Topical Review

Antigenotoxic Potential of Tea

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Introduction:

The practice of disease prevention is the most effective means for improving human health. Therefore, different approaches have been actively used, e.g. sanitation, vaccination and life style modifications. With increased awareness of our environment it becomes clear that environmental mutagens and carcinogens (e.g. automobile exhaust, food borne carcinogens, cigarette smoke, radiation etc.) can cause a variety of genetic disorders including cancer. Two general studies have been suggested to cope up with this problem: 1) reducing the exposure of an individual to known mutagen as much as possible and 2) taking advantage of the inhibitors of mutagenesis with the final purpose of their eventual application as antigenotoxic agents. Since exposure to the environmental mutagens is often unavoidable, the latter field has been widely explored with the several components of the diet. The advent of natural products as chemotherapeutic agents against human ill health effects attributable to mutations is the most valid approach due to their relative low cost and non-toxic effects.

Various short-term assays, which are used for monitoring environmental mutagens, may also be deployed for the detection of antigenotoxic/ antimutagenic substances too. Inhibitors of mutagenesis assessed by the use of *Salmonella typhimurium* reverse mutation assay (Ames Test) detect antigenotoxic potential in microbial test system. Besides this prevention of chromosomal aberrations, micronucleus and Sister Chromatid Exchange (SCE) induction contributes to the evaluation of reduction in genotoxic risk associated with exposure to physical and chemical agents and predicting anticarcinogenic agents. Identification of chemotherapeutic agents through the use of dominant lethal mutation assay determines its utility in detecting germ cell antimutagens. Hence the above techniques coupled with antimutagenicity testing could provide greater insight into chemoprevention of specific types of DNA damage and helpful in screening natural antimutagenic and anticarcinogenic agents for their chemopreventive activity.

Tea is the most popular and widely consumed beverage possessing many health beneficial effects. The pharmacological and medicinal properties of tea including antioxidant, antipyretic, anti-inflammatory and anticarcinogenic effects are well documented in the literature. Of the approximately 2.5 million metric tons of dried tea manufactured annually, only 20% is green tea and less than 2% is oolong tea and rest 78% is black tea which contains more than 500 chemical constituents (Graham, 1992). These include flavanols, flavandiols, flavonoids, and phenolic acids, carbohydrates, minerals and proteins etc. Most of the polyphenols present in green and black teas are flavonols, tannins commonly called as catechins. Some of the major catechins present in tea are (-)- epigallocatechingallate (EGCG), (-)- epicatechin-3-gallate (ECG), (-)-epicatechin (EC), (-)- epigallocatechin (EGC), Theaflavins (TF) and Thearubigins (TR) (Table 1). TFs are astringent compounds, which contribute importantly to the color and taste of the black tea beverage. During black tea manufacture some of the catechins mass is converted to a less well

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Table 1.
Composition of the Green and Black Tea Extracts & Polyphenols

Polyphenolic Constituents	Green tea extract (%)	Green tea polyphenols (%)	Black tea extract (%)	Black tea polyphenols (%)
Epicatechin	2.5	7.8	0.85	5.6
Epigallocatechin	10.3	4.7	0.97	1.4
Epicatechin gallate	2.3	13.2	1.7	10.6
Epigallocatechin gallate	11.2	40.7	2.9	15.3
Theaflavin	0.00	0.00	0.51	3.2
Theaflavin 3-gallate	0.00	0.00	0.46	2.8
Theaflavin 3'-gallate	0.00	0.00	0.30	1.3
Theaflavin digallate	0.00	0.00	0.22	2.1
Gallic acid	0.00	0.00	0.15	5.2
Caffeine	5.6	0.76	5.0	0.76

defined group of compounds known as thearubigins. The individual polyphenolic composition of black and green tea is given in Table 2.

