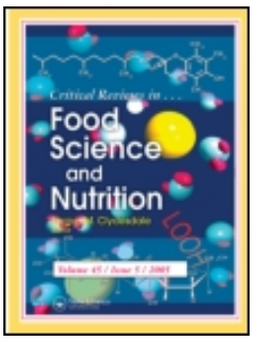

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Black Tea Polyphenols: A Mechanistic Treatise

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Black Tea Polyphenols: A Mechanistic Treatise

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Dietary interventions are among the emerging trends to curtail physiological malfunctioning like cancer, diabetes, cardiac complications, etc. The essence of phytonutrients has developed the concept of nutraceuticals at the junction of diet health linkages. In this context, theaflavin & thearubigins are the oxidized derivatives of black tea catechins during fermentation having nutraceutical potential owing to esterification of hydroxyl ring with digallate esters. Theaflavin may influence activation of transcription factors such as NFnB or AP-1 that ultimately hinder the formation of nitric oxide expression gene. Likewise, black tea contains a unique amino acid theanine acts as neurotransmitter owing to its ability to cross the blood–brain barrier. Moreover, it boasts immunity by enhancing the disease-fighting ability of gamma delta T cells. Theaflavin & thearubigins act as safeguard against oxidative stress thereby effective in the cardiac functioning. The mechanistic approach of these antioxidants is likely to be associated with inhibition of redox sensitive transcription factors & pro-oxidant enzymes such as xanthine oxidase or nitric oxide synthase. However, their involvement in antioxidative enzyme induction as in glutathione-S-transferases is also well documented. They act as curative agent against numerous pathological disorders by disrupting the electron chain thus inhibiting the progression of certain ailments. Black tea polyphenols established themselves as strong antioxidants due to their standard one-electron potential, and their vitality is dependent on the concentration of polyphenols and pH for their inclusive execution. Present review is an attempt to enrich the readers regarding the health promoting aspects of black tea polyphenols. Concomitantly, it needs core attention of researchers for the exploitations of black tea flavanols as an important dietary constituent for the vulnerable segment.

Keywords Black tea, polyphenols, flavanols, cancer, oxidative stress, theaflavin, thearubigins

INTRODUCTION

Dietary guidelines focus on the dynamic aspects of phytonutrients as they exert beneficial effects on human health particularly against cardiovascular complications, neurodegenerative diseases, diabetes, and numerous oncogenic events. This veracity has encouraged the supplementation of plant-derived nutraceuticals that, in turn, modulate the onset of chronic ailments. Epidemiological studies have correlated the capacity of numerous phytochemicals particularly polyphenols with improved health claims (Jayasekera et al., 2011). Owing to the health protective functions, black tea and its constituents are extensively investigated dietary source of polyphenols (Turkmen et al., 2006; Almajano et al., 2008).

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Tea, a popular beverage after water, made from the leaves of tea plant (*Camellia sinensis)*. The historians have linked its consumption almost 5000 years back (Yang et al., 2009). On the basis of fermentation, tea is mainly divided into four distinctive types white, green, oolong, and black tea that differ in terms of processing method and chemical profile (Cabrera et al., 2003). It has been reported that during 2008, the total production of tea was 3.7 billion kg (Letchoumy et al., 2008). Green tea account for approximately 20% of total tea produced and is consumed primarily in East and South East Asia. Contrarily, black tea that occupied approximately 78% of world tea production is consumed mainly in North America, Europe, and North Africa. Green tea is prepared by pan-frying or steaming fresh tea leaves at elevated temperature to inhibit polyphenol-oxidase mediated processes, whereas oolong tea is semifermented product (Imran et al., 2012). During the manufacturing of black tea, leaves are crushed and subjected to enzymatic oxidation process called fermentation (Hsu et al., in press). Subsequent oxidative

Table 1 Chemical composition of black tea

Constituents	Concentration (%)
Catechins	3–10
Theaflavins	3–6
Carbohydrates	15
Thearubigins	12–18
Protein	1
Flavonols	6–8
Mineral matter	10
Phenolic acids	10–12
Volatiles	1
Amino acids	13–15
Methylxanthine	8–11

