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Review Article

Protective Effect of Tea on Different Diseases

Aniket Adhikari[1]* and Madhusnata De[2]

[1]*Research Scholar, Department of Genetics, Vivekananda Institute of Medical Sciences, Ramakrishna Mission Seva Pratishthan, Kolkata, India*

[2]*Professor, Department of Genetics, Vivekananda Institute of Medical Sciences, Ramakrishna Mission Seva Pratishthan, Kolkata, India*

***Corresponding Author:** Aniket Adhikari, Research Scholar, Department of Genetics, Vivekananda Institute of Medical Sciences, Ramakrishna Mission Seva Pratishthan, Kolkata, India.

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Abstract

Tea is the most widely consumed beverage worldwide. The inhibition of tumorigenesis by tea extracts and tea polyphenols has been demonstrated in different animal models. Tea is consumed in different forms such as oolong, green and black. Being rich in natural antioxidants, tea is used in the management of different types of cancer, cardiovascular disease and cell signaling. The present review focuses on the protective effects of tea on different diseases.

Keywords: Tea; Cancer; Cardiovascular Disease; Polyphenols

Introduction

Tea is one of the most widely consumed beverages in the whole world, second only to water, and its medicinal properties have been widely explored. It is believed that tea originated from China around 2737 B.C., although earliest documented evidence as mentioned in a Chinese dictionary can be traced back to 350 B.C. [1]. Tea was brought to Europe in 1559 A.D. The tea plant, Camellia sinensis, is a member of the Theaceae family. The three major forms of tea black, green and oolong are produced from the leaves of the tea plant. Tea leaves are dark green in colour, alternately arranged, oval in shape and have serrated edges. Green tea beverage contains 30 - 42% catechins by dry weight [2]. These catechins are present in higher quantities in green tea than in black or oolong tea, because of differences in the processing of tea leaves after harvest. For the green variety, fresh tea leaves from the plant Camellia sinensis are steamed and dried to inactivate the polyphenol oxidase enzyme, a process that essentially maintains the polyphenols in their monomeric forms. Black tea, on the other hand is produced by extended fermentation of tea leaves leading to the formation of polymeric compounds, thearubigins and theaflavins. Oolong tea is a partially fermented product and contains a mixture of the monomeric polyphenols and higher molecular weight theaflavins [2]. All these varieties of tea contain significant amounts of caffeine (3 - 6%) which is unaffected by the different processing methods [3]. There are several polyphenolic catechins in green tea, viz. (−) epicatechin (EC), (−) epicatechin-3-gallate (ECG), (−) epigallocatechin (EGC), (−) epigallocatechin-3-gallate (EGCG), (+) catechin and (+) gallocatechin (GC). EGCG, the most abundant catechin in green tea, accounts for 65% of the total catechin content. A cup of green tea may contain 100 - 200 mg of EGCG, trace amounts of catechin and gallocatechin [4]. Black tea contains 2 - 6% theaflavins, > 20% thearubigins, and 3 - 10% catechins in the water-extractable portion. Tea leaves also contain flavonols, such as quercetin and myricetin, as well as nitrogenous compounds, such as caffeine and theobromine. Caffeine accounts for 2 - 5% of the water-extractable material in green, oolong, and black tea. Many health benefits including prevention of cancer, heart disease, hepato cellular carcinoma, cataracts etc have been ascribed to the consumption of this beverage.

Green Tea

Green tea and its constituent catechins are best known for their antioxidant properties, which has led to their evaluation in a number of diseases such as cancer associated with reactive oxygen species (ROS). The chemical composition of green tea is complex. It contains proteins (15 - 20% dry weight), the amino acids constituents of protein such as theanine or 5-N-ethylglutamine, glutamic acid, tryptophan, glycine, serine, aspartic acid, tyrosine, valine, leucine, threonine, arginine, and lysine and contributed towards (1 - 4% dry weight); carbohydrates (5 - 7% dry weight) such as cellulose, pectins, glucose, fructose, and sucrose; minerals and trace elements (5% dry weight) such as calcium, magnesium, chromium, manganese, iron, copper, zinc, molybdenum, selenium, sodium, phosphorus, cobalt, strontium, nickel, potassium, fluorine, and aluminum; and trace amounts of lipids (linoleic and a-linolenic acids), sterols (stigmasterol), vitamins (B, C and E), xanthic bases (caffeine, theophylline etc), pigments (chlorophyll, carotenoids etc) and volatile organic compounds (aldehydes, alcohols, esters, lactones, hydrocarbons etc) [5]. The yellowish green color of the unoxidized extract is attributed to the chlorophyll content. A cup of green tea contains about 300 to 400 mg of polyphenols, which are essentially colorless. Of the polyphenols, epigallocatechin gallate (EGCG) and epigallocatechin (EGC) are the most important and it is estimated that a typical cup of green tea contains 10 to 30 mg of