Table 2.
Catechins Constituents in Green and Black tea

Catechins	Green tea (mg/ml)	Black tea (mg/ml)
(+) Catechin (C)	21	20
(+) Gallocatechin (GC)		
(-)-Epicatechin (EC)	98	37
(-)-Epicatechin-3-gallate(ECG)	90	73
(-)-Epigallocatechin (EGC)	411	42
(-)-Epigallocatechin-3-gallate (EGCG)	444	128
Theaflavnoids	0	64
Theaflavin (TF)	0	22
Theaflavin gallate A(TFA)	0	20
Theaflavin gallate b(TFB)	0	13
Theaflavin digallate (TFDG)	0	9
Thearubigins	0	23

Epidemiological and experimental studies displayed the beneficial effects of tea and its polyphenols and utility as chemopreventive agent. The antimutagenic and anticarcinogenic activities of both green tea and black tea along with their polyphenolic constituents have been characterized in microbial and mammalian somatic and germinal test systems. (Katiyar and Mukhtar, 1997).

Epidemiological Studies:

Epidemiological studies have provided sufficient evidence suggesting the beneficial role of tea drinking on human health. Drinking of both the varieties of tea has been shown to inhibit genotoxic potential of various mutagens and carcinogens. The chemopreventive role of green tea among cigarette smokers has been demonstrated by the reduction observed in sister chromatid exchange frequency in mutagen stimulated peripheral blood lymphocytes (Shim et al, 1995). The protective effect of tea has been suggested mainly due to the ability of tea polyphenols to inhibit endogenous formation of nitroso compounds, which are considered as major causative factors in gastric cancer (Yang and Wang, 1993).

I. Antimutagenic activity of tea and its polyphenols in *microbial systems*

A. *Salmonella typhimurium* reverse mutation assay

The use of *Salmonella typhimurium* reverse mutation assay in genetic toxicology is now firmly established both for fundamental studies in mutagenesis and carcinogenesis (Flamond *et al.,* 2000; Kappers *et al.,* 2000). The *Salmonella typhimurium* reverse mutation assay (Ames Test) is the widely used method to assess the mutagenic potential of chemicals which can cause base pair and frame-shift mutations in the genome of this organism (Maron & Ames, 1983). At the same time this useful tool is also being employed to evaluate the antimutagenic potential of various synthetic or natural products (Heddle *et al.,* 1999).

The antimutagenic activity of tea extracts and polyphenols including ECG and EGCG against various mutagens and carcinogens has been demonstrated using microbial systems (Liu *et al.,* 1998). EGCG and ECG showed inhibitory against the mutagenicity of MNNG in *Salmonella typhimurium* TA98 and TA100 with and without rat liver S9 mix. (Okuda *et al.*, 1984). EGCG also has a strong inhibitory effect against the mutagenicity of BaP diol epoxide in TA 100 strain without S9 mix (Okuda *et al.,* 1984**)**. Theaflavins, gallate esters and catechins inhibited mutagenicity of PhIP in *Salmonella typhimurium* TA 98 (Apostolides *et al.,* 1997). The gallate esters of the catechins EC, EGC, EGC and EGCG, theaflavonoids TF, TFMG and TFDG and glucose had low IC_{50} in the 80-250 µM range against mutagenicity of 10 µM PhIP. Non-polyphenolic fraction of green tea suppressed 3-amino-1, 4-dimethyl-5H-pyrido[4,3-b]indol (Trp-P-1) or mitomycin C (MMC) induced umu C gene expression in *Salmonella typhimurium* TA1535/ psk 1002 in the presence or absence of S9 metabolizing enzyme mixture. (Okai & Okai, 1997). Standard black and green tea extracts have been known to inhibit mutagenicity caused by PhIP, in the *Salmonella typhimurium* reverse mutation assay with TA98 containing S9 fraction from the liver of rats induced with alpha-naphthoflavone and Phenobarbital (Apostolides & Weisburger, 1995). The inhibition of the mutagenicity of PhIP by gallated catechins and theaflavins has been found due to inhibition of the conversion of the procarcinogen PhIP, to the proximate carcinogen N-OH-PhIP (Hayatsu *et al.,* 1992). Antimutagenic activity of green and black tea extracts was also observed towards food mutagen MeIQx in the direct plate assay with *Salmonella typhimurium* in a *in vitro* gastrointestinal model (Krul *et al.,* 2001). In addition tea also exhibited antimutagenic potential against mutagenicity of heterocyclic amines in *Salmonella typhimurium* (Stravic *et al.,* 1996). The antigenotoxic effects of specific tea polyphenols, polyphenon 60 and polyphenon 100 from green tea and polyphenon B from black tea were tested against a battery of genotoxic carcinogens in *Salmonella typhimurium* TA98, TA100 and TA1535 the tester strains. (Weisburger *et al.,* 1996; Hara, 1994). The results indicated that tea polyphenols sharply decreased the mutagenicity of a number of aryl-and heterocyclic amines of AFB_{1}, B[a]P, DBE and more selectively, of 2-nitropropane, all when an induced rat liver S9 fraction was included. Antimutagenic and antioxidative effects of theaflavins from black tea were reported using *Salmonella typhimurium* TA104 (Shiraki *et al.,* 1994). All theaflavins tested, TF, TFA, TFB and TFDG, suppressed mutagenicity induced by H_2O_2, and inhibited peroxidation of rabbit erythrocyte ghosts induced by t-butyl hydroperoxide.