Source: Sharangi (2009).

condensation of the catechins during the fermentation leads to production of theaflavins (TFs) (benzotropolone dimers of catechins) as well as higher molecular weight polymers, i.e., thearubigins (TRs). Both constituents are responsible for specific taste and color of black tea. Polyphenolic compounds including substantial amounts of flavonoids dominate typical composition of black tea (Bursill et al., 2007). Flavonoids are classified into six groups based on structure and position of the heterocyclic oxygen carbon oxygen ring, i.e., flavones, flavanones, isoflavones, flavonols, flavanols, and anthocyanins. Flavanols consist of unoxidized catechins including TF and TRs, while flavonols are characterized by quercetin, kaempferol, and myricetin. Tea also contains phenolic acids (caffeic, quinic, and gallic acids), caffeine, theobromine, theophylline, and many flavors compounds enriched with linalool (Dimpfel et al., 2007). In addition, tea carries unique amino acid, theanine that has been extensively studied for biological activities. Tea composition is likely to be associated with origin, fermentation conditions, and processing (Table 1). Black tea health claims are allied to the TF, TRs, catechins, theanine, and flavonols (Mei et al., 2009). The brief description of tea phytochemicals is given below.

THEAFLAVIN

Theaflavins constitute a complicated structure of hydroxy-substituted benzotropolone ring that is synthesized by condensation of catechins in their hydroxylated B rings (di and tri forms), attaching with benzotropolone catechins (Ju et al., 2007). The reaction of abridgment initiates by B ring oxidation to the quinines, with addition of the gallocatechin quinone to the catechin quinone that ultimately brings down decarboxylation termed as Michael addition reaction (Kaur et al., 2007).

Theaflavin is a mixture of four compounds termed as theaflavin (TF1), theaflavin-3-gallate (TF2A), theaflavin-3′-gallate (TF2B), and theaflavin-3, 3′-digallate (TF3). The molecular formulas of TF1, TF2 (including TF2A and TF2B), and TF3 are $C_{29}H_{24}O_{12}$, $C_{39}H_{28}O_{16}$, and $C_{43}H_{32}O_{20}$, respectively. Their chemical structures and route of formation is shown in Fig. 1. Several in vitro researches in TF chemistry have chalked out their new analogs. In this context theaflavate A is a famous resultant product of epicatechin gallate (EC) oxidation by potassium ferricyanide (Halliwell, 2007). Alongside to theaflavate A, other active forms of TFs including isotheaflavin-3′-o-gallate and neotheaflavin-3-o-gallate have also been reported containing a benzotropolone moiety common in their structure (Inami et al., 2007). TFs are natural antioxidant and metal chelators due to the presence of hydroxy groups; however, the gallic acid moiety is also a key contributor in this regard (Kumar et al., 2007; Lambert et al., 2007a). The majority of studies have reported elevated antioxidant efficiency of TFs by the esterification of hydroxyl ring with digallate esters (Lambert et al., 2007b). Furthermore, it has been revealed that the rate constant of TFs as a superoxide scavenging is higher in comparison with epigallocatechin gallate (EGCG) (Maeta et al., 2007). Likewise, preventive role of TFs in lipid preoxidation is mainly attributed to its ability to cease the chain reaction of lipid oxidation. Apart from free radical scavenging and metal chelating abilities, TF has potential to activate certain antioxidant enzymes like glutathione-S-transferases (GST), glutathione peroxides (GPX), superoxide dismutase (SOD), and catalase (CAT), which ultimately resulting lipid peroxidation reduction (Maki et al., 2009; Mazzanti et al., 2009).