EGCG. Several epidemiological studies as well as studies in animal models have shown that green tea can offer protection against various cancers such as skin, breast, prostate and lung [6,7]. In addition to the cancer chemopreventive properties, green tea and EGCG have been shown to be anti-angiogenic (prevention of tumor blood vessel growth) [8,9] and anti-mutagenic [10,11]. Decaffeinated green tea extract is available as Polyphenol E.

Black Tea

Black tea is made from leaves that have been withered before being rolled and dried [12]. Quantitatively, black tea is the major type of tea produced worldwide [1]. In black tea, catechins, theaflavin (TF) and thearubigins (TR) accounts for 3 - 10, 2 - 6 and > 20% respectively. Theaflavins consist of two catechin molecules joined together and account for about 10% of the converted catechins, whereas the thearubigins are more complex flavonoid molecules, whose structural chemistry are still unknown, and may account for up to 70% of flavonoids in black tea [13]. Researchers from New Jersey, USA have shown that theaflavin-2 (TF-2), a compound unique to black tea and oolong tea kills cancer cells. Theaflavin-2 suppresses the activity of a gene that induces the inflammatory enzyme cyclooxygenase (COX 2), while also reducing the activity of other inflammatory molecules such as TNF-α and nuclear factor-kappa B (NF-$_{k}$B). Theaflavin-2 was also shown to produce a pattern of gene regulation similar to that found in the cancer cells.

Oolong Tea

Oolong tea also known as blue green tea or wu long tea is produced by partial oxidisation. It is rolled by hand or machine and pan fried and then allowed to oxidize. This process is repeated several times until the desired level of oxidation is achieved. It contains catechins, theasinensins and other polymerized catechin derivatives but the amount of cathechin content is less than that of green tea. Tea leaves also contain flavonols, such as quercetin and myricetin, as well as nitrogenous compounds, such as caffeine and theobromine. Caffeine accounts for 2 - 5% of the water-extractable material in green, oolong, and black tea. Oolong tea extract (OTE) contains substances, notably polyphenols that have antibacterial properties against oral pathogens, such as *Streptococcus mutans*, the bacteria closely associated with dental caries [14,15].

Effects of Tea on Health

Anticarcinogenic Effects

Studies in animal models have demonstrated that green tea and EGCG can inhibit carcinogenesis at all stages, viz. initiation, promotion and progression [16]. In animal model green tea and EGCG have also been shown to inhibit the process of angiogenesis, tumor metastasis and invasion [17-19] Species differences in the pharmacokinetics of green tea and EGCG in humans and rodents may account for the more definitive evidence of the cancer chemo-preventive effect of green tea [20]. It is reported that both green and black tea exhibit potential chemo-preventive property against Ph1P induced tumourogenesis in Fischer rats [21]. Important information on the mechanism of action of tea polyphenols has been obtained by examining the influence of EGCG and ECG on protein kinase activator, an enzyme involved in the cell activation process and growth of tumour. While EGCG blocks the interactions between proteins and ligands [22], both EGCG and ECG inhibit the gap junctional intercellular communication caused by tumour promoters [23]. Tea may affect the metabolism of carcinogens by induction or inhibition of various cytochrome P450s, but the practical importance of this mechanism is not known. Among the phase II enzymes, tea increases glucuronyl transferase activity, which may facilitate the detoxification pathway of certain carcinogens. Inhibition of tumour promotion-related enzymes, such as lipoxygenase and cyclooxygenase [24,25], ornithine decarboxylase [26-28] protein kinase C [28-30] and 5α steroid reductase isoenzymes [31] helps in the prevention of cancer.

