact that the higher doses of tea are used in animal studies than those consumed by humans and in animal studies, the experimental conditions are generally optimized for the evaluation of a protective effect. Large scale well-controlled human clinical trials are necessary to establish the health promoting effects of tea consumption. Only based on these findings, recommendations to human population could be made.

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Table 1

Reported Effects of Tea on Skin, Prostate, Lung and Breast Cancer in Humans.

Effects of tea in humans	References
SKIN CANCER	
Significant marked decrease risk of skin squamous cell carcinoma by intake of black tea	[16]
Protective effect of tea on cutaneous malignant melanoma risk	[17]
Treatment with Polyphenon E ointment showed complete clearance of all baseline and new anogenital warts in immunocompetent patients	[18]
PROSTATE CANCER	
In patients with androgen independent prostate carcinoma, green tea supplementation	[19]
caused Grade 1 or 2 toxicity in 69% of patients along with Grade 3 toxicity and one episode of Grade 4 toxicity	[20]
The risk of PCa declined with increasing frequency, duration and quantity of green tea supplementation in a case-control study in China	[21]
In patients with hormone refractory prostate cancer, green tea had minimal clinical activity	
In high-grade prostate intraepithelial neoplasia volunteers, green tea catechins-treated men showed PSA values constantly lower with respect to placebo-treated ones with reduced lower urinary tract symptoms	[22]
Dose-dependent decrease in the risk of advanced PCa by intake of green tea in Japan	[23]
Significant reduction in serum levels of PSA, hepatocyte growth factor and vascular endothelial growth factor in men with prostate cancer after treatment with Polyphenon E	[24] [25]
Treatment with Polyphenon E caused changes in the levels of serum PSA, serum insulin-like growth factor axis and oxidative DNA damage in blood leukocytes	[26]
LUNG CANCER	
Reduced risk of lung cancer in male cigarette smokers by tea drinking in Uruguay	[27]
Reduced risk of lung cancer among non-smoking women by consumption of green tea	[28]
Decrease in urinary 8-hydroxydeoxyguanosine after drinking decaffeinated green tea among smokers in a phase II trial	[29]
Protective effect of black tea in non-smoking women	[31]
In a case-control study in Taiwan, higher risk of lung cancer in smokers who never drank green tea, as compared to smokers who drank more than 1 cup/day of green tea	[32]
BREAST CANCER	
Consumption of more than 5 cups of green tea/day by stages I and II breast cancer patients showed a lower recurrence rate and a longer disease-free period compared to those consuming less than 4 cups/day	[33]
Reduced risk for breast cancer with green tea consumption and a possible late-stage, promotional effect of black tea on breast cancer	[34]
Decreased risk of developed breast cancer in a case-control study with breast cancer confirmed patients by ingestion of green tea	[35]
Increased green tea consumption of more than 3 cups/day was inversely associated with breast cancer recurrence	[36]
No association between green tea drinking and breast cancer risk	

* This list provides selected examples.