THEARUBIGINS

Recent studies have documented TRs as the most copious group of phenolics found in black tea, contributing almost 60% of the solids in typical black tea (Nagao et al., 2009; Schneider and Segre, 2009). Among the black tea polyphenols, TRs having anti-initiating properties against cancer cells referred as polymeric black tea polyphenols (PBPs) (Patel et al., 2007). They are providing reddish tonality to black tea in contrast with green and white tea. The color of a black tea, however, is not only affected by the TRs, but some other intrinsic compounds like unoxidized polyphenols and TFs are also involved (Das et al., 2009; Schneider and Segre, 2009). Originally, TRs formation (Figure 1) is initiated after conversion of 75% the phenolic flavan-3-ol molecules from catechins. Nutraceutical properties of tea are accredited to the presence of TRs, which not only help mitigate various ailments but also enhance its credit and integrity toward the consumer acceptance. Numerous studies have investigated that the TRs in tea is intricate due to their varying concentrations that are often found in a chaotic manner as 20% in black tea leaf and 60% as solids in final black tea infusion (Gupta et al., 2009; Thielecke and Boschmann, 2009). TRs have gained special interest for their ability to activate phase II enzymes by inducing the transcriptional upregulation in liver and lungs after elevation of Nrf2-mediated antioxidant-responsive element binding. However, PBP extract has not been reported for the alteration of Nrf2 or Keap1 at the transcriptional level may increased by posttranslational modifications such as phosphorylation and decreased ubiquitination. Pretreatment of TRs is