Evaluation of antimutagenic potential of aqueous black tea extract (ATE) in Ames Test using TA 98 and TA 100 tester strains revealed that addition of 500µl of 1, 2 and 4% ATE to the BaP and CP treated plates resulted in a dose dependent inhibition in the number of his^+ revertant colonies. Similarly, supplementation of BTP at the concentration of 100, 200 and 400 mg/plate also lead to a significant inhibition in BaP and CP induced his^+ revertant colonies. The antimutagenic activity profile of BTP was found to be higher than ATE, which may be attributed due to higher amount of polyphenolic ingredients. (Taneja and Shukla, 2002).

B. In other microbial systems

Antimutagenic profile of both black and green tea and their polyphenolic constituents are well documented in the literature. A homogenate of Japanese green tea gave high bioantimutagenic activity against spontaneous mutations resulting from altered DNA-polymerase III in strain NIG1125 of *Bacillus subtilis* met his mut-1 (Kada *et al.,* 1985). Green tea and black tea decreased the mutagenic activity of MNNG in *Escherchia coli* WP2 (Jain *et al.,* 1989). Pre-incubation together of the MNNG and tea extracts, before the exposure of the cells, also reduced the mutagenic activity of MNNG. EGCG reduced spontaneous mutations in strain NIG1125 of *B. subtilis (met his mut-1)*, due to the inhibition of a function of error-prone DNA replication involving an altered DNA polymerase III (Kada *et al.,* 1985). ECG, EGC and EGCG reduced UVC (254 nm)-induced mutations in *E. coli* B/r WP2 by altering the fidelity of DNA replication. (Shimoi *et al.,* 1986). The antimutagenicity of catechins was identified against UV-induced in *Escherichia coli* B/r WP2 (Shimoi *et al.,* 1986). Tea extracts inhibited mutagenicity of 1-methyl -1,2,3,4-tetrahydrodiol-b-carboline-3-carboxylic acid on treatment with nitrite in the presence of ethanol (Higashimoto *et al.,* 2000).

II. Antimutagenic activity of tea and their polyphenols in *mammalian invivo* cytogenetic assays (somatic cell assays)

Cytogenetic tests are well identified for evaluation of mutagenic damage caused by environmental toxicants to the chromosomes (Preston *et al.,* 1987). *In vivo* bone marrow tests, which include metaphase chromosome analysis, the Micronucleus assay and Sister chromatid exchange (SCE) assay are used to identify clastogenic compounds, that is, those which are capable of inducing structural damage to chromosomes. Chromosomal aberrations indicate the clastogenic effect induced by mutagens cytogenetically observed as gaps, breaks exchanges and multiple aberrations in metaphase-arrested cells. The micronucleus test is a method devised primarily for screening of mutagenic chemicals for chromosome-breaking effects Micronuclei are the acentric chromosome fragments, which lag behind at the anaphase phase of cell division on exposure to genotoxicants. Whereas, Sister Chromatid exchanges represent reciprocal exchanges in the DNA between two sister chromatids of duplicating chromosomes and their reunion at apparently homologous loci, which are induced on exposure to genotoxicants**.** All three tests are widely used for the screening purposes and are regarded as of particular importance by many regulatory authorities. These tests are employed in the whole animal, so obvious deficiencies in artificial metabolic activation systems used in *in vitro* systems are minimized.