Tea Flavonoids and Cancer

Interaction of tea flavonoids with procarcinogens plays a prominent role for the beneficial effects of tea against cancer initiation. Cancer of the colon, breast and pancreas are associated with formation of heterocyclic amines and the genotoxic carcinogens from cooked food and meat that can be prevented by tea polyphenols [23]. Phase I enzymes are known to induce tumour formation by activating procarcinogens which modify genomic DNA and black tea polyphenols probably inhibit cytochrome P450 dependent bioactivation of the carcinogen [32]. Most of the commonly consumed teas (green, black and oolong) are shown to possess similar antimutagenic efficacy [33-39]. This leads to a general conclusion that development of cancer is prevented by tea consumption through antimutagenic protection paralleling to their antioxidant efficacy. EGCG has been most extensively studied against mutation and ROS-scavenging property and is perhaps the most potent antimutagenic agent protecting DNA scissions and non-enzymatic interception of superoxide anions. ECG emerges as the most potent enzymatic scavenger amongst the green tea polyphenols [40]. Antimutagenic property of black tea and its constituents has been widely documented in many reports, especially in Salmonella strains [41]. The effects of specific tea polyphenols (polyphenol 60 and polyphenol 100 from green tea and polyphenol B containing mixture of polyphenols from black tea) have been examined against a number of genotoxic carcinogens in Salmonella strains TA98, TA100 and TA1535. All of these polyphenols sharply decreased mutagenicity of a number of aryl and heterocyclic amines of aflatoxin B1, 1, 2-dibromomethane, 2-nitropropane, involving an cancer induced rat liver S9 fraction [42].

Cancer of Ectodermal or Endodermal origin

Oral Cancer

Oral cancer is the fifth most common cancer worldwide [43]. Oral pre malignancies are also very common in betel quid chewers and formation of micronucleus has been observed in precancerous lesions of the oral cavity of betel quid chewers [44]. The antioxidant properties of tea play a vital role to reduce the cancer biomarker (micronuclei) in oral cancer. The polyphenolic component of tea decreases its antioxidant property with combination of milk. The milk protein casein binds the antioxidant portion of the tea and reduces its property. So black tea i.e. tea without milk plays an important role for scavenging the free radicals thereby promoting good health (Adhikari and De 2013). It has been suggested that tea may play a role in the prevention of oral cancer [7]. One double-blind, randomised intervention trial suggest that treating patients with a mixture of black and green tea components could improve the clinical manifestations of precancerous oral lesions [45]

Leukoplakia and Erythroplakia (possible pre-cancerous conditions)

Leukoplakia and erythroplakia are terms used to describe certain types of abnormal tissue that can be seen in the mouth or throat: Leukoplakia is a white or gray patch. Erythroplakia is a flat or slightly raised, red area that often bleeds easily if it is scraped. Erythroleukoplakia is a patch with both red and white areas.

Oral cavity and oropharyngeal cancers

Several types of cancers can start in the mouth or throat.

Squamous cell carcinomas

More than 9 of 10 cancers of the oral cavity and oropharynx are squamous cell carcinomas, also called squamous cell cancers. These cancers begin in early forms of squamous cells, which are flat, scale-like cells that normally form the lining of the mouth and throat. The earliest form of squamous cell cancer is called carcinoma *in situ,* meaning that the cancer cells are present only in the outer layer of cells called the epithelium. Antimetastatic effect of black tea polyphenol extracts (BTE), which contain polyphenols including gallic acid, gallocatechin, catechin, epigallocatechin-3-gallate, epicatechin-3-gallate, and theaflavin 3,3'-digallate, in an oral squamous cell culture system by showing a nearly complete inhibition on the invasion of SCC-4 cells via reduced activities of MMP-2 and u-PA [46].

Verrucous carcinoma

Verrucous carcinoma is a type of squamous cell carcinoma that makes up less than 5% of all oral cancers [47]. It is a low-grade (slow growing) cancer that rarely spreads to other parts of the body, but it can grow deeply into surrounding tissue. Black tea exhibited antimutagenicity with N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) in the Salmonella typhimurium TA100 strain and the tumor volumes for the groups treated with different concentrations of black tea were smaller than the control groups. black tea had an improved antimutagenic effect and *in vivo* buccal mucosa cancer preventive activity compared with the untreated control in mice [48].

Minor salivary gland carcinomas

Minor salivary gland cancers can develop in the glands in the lining of the mouth and throat. There are several types of minor salivary gland cancers, including adenoid cystic carcinoma, mucoepidermoid carcinoma, and polymorphous low-grade adenocarcinoma.