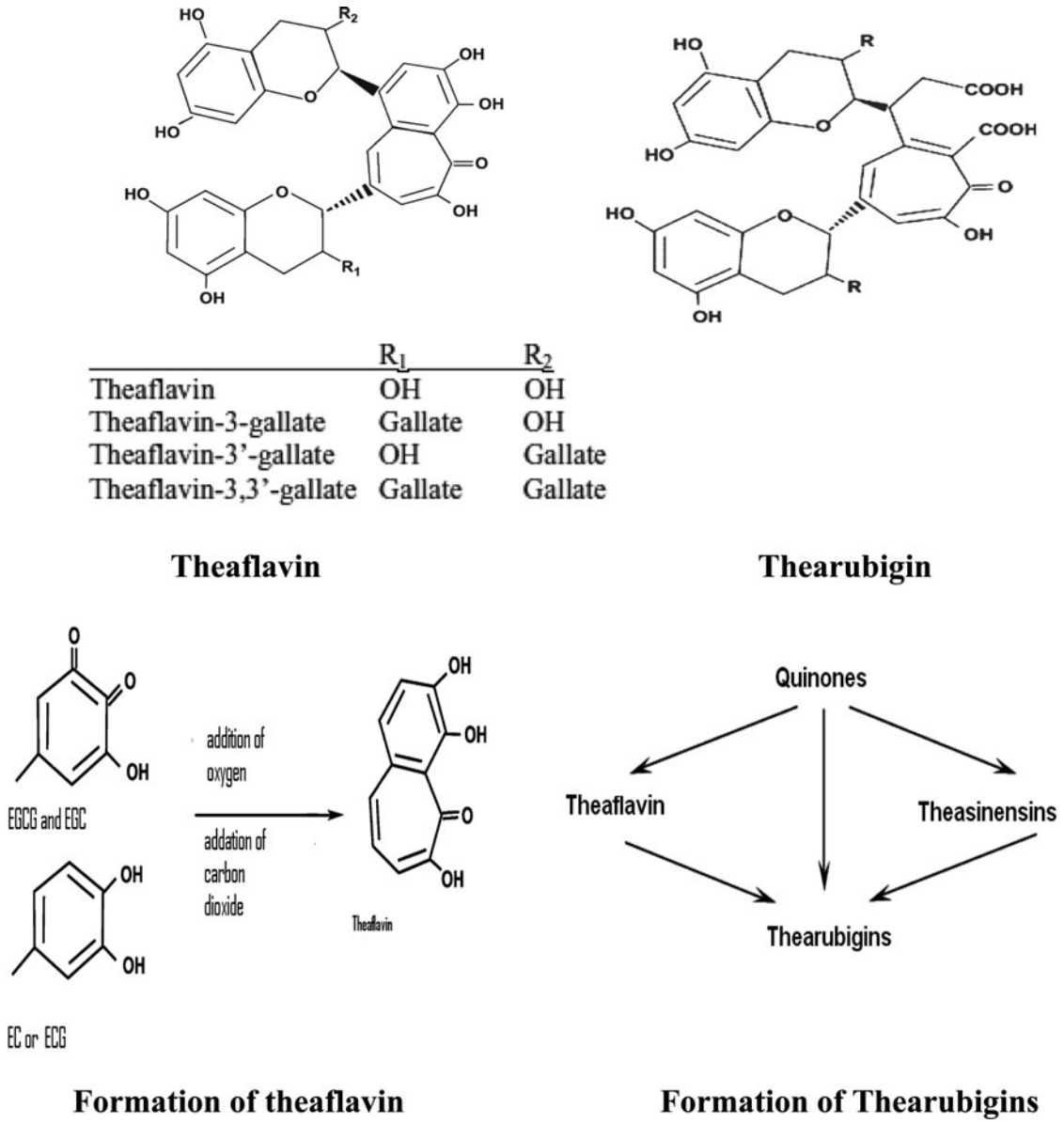

Figure 1 Structure and mode of formation of flavanols.

responsible for the nuclear translocation of PKC and PI3-kinase-mediated phosphorylation of Nrf2, critical for the release of Nrf2 from Keap1 and its subsequents. Moreover, their anticancer concerns are probed due to their ability to decrease carcinogen DNA adducts by inactivation of carcinogen-induced phase I enzymes such as CYP450 1A1 and 1A2 (Patel and Maru, 2008).

THEANINE

Theanine (gamma-glutamylethylamide, or 5-N-ethyl-glutamine) (Fig. 2) is a glutamic acid analog commonly identified in tea (*Camellia sinensis*). Synonymously termed as L-theanine, (Table 2) due to its molecular orientation and classified as levorotary enantiomer. L-Theanine is a predominant amino acid, 1–2% of the dry weight of the leaves comprises about 50% of total protein (Palva and Palva, 2007). It was first identified by Sakato in tea leaves as the main free amino acid component that can influence the major umami constituents of tea (Hideyuki et al., 2002). Various health effects have been associated with L-theanine, such as neuroprotective effects, which ultimately enhanced nervous attention. On the basis of two parallel techniques, i.e., electroencephalographic (EEG) and behavioral modules indicate that L-theanine influences functionality of brain (De Mejia et al., 2009). Current consensus regarding theanine has explained its effect in mitigation of mental and physical stress due to its ability to cross the blood–brain barrier (Boris et al., 2009). Moreover, it enhances cognition and behavior in a systematic manner with caffeine.

Table 2 Promising Characteristic of black tea polyphenols

Name of constituents	Silent features	Health claims	Sources	References
Catechin	White in color crystalline structure Mol. Wt. 302.2357 Boiling point 642.4 Density is 1.799 g/cm^3	Act as strong antioxidant. Provide protection against cancer, obesity, and diabetic	Green tea, black tea, onion garlic, etc.	Boris et al., 2009
Theaflavin	Orange-colored crystalline structure Mol. for $C_{29}H_{24}O_9$ For. Wt. 516.5 Boiling point 1003.9° Density 1.87 g/cm^3	Strong antioxidant provide protection against cancer and other life related disorders	Black tea	Popkin, 2010
Thearubigin	Dark brown crystalline structure Heterogeneous in nature Molecular mass 700–40,000 Da. Water soluble and acidic	Provide multiplicity of health claims dominated by oxidative stress and cardiovascular compliances	Black tea	Popkin, 2010
Theanine	Gammaglutamylethylamide analog amino acid levorotary enantiomer GRAS by FDA Mol. Wt. 174.20 mp. 202–215°C	Neurotransmitter enhance resistance against Alzheimer disease	Green and black tea	Rains et al., 2011
Quercetin	Yellow crystalline powder mp. 310–317°C stable under normal conditions Mol. for $C_{15}H_{10}O_7$	Strong antioxidant status. Important in oral health reduce cholesterol	Vegetables like cabbages broculis, onion, and green and black tea	Amić and Lučić, 2010
Myricetin	White powder that was slightly soluble in water Mol. Wt. 318. 2351 mp. 300°C mp. 745.45°C	Metal chelating and cancer inhibiting properties	Black tea, green tea onion and mango peel	Amić and Lučić, 2010
Kaempferol	Yellow solid having the crystalline structure. Boiling point 276–278°C. sparingly soluble in water readily soluble in hot organic solvents	Reduce cancer and act as antibacterial agent	Walnut is its richest source also reported in green and black tea	Amić and Lučić, 2010