The applicability of *in-vivo* cytogenetic assays in determination of antigenotoxic potential of dietary compounds is well-documented (Bronzetti, 1997). Studies conducted with green tea polyphenolic ingredients have shown that it possesses a potential in inhibiting genotoxicity of polycyclic aromatic hydrocarbons, nitrosoamines etc in mammalian test system (Kuroda & Hara, 1999). Tea and their polyphenols inhibited mitomycin C induced micronuclei induction in V79 cells (Liu *et al.,* 1998). Moreover oral administration of 0.1% green tea reduced BaP induced micronuclei in peripheral blood of mice (Sasaki *et al.,* 1993). Tea polyphenols, EGCG, and TFG sharply reduced the mutagenicity of IQ and PhIP, and induced DNA repair in rat hepatocytes (Weisburger *et al.,* 1996). ECG and EGCG had inhibitory effects against 6TG-resistant mutations induced by 4NQO in cultured Chinese hamster V79 cells (Kuroda, 1996). The antimutagenic activity of the catechins was found only when the cells were post-treated with catechins during the mutations expression time after treatment with 4NQO: and were not found by simultaneous treatment with 4NQO and catechins. (Kuroda, 1996). This suggests that the catechins may act intracellularly as bio-antimutagenic blocking agents or suppressive agents. In addition extracts of green tea effectively suppressed aflatoxin B1 (AFB1) induced chromosome aberrations in bone marrow cells in rats (Ito *et al.,* 1989). In another

report green tea and black tea retarded 4(methylnitrosamino)-1-(3-pyridyl)-1-butanone bioactivation, DNA methylation in A/J mice (Shi *et al.,* 1994). Crude tea extracts decreased the mutagenic activity of *N-methyl-N'-nitro-N-nitrosoguanidine in vitro* and in intragastric tract of rats (Jain *et al.,* 1989). Black and green tea imparted protection against 2-amino-3-methylimidazo [4,5-f]quinoline-induced DNA adducts and colonic aberrant crypts in the F344 rat (Xu *et al.,* 1996). Anticlastogenic effects of black tea and its two active polyphenols theaflavins and thearubigins was identified towards CP and DMBA in SCE and chromosomal aberration assay *invivo* in Swiss albino mice (Gupta *et al.,* 2001). Protective effect of green tea has been observed against BaP induced mutations in the liver of big Blue mice (Jiang *et al.,* 2001). Chemopreventive effect of green tea has been attributed against cigarette smoke induced mutations (SCE) in humans (Lee *et al.,* 1997). Tea exhibited anticlastogenic activity against environment tobacco smoke in the sister chromatid exchange assay (Zhao *et al.,* 2000). Green tea antioxidant strongly inhibited the increase in SCE and micronuclei induced by fried fish extract and its component MeIQ in V79 or IAR20 cells (Liu, 1990). Besides this in another study green tea exhibited chemopreventive effects on SCE induction among cigarette smokers (Shim *et al.,* 1995). Tea tannin components inhibited the induction of sister chromatid exchanges and chromosome aberrations in mutagen-treated cultured mammalian cells. (Imanshi *et al.,* 1991). Hot water extracts of green tea effectively suppressed aflatoxin B1 (AFB1) induced chromosome aberrations in bone marrow cells in rats which were given green tea extract 24 h before they were injected with AFB1 (Ito *et al.,* 1989). The suppressive effect of green tea extracts on AFB_1-induced chromosome aberrations was directly related to the dose of green tea extract when given in the range between 0.1 and 2 g/kg. Catechins have been found to inhibit tobacco specific 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK) induced DNA strand breaks in rat hepatocytes (Liu & Castonguay, 1991). Green tea suppressed NNK induced levels 8-OH-guanosine levels, in lung DNA (Xu *et al.,* 1992). Administration of 2% green tea as sole source of drinking solution for 2 weeks reduced 2-Nitropropane -induced levels of 8-OH-deoxyguanosine adducts in liver nuclear DNA. Reductions in levels of DNA adducts were also found in rats given extracts of 2% green tea or 1% black tea for 8 weeks before oral administration of IQ (Xu *et al.,* 1996). The amount of IQ and other promutagens decreased in both urine and feces. Binding of AFB_1 to hepatic nuclear DNA was inhibited in rats given 0.5% instant green tea for 2 or 4 weeks before a single injection of AFB_1 (Quin *et al.,* 1997). The oral administration of 0.2% green tea or 0.1% black tea for 28 days decreased the extent of micronuclei formation in the peripheral blood of mice subsequently treated with BaP and 3-methylcholanthrene (Sasaki *et al.,* 1993). It was also found that green tea given by stomach perfusion had distinct inhibitory effects on micronuclei by in the colon crypt cells of C57BL mice (Zao *et al.,* 1992)