Tea and Dental Health

Drinking tea has been associate with a number of beneficial effects in preventing tooth decay [49]. Epidemiological surveys have reported that some populations who drink tea on a regular basis have a reduced number of carious teeth [50-52]. Lingstrom., et al. [53] found that frequent mouth rinsing with black tea infusion may contribute to oral health by inhibition of plaque, its acidity and its cariogenic microflora. Tea contains polyphenols, that were shown to have antibacterial properties against cariogenic bacteria, especially *S. mutans* [54,55]. The polyphenols in green tea are reported to have an inhibitory effect on growth and cellular adherence of *Porphyromonas gingivalis*, an oral bacterium that causes periodontal disease [56]. Apart from their polyphenol content, both green and black tea, are natural sources of fluoride and effective vehicle for fluoride delivery to the oral cavity. According to Simpson., *et al.* [57] after cleansing the mouth with tea, approximately 34% of the fluoride is retained and show a strong binding ability to interact with the oral tissues and their surface integuments. This fluoride content may have a beneficial impact on caries and may carry out a wide range of biological activities including prevention of tooth loss and oral cancer [58,59].

Stomach cancer

Green tea consumption is associated with lower risk of stomach cancer. Among drinkers of green tea, the risk of stomach cancer does not depend on the age when habitual green-tea drinking started. Green tea may disrupt gastric carcinogenesis at both the intermediate and the late stages [60]. Experimental and epidemiological studies indicated green tea possessed antimicrobial, immunostimulant, anti-oxidant and anti-inflammatory effects [61,62], and these properties made green tea, as a potential cancer preventive agent on the basis of numerous *in vitro* and *in vivo* studies [2,63,64]. Green tea is shown to have a preventive effect on gastric cancer by a meta-analysis with pooling case-control studies [65].

Esophageal cancer

Population-based, case-control study of esophageal cancer in urban Shanghai suggests a protective effect of green tea consumption. These findings are consistent with studies in laboratory animals, indicating that green tea can inhibit esophageal carcinogenesis. However, only a few epidemiologic studies have evaluated green tea as a potential inhibitor of human esophageal cancer [66]. The present meta-analysis are that any association between green tea and risk of esophageal cancer remains unclear. Subgroup analyses indicated that greater consumption of green tea might reduce the risk of esophageal cancer in female subjects. However, the results are based on limited research [67].

Lung Cancer

Small-cell lung carcinoma (SCLC)

Several cancers such as cancer in the lung is associated with cigarette smoking and tobacco use [68]. Formation of nitrosamines, the carcinogens also found in tobacco, can be prevented by phenolic compound present in green tea [69,70]. Pretreatment with black or green tea, decaffeinated tea and EGCG reduces the number of lung tumors induced by chemical carcinogens [71,72]. Studies with tea and its constituents (black and green) on sponta-

neously developing and induction of tobacco-specific nitrosamine (NNK) lung tumour show parallel results [73,74].

Non-small-cell lung carcinoma (NSCLC)

Green tea inhibits cycolooxygenase-2 in non-small cell lung cancer cells through the induction of Annexin-1 [75]. TF3, one of the major theaflavin monomers in black tea, Annexin and EGCG in combination with ascorbic acid (AA), a reducing agent can synergistically inhibit the proliferation of lung adenocarcinoma SPC-A-1 cells, and increased its cell population in G0/G1 phase of cell cycle. It suggested that the combination of EGCG with AA and TF3 with AA may be potent anticancer agents for cancer therapy [76]. Growth inhibition of human non-small lung cancer cells has been shown h460 by green tea and ginger polyphenols [77].

Colon Cancer

Epigallocatechin-3-gallate (EGCG) is an important bioactive constituent of green tea extract (GTE) that is widely believed to reduce proliferation of many cancer cell lines. Pro-apoptotic action of EGCG/GTE mediated positive effects on viability and mitogenicity of COLO 205 [78]. Green tea and colorectal cancer association, based on eight studies conducted in native China [79,80] and Japanese [81-85], indicated a statistically significant 18% reduction in risk associated with high green tea consumption. Black tea consumption is rare in Japan [81,82,86], whose main tea beverage is green tea. A protective effect of both green and black tea against the development of pre-cancerous lesions in rat colon also has been shown [87-90]. *In vivo* animal studies have demonstrated that both green and black tea extracts or specific tea polyphenols inhibit the development of carcinogen-induced colorectal tumour in rodents [91-94].