In addition, L-theanine helps boast immunity against infection by enhancing the disease-fighting ability of gamma delta T cells (Sugiyama and Sadzuka, 2003). Recently, array of biochemical modulations proved theanine effective to enhance the activity of several antitumor agents, including doxorubicin (DOX) (Popkin, 2010). In addition to neurofunctionality and antitumor activities, its role as hepatic protective agent is also well documented. During oxidative stress it protects the liver damage due to increase in glutathione level via metabolism through glutaminase and c-GTP (Van der Pilji et al., 2010).

FLAVONOLS

Flavonols are often termed as aglycons due to their occurrence in plants in the form of glycosides. Mostly, glucose and galactose sugar moieties are attached with aglycons, responsible for their rapid metabolism (Baoru et al., 2009; Ou et al., 2002). Their composition and availability is influenced by numerous factors like plant variations, soil, season, light, degree of ripeness, food preparation, and processing (Ross et al., 2000). They are formed by the combination of derivatives synthesized from phenylalanine (via shikimic acid pathway) and acetic acid; nevertheless, formation of phenylalanine from phenylpyruvate is a crucial step. Furthermore, their absorption is dependent on attached sugar moiety on flavonol glycosides thereby effecting absorption rate (Noelia et al., 2010). They comprised kaempferol, myricetin, and quercetin (Fig. 3), whereas kaempferol is potentially present in broccoli, grapefruit, brussels sprout, and apple (Smith et al., 2000). It has yellowish tonality with boiling point ranging from 276–278°C

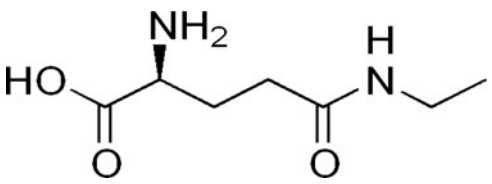

Figure 2 Structural representation of theanine.

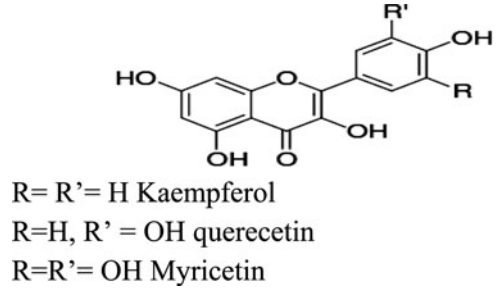

Figure 3 Structural representation of flavonols.

(Table 2). It is sparingly soluble in water but readily soluble in hot ethanol, diethyl ether, and other organic solvents (Rains et al., 2011). Its consumption through tea and other natural commodities has closely been associated with reduced cardiac complications and used in antidepressant drugs (Amić and Lučić, 2010).

Myricetin is predominantly found in many fruits like grapes, berry, some vegetables, herbs, and walnuts. In vitro research has proved myricetin as an active ingredient to reduce low-density lipoprotein (LDL) cholesterol by increasing the uptake and modifying the white blood cells that ultimately responsible for scavenging the free radicals that produced due to oxidation of LDL. In some scientific studies, high myricetin consumption resulted in lowering the onset of prostate cancer. Quercetin works as anti-inflammatory, antioxidant, and polar auxin transport inhibitor. Furthermore, in vivo study conducted on rats confirmed that its administration can increase energy expenditure (Amić et al., 2007a).