Aqueous Tea Extract (ATE) at a concentration of 1, 2 and 4% was when given as a sole source of drinking solution for 2 weeks resulted in inhibition of chromosomal aberrations, micronuclei and SCE's induced by BaP or CP (Table 3 and 4). The anticytotoxic potential of ATE was also evident as the status of mitotic index, which declined in BaP/CP alone treated group was found to be increased. Similarly, the oral dosage of 40 and 80 and 160 mg/kg.b.w of BTP for five consecutive days prior to BaP/CP injection also lead to more significant inhibition in chromosomal aberrations, micronuclei induction and SCE's. Different kinds of chromosomal damages including gaps, breaks, exchanges and multiple aberrations induced by BaP or CP were found to be inhibited. Furthermore, BaP and CP induced cytotoxicity was also found to be protected by different doses of BTP. Hence the study reveals that administration of black tea has potential in suppressing chromosomal aberrations, micronuclei induction, SCE's and cytotoxicity produced by mutagens *in vivo.* (Shukla and Taneja, 2002).

Table 3.
Antimutagenic Effect of ATE and BTP on BaP Induced Chromosomal Aberrations in Swiss Albino Mice Bone Marrow Cells.

Treatment Groups	Mitotic Index (Mean ± S.E.)	% Chromosomal aberrations with (Mean ± S.E.)			Multiple damage	Incidence of aberrant cells(%) (Mean ± S.E.)	Suppression (%)
		Breaks	Fragments	Exchanges			
Untreated	4.67 ± 0.47	0.77 ± 0.17	0.71 ± 0.020	0.02 ± 0.01	0.97 ± 0.26	2.47 ± 0.61	-
BaP	3.01 ± 0.38#	3.77 ± 0.89	4.53 ± 1.07	0.98 ± 0.12	2.50 ± 1.01	11.78 ±1.82#	-
1% ATE + BaP	3.69 ± 0.36	3.53 ± 0.63	4.22 ± 0.96	0.81 ± 0.19	2.16 ± 1.07	9.51 ± 1.1 7	19.2
2% ATE + BaP	4.01 ± 0.37*	2.94 ± 0.59	4.10 ± 0.89	0.65 ± 0.18	2.02 ± 0.89	8.52 ± 1.03	27.6
4% ATE + BaP	4.36 ± 0.39*	2.19 ± 0.48	2.17 ± 0.67	0.51 ± 0.10	1.86 ± 0.78	6.10 ± 0.81*	48.2
BTP (40) + BaP	3.89 ± 0.38#	2.28 ± 0.39	3.13 ± 0.67	0.65 ± 0.09	1.76 ± 0.61	7.93 ± 0.92	32.7
BTP (80) + BaP	4.09 ± 0.36	2.23 ± 0.63	2.72 ± 0.46	0.37 ± 0.09	1.26 ± 0.57	6.90 ± 0.80*	41.4
BTP (160) + BaP	4.58 ± 0.37*	1.64 ± 0.19	2.10 ± 0.59	0.22 ± 0.09	1.02 ± 0.29	4.43 ± 0.61*	62.4

Significant difference from Gr. I, $p<0.05$

* Significant difference from Gr. II, $p< 0.05$

III. Antimutagenic potential of black tea and their constituents in mammalian germ cells using dominant lethal mutation assay:

Dominant lethal assay analyzes the meiotic mutagenic damage induced by genotoxicants, which results in the death of embryo. A positive result in the Dominant lethal test (DLT) provides evidence for damage transmitted via the gametes. DLT is widely used to assess mutagenic potential of chemicals in whole animals and to detect agents, which produce chromosomal aberrations in sperms and thereby affect the viability of progeny (Green *et al.,* 1987; Ashby & Clapp, 1995).