Breast Cancer

It is found that increased consumption of green tea is associated with decreased numbers of axillary lymph node metastases especially among premenopausal patients with stage I and II breast cancers [95]. A potential beneficial influence for breast cancer associated with moderate levels of tea consumption (three or more cups per day) among younger women is shown by Kumar., *et al* [96]. EGCG can inhibit the activation of HIF-1α and NFκB, and VEGF expression, thereby suppressing tumour angiogenesis and breast cancer progression [97]. Green Tea Polyphenol (GTP) reduce the incidence and progression of breast cancer and induce apoptosis of MDA-MB-231, an estrogen receptor negative highly invasive human breast cancer cell line [98].

Skin Cancer

Protective activities of tea against skin cancer have been studied extensively in UV-induced or chemically induced tumorigenesis models in mice [99]. The results show that both tea polyphenols and caffeine, when applied topically to the skin, inhibit skin carcinogenesis. When tea polyphenols are administered orally, their low bioavailability in the skin may limit the inhibitory effect. Therefore, the contribution of caffeine is more important to the inhibition carcinogenesis. The studies by Conney., *et al.* (2007) indicates that caffeine inhibits UVB-induced carcinogenesis in SKH-1 mice by enhancing apoptosis of DNA damaged cells and premalignant cells [100]. Initiation of skin carcinogenesis by AP1 is effectively blocked by EGCG and theaflavin-3-3-digallate [101-104].

Prostate Cancer

Gupta., *et al.* [105] reported that oral infusion of green tea polyphenols significantly inhibit tumour incidence and burden in the prostate as well as the metastases of the tumor to distant sites in an autochthonous transgenic adenocarcinoma of the mouse prostate (TRAMP) model. This inhibition is associated with decreasing insulin-like growth factor (IGF)-1 level and suppression of phosphorylation of Akt and Erk 1/2 [106].

Liver Cancer

Oral administration of black and green tea is shown to decrease the incidence of NNK-induced liver tumours in rats and the progression of diethylnitrosamine-induced liver tumours in mice [99].

Bladder and Pancreatic Cancer

Oral administration of green tea or green tea polyphenols during the promotion or entire experimental period inhibited N-butyl-N-(4-hydroxybutyl)-nitrosamine-induced urinary bladder tumours in rats. Inhibitory activity of tea is observed on nitrosamine-induced pancreatic cancer and related ductal lesions in hamsters [99].

Cancer of Mesenchymal origin

Sarcomas are given a number of different names based on the type of tissue that they most closely resemble. For example, osteosarcoma resembles bone, chondrosarcoma resembles cartilage, liposarcoma resembles fat, and leiomyosarcoma resembles smooth muscle.

Osteosarcoma

The ability of a polyphenolic fraction of green tea (GTP) has been shown to have antitumor effects on various malignant cell lines to inhibit growth and induce apoptosis in human osteosarcoma SAOS-2 cells. GTP is a candidate therapeutic for osteosarcoma that mediates its antiproliferative and apoptotic effects via activation of caspases and inhibition of NF-kappaB [107]. Green tea extract tested strongly suppressed the growth of tumors without adverse effects in nude mice, suggesting potential as an anticancer agent [108].

Chondrosarcoma

Epigallocatechin-3-gallate (EGCG), the major polyphenol in green tea, has been shown to inhibit tumorigenesis and cancer cell growth in animal models. EGCG induced cell apoptosis in human chondrosarcoma cell lines but not primary chondrocytes. EGCG induced upregulation of Bax and Bak, downregulation of Bcl-2 and Bcl-XL, and dysfunction of mitochondria in chondrosarcoma. Treatment of chondrosarcoma cells with EGCG induced p38 and c-jun-NH2-kinase (JNK) phosphorylation [109].

Liposarcoma

Liposarcoma is a malignant tumor that arises in fat cells in deep soft tissue. A nutrient mixture (NM) containing lysine, proline, ascorbic acid, and green tea extract has shown significant anticancer activity against a number of cancer cell lines. NM significantly inhibited liposarcoma cell growth, MMP activity, and invasion and induced apoptosis *in vitro*-important parameters for cancer development, suggesting NM as a potential treatment strategy for liposarcoma [110].

Leiomyosarcoma

EGCG significantly lowered the concentration of curcumin required to inhibit the AKT-mTOR pathway, reduce cell proliferation and induce apoptosis in uterine leiomyosarcoma cells [111].

Tea and Chromosome

Black tea and its two polyphenols (TF and TR) are investigated against chemically induced genetic damage as measured by chromosome aberrations and sister chromatid exchanges in mice [112]. The frequency of sister-chromatid exchange in lung cells is lower in smokers who consumed green tea [113]. Administration of tea extract for prolonged periods also showed protective effect on arsenic toxicity [114]. Chromosome breaks have been reported in oral exfoliated cells in chewers of betel quid with or without tobacco. Micronucleus formation has been observed in precancerous lesions of the oral cavity of betel quid chewers [44]. Administration of black tea to subjects with oral leukoplakia resulted in a gradually reversal of the leukoplakia both on clinical observation and at cellular level as assessed by MN and chromosomal studies [115].