MECHANISTIC APPROACH OF BLACK TEA

The emphasis of phytochemical research has shifted researcher focus toward their disease preventive behavior by executing their functionality against lipid oxidation, nucleic acids, or proteins degeneration (Bai et al., 2007). Thereby, phytochemical pharmacokinetics work well in case of several chronic diseases like cancer, whereas more pronounced effects were observed in cardiovascular compliances, cataract, age-related macular degeneration, and aging (Cirico and Omaye, 2006). Although human cells are enriched with variety of endogenous antioxidants but still require some exogenous antioxidants to maintain an appropriate level of antioxidants to quench the reactive oxidative species (Maeta et al., 2007). Antioxidants protect the body by neutralizing the free radicals via donating electrons and thus ending the scavenger property (Amić et al., 2007b; Maeta et al., 2007). Black tea is considered as a dietary source of antioxidant nutrients like TFs, TRs, quercetin, myricetin, and kaempferol (Table 1). Black tea is a proven nutraceutical agent through inhibition of redox sensitive transcription factors and some "prooxidant" enzymes, like nitric oxide synthase, lipoxygenases, cyclooxygenases, and xanthine oxidase. Moreover, it can induce certain antioxidant enzymes mainly glutathione-S-transferases and superoxide dismutases (Amić and Lučić, 2010). Tea polyphenols with vicinal hydroxyl groups are also strong chelators of redoxactive transition metals (e.g., iron and copper) (Chlebda et al., 2010) may contribute to their overall antioxidant activity. It has been proposed that the stability of such complexes increases as a function of increasing pH as metals are not so efficient electrons acceptor as they are generally surrounded by negative charges. Studies have demonstrated antioxidant activity of black tea while using oxygen radical absorbance capacity (ORAC) assay and found to posses higher antioxidant activity against peroxyl radicals as compared with vegetables like garlic, spinach, and kale (Mukai et al., 2005). Moreover, both catechins and TFs exhibited strong antioxidant properties as compared with that of glutathione and tocopherol (Kim et al., 2005). Individual fraction of theaflavin, (TF3) has shown higher antioxidant activity than EGCG, a precursor of TF3 (Kim et al., 2005; Phung et al., 2010) probably due to presence of more hydroxyl (OH) groups. Investigations regarding TF structure have shown that order of reactivity is dependent upon the position of hydroxyl groups within the TF molecules. Similarly, theaflavin TF3 showed higher antioxidant activity followed by TF2 and least is documented in TF1 (Auvichayapat et al., 2008). It has been proved that TF in their gallate form exhibits stronger antioxidant activity as compared with individual TF moiety (Nagao et al., 2009). It has also been reported that in vivo free radical scavenging activity is moderately influenced by the value of standard one-electron potential (Table 3), higher in black tea polyphenols (BTP) as compared with vitamin C and tocopherol (Henning et al., 2011). TF also possess ability to inhibit prooxidative enzymes. Study conducted on human leukemia cells HL-60 indicated that TF digallate efficiently reduced the xanthine oxidase activity, which catalyses oxidation of hypoxanthine and xanthine enzymes and convert into uric acid leading to superoxide radical and hydrogen superoxide formation. Furthermore, radical scavenging activity was proved through reduction of NADPH-cytochrome P-450 reductase activity after application of 2-amino-3-methylimidazo quinoline (Amić et al., 2008) as a reaction substrate (Cavia et al., 2010). Studies on human white blood cell (macrophages) exposed the ability of TFs as a nitric oxide synthase (NOS) inhibitor. Polyphenols of black tea also prevent the action of cancer promoting enzymes like cyclooxygenase COX-2 and 5-, 12-, and 15-lipoxygenase that can actively participate in enzymatic induced lipid peroxidation in human colon mucosa and tumor tissues (Lee et al., 2006; Martín et al., 2010). Strong interaction of polyphenols and transition metals in case of black tea is evidence of its antioxidative activity, forming complex with iron or copper ions and thus prevent free radicals initiation by inhibiting the lipid peroxidation mechanism (Young and Woodside, 2001; Mladěnka et al., 2010). However, iron binding ability of black tea polyphenols can impair the iron absorption in the gastrointestinal tract (Balentine et al., 1997; Mukhtar and Ahmad, 2000). This binding with iron can be