Clastogenicity induced by genotoxicants leading to non-disjunction in chromosomes in meiotic cycle resulting in chromosomal deficient embryo, which dies in utero, is the cause of dominant lethality (Green et al., 1987; Ashby & Clapp, 1995). However dietary agents have been found to inhibit the clastogenetic damage induced by many xenobiotics in germ cells (Ferguson, 1994; Waters *et al.,* 1998). The antimutagenic properties of tea and its polyphenols are well documented in mammalian somatic cell assays (Katiyar & Mukhtar, 1996; Kuroda & Hara, 1999). However, no study on the effect of tea on germ cell has been conducted.

The work carried out in our laboratory demonstrates the antimutagenic potential of ATE and BTP against BaP and CP induced dominant lethal mutations in male Swiss albino mice. (Shukla and Taneja, 2002) In different sets of experiments BaP and CP were injected through i.p. route at the dose of 100mg/kg/b.w and 60mg/kg.b.w respectively. Soon after BaP/CP injection the animals were mated with untreated virgin females for three weeks of mating intervals. The females were analysed for living and dead

Table 4.

Antimutagenic Effect of ATE and BTP on CP Induced Chromosomal Aberrations in Swiss albino Mice Bone Marrow Cells.

Treatment Groups	Mitotic Index (Mean ± S.E.)	% Chromosomal aberrations with (Mean ± S.E.)			Multiple damage	Incidence of aberrant cells(%) (Mean ± S.E.)	Suppre-ssion (%)
		Breaks	Fragments	Exchanges			
Untreated	4.67 ± 0.47	0.77 ± 0.17	0.71 ± 0.020	0.02 ± 0.01	0.97 ± 0.26	2.54 ± 0.66	-
CP	2.89 ± 0.38#	7.58 ± 0.89	8.63 ± 1.07	0.96 ± 0.12	3.76 ± 1.01	19.86 ± 2.02 #	-
1% ATE + CP	3. 19 ± 0.36	7.0 3 ± 0.63	7.51 ± 0.96	0.87 ± 0.19	2.16 ± 1.07	16.98 ± 1.57	14.5
2% ATE + CP	3.68 ± 0.37*	6.14 ± 0.59	6.51 ± 0.89	0.67 ± 0.10	2.02 ± 0.89	15.35 ± 1.17	22.7
4% ATE + CP	4. 01± 0.39*	5.68 ± 0.58	5.78 ± 0.67	0.51 ± 0.30	1.86 ± 0.78	12.10 ± 1.06*	38.6
BTP(40) + CP	3.86 ± 0.47	6.77 ± 0.17	5.71 ± 0.50	0.69 ± 0.01	1.97 ± 0.26	13.36 ± 1.42	24.4
BTP(80) + CP	4.18 ± 0.38	6.18 ± 0.89	4.51 ± 0.67	0.53 ± 0.32	1.66 ± 1.01	12.17± 1.27*	38.7
BTP(160) + CP	4.48 ± 0.36	4.53 ± 0.63	3.21 ± 0.96	0.38 ± 0.29	1.16 ± 1.07	9.55 ± 0.97*	51.9

Significant difference from Gr. I, $p<0.05$

*Significant difference from Gr. II, $p< 0.05$

implants. During three weeks of mating BaP/CP administration resulted in decrease in the number of living implants and increase in dead implants. However Pre-treatment of 1, 2 and 4% ATE as sole source of drinking solution for 2 weeks prior to BaP or CP injection resulted in dose dependent inhibition of dominant lethality (Table 5 and 6) . The numbers of living implants were found to be increased by ATE. The induction of post implantation by BaP/CP was found to be protected by ATE. Similarly, oral dosage of 40, 80 and 160 mg/kg.b.w of BTP for 5 consecutive days also lead to more significant inhibition of dominant lethal mutations induced by either by BaP or CP. The status of declination in the number of living implants by BaP/CP treatment was found to be protected by BTP. Furthermore significant inhibition of BaP/ CP induced post implantation losses was also notified by treatment of BTP. Hence the study reveals that black tea has a potential in inhibiting meiotic mutagenic damage induced by germ cell mutagens.