Signal transduction and cell cycle effects

Inactivation of carcinogens by EGCG mediates through inhibition of phase I enzymes and activation of phase II enzymes [69,116]. Flavonoids help to maintain normal cell growth by blocking the activation of an oncogene AP1 (activator protein), maintaining cell-cell communication and increasing apoptosis of malfunctioning cells. The factors NF-KB (nuclear factor kappa B) and AP1 are redox-regulated components of the signal transduction cascade and, thus, sensitive to the oxidant/antioxidant status of the cell [117]. EGCG and theaflavins were examined for inhibitory effects on 12-otetradeconylphorbol-13-acetate (TPA) induced protein kinase C (PKC) and transcription activator protein-1 binding activities in N1H 3T3 cells. Fujiki., *et al.* [22] demonstrated that EGCG and other tea polyphenols inhibit growth of human lung cancer cells with a G2/M phase arrest of the cell cycle. The involvement of the tumor necrosis factor α pathway in the inhibition process has been suggested. EGCG and other tea polyphenols have been shown to inhibit the phosphorylation of Rb by Cdk2/4 [118] and the binding of epidermal growth factor and TPA to their respective receptors and thus inhibit tumor promotion [118,119]. Green tea polyphenols also enhance apoptosis, and this has been shown in many cancer cell lines such as PC-9, H661, KATO III, DU145, A431, LY-R, HaCaT, W138 and Molt-43 [120].

Tea and Cardiovascular Disease

Green tea consumption has been associated with a lower Incidence of coronary artery disease in Japanese populations [121]. Miura., *et al.* [122] showed that oral intake of green tea extract by human volunteers increased resistance of plasma LDL to oxidation *in vivo,* an effect that may lower the risk of artherogenesis. In the apolipoprotein E-deficient mouse model of atherosclerosis, green tea extract administered in drinking water, prevented the development of atherosclerosis without affecting plasma lipid or cholesterol levels [123]. Similarly, EGCG at a dose of only 10 mg/kg given intraperitoneally significantly inhibited the developing atherosclerotic plaques in Apo E deficient mice [124]. Green tea has long been believed to possess hypotensive effects in popular Chinese medicine. Yang., *et al.* [125] concluded that habitual moderate strength green tea or oolong tea consumption, 120 mL/day or more for 1 year significantly reduces the risk of developing hypertension in the Chinese population. Hodgson., *et al.* [126] reported

that long-term regular ingestion of green tea may have a favorable effect on blood pressure in older women. Singh., *et al.* [127], and Murakami and Ohsato [128] reported that dietary green tea intake preserves and improves arterial compliance and endothelial function. The oxidation of LDL cholesterol, associated with a risk for atherosclerosis and heart disease, is inhibited by green tea due to EC and EGCG antioxidant activity. The in vitro antioxidant activity of EGCG on LDL oxidation is stronger than EC [129]. Raederstorff., *et al.* [130] investigated the dose-response and the mechanism of action of EGCG on these parameters in rats which were fed a diet high in cholesterol and fat. After 4 weeks of treatment, total cholesterol and LDL cholesterol plasma levels were significantly reduced in the group fed 1% EGCG when compared to the non-treatment group [131-135].

Conclusions

Tea is considered as one of the most promising dietary agents for the prevention and treatment of many diseases and consequently, it is being studied extensively worldwide. Numerous studies in a variety of experimental animal models have demonstrated that catechins (EGCG, EGC, ECG and EC) possess antioxidant, antimutagenic, antidiabetic, anti-inflammatory, antibacterial and antiviral and cancer preventive properties. Most of the effects of tea are associated with flavonoids and their antioxidant potential. The polyphenols present in tea can also decrease the risk factor of specific type of cancers by inducing phase I and phase II metabolic enzymes that increase the formation and excretion of detoxified metabolites of carcinogens.We have screened 311 subjects from different areas of Eastern, North Eastern India and also from RKMSP Hospital, Kolkata, out of (311 subjects) which 61.09% has betel quid chewing habit. Percentage of micronuclei, which acts as a cancer biomarker are lower after supplementation of black tea.

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