Table 3 Standard electron potential of some prominent antioxidants

Antioxidants	Standard electron potential (mV)
Ascorbate	280
Alpha tocopherol	480
Uric acid	590
Glutathione	920
(-)-Epigallocatechin gallate	430
(-)-Epigallocatechin	430
(-)-Epicatechin	570
(-)-Epicatechin gallate	550
Theaflavin	510
Theaflavin digallate	**540**

Source: Luczaj and Skrzydlewska (2005).

mitigated by enhancing the magnitude of ascorbic acid (Duffy et al., 2001; Widlansky et al., 2005). Another theory, regarding the antioxidative mechanism of black tea, revealed that its antioxidant response might be due to its ability to increase the activity and concentration of antioxidants in the living organism. This has been supported by research study, in which black tea dried leaves supplemented in rat's diets resulted in liver protection (Hodgson et al., 2002). Similarly, other experiments showed the improvement in serum superoxide dismutase (SOD) activity after oral administration of black tea to mice exposed to the strong carcinogen, i.e., 3-methylcolanthrene (Di et al., 2011; Hodgson et al., 2000). Many investigations revealed that black tea consumption causes an increase in plasma antioxidative activity from 20 to 40% depending upon condition and applied assay (Hakim et al., 2003; Rietveld and Wiseman, 2003). Evidence for antioxidative potential of black tea is obvious from attenuation of free radicals interaction with some cordial molecules like lipids, DNA, and proteins. It was proved that TF digallate has stronger inhibitory action against macrophage-mediated (white blood cell) LDL oxidation in comparison with EGCG and gallic acid due to its ability to protect membrane phospholipids oxidation (Maron et al., 2003; Sinisalo et al., 2010). Experiments on rats drinking black tea demonstrated inhibition of lipid peroxidation in their livers (Macedo et al., 2011). Antioxidative properties of black tea are also supported by the fact that resultant beverage as well as unoxidized catechins is able to inhibit changes in natural porosity of cell membranes resulting from oxidative stress. Moreover, black tea inhibition of cytochrome P-450 1A1 activity reduces the activation of benzopyrene (BaP), procarcinogen that participates in DNA damage (Roy et al., 2010). Similarly, black tea administration in rats for 10-day as gavages significantly decreased 8-OHdG generation (8-Oxo-2′-deoxyguanosine; a marker of DNA damage) induced by the colon carcinogen, 1, 2-dimethyl hydrazine (Huange et al., 2010; Miranda et al., 2008). However, remarkable decrease was found in the level of 8-OHdG in blood profile of smokers addicted to black tea. Experiments on RAW 264.7 mice macrophages revealed that TFs, especially TF3 effectively prevents activation of transcription factor (NFnB) thus avoiding expression of nitric oxide synthase (iNOS) (Yang et al., 2009). Experiment conducted on prokaryotes macrophages (106 cells/well) disclosed that black tea TFs and catechins abrogate NO production up to 70%. Incubation of 21BES cells with TF digallate (TF3) showed inhibited c-jun protein phosphorylation considered responsible for the binding of transcription factor AP-1 that plays a vital role in transformation and proliferation of cells (Shen et al., 2010).

RECENT INNOVATION IN ANTIOXIDANT ACTIVITY OF BLACK TEA

In a recent study, antioxidant role of black tea polyphenols and bovine lactoferrin (bLF) was determined using the hamster buccal pouch (HBP) to evaluate the inhibitory effects of both substances on the onset of 7, 12-dimethylbenz anthracene (DMBA)-induced cancer insurgence. The chemopreventive role of beta lactoferon and black tea polyphenols was accredited to their ability to modulate DMBA-induced DNA damage as well as the performance on different carcinoma proteins (von Staszewski et al., 2010). Moreover, a comparative trial was conducted to demonstrate the effects of consuming a high-flavonoid (HF) and low-flavonoid diet on oxidative damage in 32 healthy humans for testing the lipid peroxidation biomarkers (plasma F2-isoprostanes). Conclusion of study stressed upon the strong ex vivo activity of flavonoids as compared with in vivo activity mainly due to their low bioavailability (Jayasekera et al., 2011).