Mechanism of antigenotoxicity of tea:

The mechanisms proposed for antimutagenic effect of tea involves interaction between the reactive genotoxic species of the various promutagens and nucleophilic tea component(s) present in tea (Kuroda & Hara, 1999). Tea ingredients have property of mopping mutagenic reactive free radical intermediates generated by genotoxicants by various metabolic pathways (Johnson & Loo, 2000; Maliakal *et al.,* 2001). The second, mechanism, involves inhibition of the cytochrome P-450-dependent bioactivation of the promutagens (Wang *et al.,* 1988). Black tea exhibit potential to inhibit *invitro* cytochrome P-450-dependent metabolic activation of mutagens and display antioxidative activity (Chen & Ho, 1994; Grinberg *et al.,* 1997). Tea ingredients were found to inhibit aryl hydrocarbon hydroxylase (AHH) activity in liver microsomes (Wang *et al.,* 1988). The inhibition of cytochrome P-450 activity may be due, at least partly, to impairment of the

Table 5.

Antimutagenic Effect of ATE and BTP on BaP Induced Dominant Lethal Mutations in Swiss Albino Mice.

Treatment Groups	Mating Weeks	Living Implants/female (Mean ±SE)	Dead implants/female (Mean ±SE)	DLM rate (%)	Suppression (%)
Untreated	1	7.86± 0.32	0.32 + 0.06	-	-
	2	7.84± 0.28	0.30 + 0.09	-	-
	3	7.85±0.30	0.28 + 0.09	-	-
BaP	**1**	**5.45±0.36#**	**2.87 + 0.78#**	**31.7**	**-**
	2	6.17±0.28#	1.89 + 0.62#	21.2	-
	3	6.51±0.30	0.92 + 0.23#	18.7	-
1% ATE + BaP	1	5.94±0.38	2.16 + 0.72	24.4	21.1
	2	6.46 ±0.28	1.50 + 0.48	17.5	18.7
	3	6.96 ±0.36	0.66 + 0.28	11.3	36.4
2% ATE + BaP	1	6.30±0.28	1.84 + 0.60	19.8	37.6
	2	6.71±0.36	1.09 + 0.42	14.3	32.8
	3	7.13±0.28*	0.52 + 0.20*	9.1	51.3
4% ATE + BaP	1	6.84±0.35	1.26 + 0.38*	12.9	59.3
	2	7.04±0.36	0.89 + 0.17*	10.1	52.2
	3	7.37 ±0.28	0.41 + 0.09*	6.1	68
BTP (40) + BaP	1	6.15±0.28*	1.77 + 0.72	22.3	29.6
	2	6.61±0.28	1.10+ 0.48	15.6	30.9
	3	7.04±0.30*	0.70 + 0.18*	10.3	47.4
BTP (80) + BaP	1	6.55±0.28	1.55+ 0.60	16.6	45.8
	2	7.03± 0.30*	0.85 + 0.42	10.4	46.9
	3	7.27±0.30	0.60 + 0.15*	7.3	62.7
BTP (160) + BaP	1	6.86±0.28*	1.10 + 0.58	10.3	66.2
	2	7.10±0.35*	0.70 + 0.21*	9.4	58.4
	3	7.38 ±0.35	0.45 + 0.09*	5.5	72

Significant difference from Gr. I. $p<0.05$

* Significant difference from Gr. II, $p< 0.05$

electron flow from NADPH to the cytochrome (Wang *et al.,* 1988). Tea catechins have been shown to inhibit cytochrome P450 mediated activation of carcinogens including PAH's, AFB1 and nitrosoamines (Wang *et al.,* 1988; Yang *et al.,* 2000a). EGCG, the major catechin present in both varieties of tea has been found to modulate the activity of cytochrome P450 IA1, IA2, IA3 and NADPH reductase thereby reducing conversion of promutagens to ultimate mutagens (Matsuzki & Hara, 1986; Wang *et al.,* 1988). Both phase I and phase II enzymes were induced in rats, using black or green tea infusions (Katiyar & Mukhtar, 1996; Kuroda & Hara, 1999). Besides this tea

Table 6.

Antimutagenic Effect of ATE and BTP on CP Induced Dominant Lethal Mutations in Swiss Albino Mice.

Treatment Groups	Mating Weeks	Living Implants/female (Mean ±SE)	Dead implants/female (Mean ±SE)	DLM rate (%)	Suppression (%)
Untreated	1	7.86±0.28	0.32 + 0.06	-	-
	2	7. 84±0.36	0.30 + 0.09	-	-
	3	7.85 ±0.35	0.28 + 0.09	-	-
CP	**1**	**5.69±0.28#**	**2.03 + 0.78#**	**27.5**	**-**
	2	4.98±0.36#	3.04 + 0.62#	36.4	-
	3	6.32±0.28	1.43 + 0.23#	19.4	-
1% ATE + CP	1	5.97±0.28	1.77 + 0.72	24	12.6
	2	5.48±0.28	2.49 + 0.48	30.1	17.2
	3	6.75±0.30	1.04 + 0.28*	13.9	28.6
2% ATE + CP	1	6.16±0.28	1.55+ 0.60	21.6	21.2
	2	5.77± 0.30	2.22 + 0.42	26.4	27.6
	3	7.00±0.30	0.79 + 0.20*	10.8	44.2
4% ATE + CP	1	6.46±0.28	1.25 + 0.38	17.7	35.6
	2	6.06±0.35*	1.89 + 0.41*	22.6	37.8
	3	7.08 ± 0.35	0.68 + 0.09*	9.8	49.6
BTP (40) + CP	1	6.09±0.30	1.51 + 0.72	22.4	18.2
	2	5.84±0.30	2.34 + 0.48	25.4	21.6
	3	6.80±0.36	0.87 + 0.28*	13.3	31.4
BTP (80) + CP	1	6.38±0.36	1.24 + 0.60	18.8	31.6
	2	6.02± 0.36	1.90 + 0.42	23.1	36.4
	3	6.03±0.28*	0.54 + 0.20*	10.0	48.2
BTP (160) + CP	1	6.53±0.28	1.12 + 0.58	16.9	38.2
	2	6.20±0.30*	1.71 + 0.21*	20.8	42.6
	3	7.19±0.36	0.40 + 0.09*	8.4	56.7

Significant difference from Gr. I. $p<0.05$

* Significant difference from Gr. II, $p< 0.05$

catechins EGCG, EC, EGC and ECG have also been found to enhance the phase II enzymatic pathways resulting in detoxification of carcinogens (Kuroda & Hara, 1999; Maliakal et al, 2001). For theaflavins, polyphenolic ingredients of black tea, it has been shown that inhibition of DNA single-strand cleavage and mutagenicity induced by hydrogen peroxide in *Salmonella tyhphimurium* is due to *in vitro* antioxidant activity (Shiraki *et al.,* 1994). It has also been found to possess antimutagenic effects towards peroxy radical damage (Shiraki *et al.,* 1994).Catechins are competitive inhibitors of the NADPH-cytochrome c reductase enzyme (Katiyar and Mukhtar, 1996; Hasaniya et al, 1997).

Induction of antioxidant enzymes against oxidative stress plays an important role in inhibiting clastogenicity of genotoxicants (Liu *et al.,* 1998). Tea polyphenols are strong scavengers against superoxide, hydrogen peroxide, hydroxy radicals and nitric oxide produced by various chemicals (Katiyar & Mukhtar, 1997b). Black tea has been identified to act as powerful chemopreventor of reactive oxygen and nitrogen species (Sarkar & Bhaduri, 2001). EGCG also exhibited protective effect to the oxidative damage to cellular DNA (Johnson & Loo, 2000). EGCG is known to interact with DNA polymerase III and influence excision repair system favoring repair of genetic damage (Kada *et al.,* 1985).

Conclusion:

The levels at which tea has been consumed worldwide, aroused interest in the possibility of its use in cancer chemoprevention and other related genetic disorders. The possible beneficial health effects on tea consumption have been suggested by epidemiological studies and supported by laboratory research. Considerable work has been carried out on both varieties of tea as infusions and their principal constituents. The over view of the findings on antigenotoxicity indicate that both varieties of tea have significant antimutagenic and anticlastogenic properties. Green tea was found to have no mutational toxicity but was able to inhibit mutations at concentration levels equivalent to daily human consumption. In case of black tea reports on thearubigins shows that it has significant antimutagenic and anticlastogenic effects as in the case of theaflavins. The knowledge gained at tissue levels and biological activities of tea polyphenols would be useful in planning future epidemiological studies and human cancer prevention trials.Therefore it may be concluded that both varieties of tea has a potential to prevent cancer and other genetic disorders, but more in-depth studies are needed to study its mechanism of action.

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