Likewise, role of black tea polyphenols in reducing oxidative stress was tested in a rat model of hepatocellular carcinoma (HCC). Administrations of polyphenol-B effectively suppressed hepatocarcinogenesis, as shown by reduced preneoplastic and neoplastic lesions, modulation of xenobiotic-metabolizing enzymes, and amelioration of oxidative stress (Adhami et al., 2004; Martin et al., 2009). Scantly, it can be concluded that polyphenons acts as an effective chain breaker and act as cemopreventive agent in vivo (Murugan et al., 2009). Moreover, Widlansky et al. (2005) evaluated the effect of black tea polyphenols on oxidation, inflammation, and antioxidant protection from 66 subjects after administration of two dosages as 450 ml of black tea (acute) and 900 ml of black tea per day (chronic). Results showed that it did not improve plasma antioxidant capacity, suggesting that the benefits of black tea consumption on endothelial function may not be attributable to tea dose (Ziyin et al., 2009).

PROOXIDANT ACTIVITIES

The field of prooxidant has employed the contradict attitude of black tea polyphenols with its antioxidative characteristics. Although antioxidative properties of black polyphenols have well documented, some opposing results also been reported proposing the prooxidative properties of tea. Recently, it has been reported that administration of TF on the human bronchial epithelial (21BES) cell lines, enhanced generation of hydrogen peroxide, and lead to apoptosis after 8 to 12 hours (Haslam, 2003; Lambert and Yang, 2003). Copper, which occurs in the mammalian cell nucleus, is believed to play a central role in the formation of oxygen species and produce DNA damage. Possible mechanism is copper ion (II) activated catechins autooxidation, subsequently generating copper ion (I) and semiquinone radical (Xianglin et al., 2000) This copper ion (I) combines with oxygen to produce hydrogen peroxide and forms bond with DNA to make DNA-Cu(I)OOH that might be responsible for the formation of hydroxyl radical resulting in DNA damage. Moreover, effect of copper ions (II) was also reported to catalyze the oxidation of other active black tea polyphenols, such as quercetin and myricetin, caused brake up of DNA strand and formation of 8-OHdG complex (Agarwal et al., 1991; Feng et al., 2002; Leung et al., 2001). Moreover, retrospective data have illuminated that oxidized tea polyphenols, such as semiquinone

or benzoquinone radical undergo reduction that is classified as nonenzymatic through NADH, resulting in abundant redox substances formation that will yield reactive oxygen species. Coenzyme mediated (NADH) free radicals could also facilitate the catechins initiated DNA injures. Prolonged in vivo administration of quercetin (Langley, 2000) leads to dysfunction of important antioxidant enzyme, such as glutathione, causes oxidative damages due to decrease glutathione reeducate activity and glutathione concentration. Thus, it could be said that antioxidant and prooxidant activity of black tea polyphenols is not consistent, but it dependent upon many factors like reducing potential, chelating ability, pH, solubility, bioavailability, and more important stability in tissues and cells (Meng et al., 2001).

CONCLUSIONS

Current scenario has established black tea as an effective nutraceutical product due to enriched polyphenols profile, an ultimate antioxidative entity. Although the cutting edge between functional and nutraceutical has not yet been illuminated, tea flavanols have enclosed features of an effective disease curative constituents. TF is one of the promising agents against cancer cells while TRs also contribute strongly toward the menace. Alongside, theanine and flavonols have affirmed significance and attained consumers' attention due to their minimal toxicity, high consumption safety, and health assuring perspectives. However, black tea polyphenols are also known to exhibit prooxidative properties in certain conditions. The manuscript artwork provides sufficient evidences to support black tea against various physiological threats. Furthermore, there is still a need of extensive exploration, corroboration, and refinement of respective nutraceuticals to address the remaining pitfalls and challenges in a novel way.

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