

Black Tea (*Camellia sinensis*) Extract Induced Prenatal and Postnatal Toxicity in Experimental Albino rats

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ABSTRACT

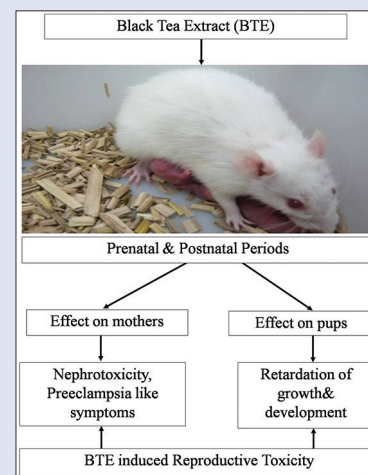
Background: Tea (*Camellia sinensis*) being the most widely drank beverage and despite having numerous beneficial role toward health and disease, its safety evaluation during pregnancy and prenatal, postnatal developmental period need to be monitored. **Objective:** This study was to evaluate the toxicity of black tea extract (BTE) in experimental pregnant rats and on their pups during prenatal and postnatal developmental periods. **Materials and Methods:** Pregnant female (120 ± 10 g) Wister albino rats were chosen for this study. Group 1 was control group where pregnant female rats were treated with saline. Group 2 and Group 3 were pregnant female rats treated with 50 mg and 100 mg BTE/kg/day, respectively, throughout prenatal and postnatal periods. All three groups of rats were provided food and drinking water *ad libitum*. Animals were examined through their urinary and serum parameters, histopathological studies, and biomorphometric studies in pups. All data were expressed as mean ± standard deviation with significance between the controls and the treated groups ($n = 6$). Collected data were subjected to the analysis of variance and Tukey test; $P < 0.05$ was considered as statistically significant. **Results:** BTE produced significant alterations in urinary calcium, creatinine, and urea during prenatal period; exhibited proteinuria, ketonuria, and histology showed nephrotoxicity during postnatal period, and BTE also showed a significant increase in serum proinflammatory cytokines and decreased anti-inflammatory cytokines level compared to control group. BTE caused significant changes in biomorphometric parameters in the pups as compared with pups of control mothers. **Conclusion:** This study confirmed the BTE-induced toxicity in pregnant rats and their pups.

Key words: Black tea extract, nephrotoxicity, preeclampsia, prenatal-postnatal development, reproductive toxicity

SUMMARY

- Black tea (*Camellia sinensis*) is the most widely drank beverage. This study was to evaluate the toxicity BTE in experimental pregnant rats and on their pups during prenatal and postnatal developmental periods. Animals were

examined through their urinary and serum parameters, histopathological studies, and biomorphometric studies in pups. BTE-induced toxicity in pregnant rats and their pups.



Abbreviations used: BTE: Black tea extract, IL-1 α : Interleukin 1 alpha, IL-1 β : Interleukin 1 beta, IL-6: Interleukin 6, IL-10: Interleukin 10, TNF- α : Tumor necrosis factor alpha.

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INTRODUCTION

Tea (*Camellia sinensis*) is native to the southern provinces of China and parts of India, Laos, Thailand, Vietnam, and Myanmar.^[1] However, tea is presently cultivated in over thirty countries around the world, and the tea beverage is second only to water in terms of worldwide consumption.^[2,3] Based on the fermentation and oxidation of the polyphenols in the tea leaves during production, tea has been classified into three types: green tea, black tea, and oolong tea.^[4] Green tea is referred to as nonfermented tea, in which the oxidation of the tea polyphenols called catechins is prevented, and thus, most of the catechins are preserved during its processing. Black tea is fully fermented, and oolong tea is semi-fermented tea leaves. In these teas, aerobic oxidation of the tea leaf polyphenolics is allowed to occur, and the catechins are enzymatically catalysed to form theaflavins and thearubigins.^[2,5] For black tea, the reaction is promoted to maximize the oxidation (fermentation), but for oolong tea, it is stopped usually half-way before it is complete. There are two main types of black

tea, crushing, tearing, and curling black tea and orthodox (rolling) black tea, produced through various stages including withering, rolling, drying, and grading.^[6] Unlike green and oolong teas which are not graded at the final stage of processing, black tea is graded based on the particle sizes to form various grades such as orange pekoe (OP), pekoe (P), broken OP, broken OP fanning (BOPF), fanning (F), and dust.^[1] The composition of tea varies with the climate, season, agricultural practices, varieties of

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plant, age of leaf, types of leaf, and processing methods.^[1,7,8] The catechin content is up to 30% of the dry weight, whereas the content of caffeine is up to 5% of the dry weight.^[2,9] There are four major catechins in order of abundance they are epigallocatechin gallate (EGCG), EGC, epicatechin gallate (ECG), and epicatechin (EC).^[9]

Several therapeutic activity is reported with tea (black, green, and oolong) extracts including anticancer,^[10] anti-atherosclerosis, and as cardioprotective agents.^[11] Black tea extract (BTE) is associated antiarthritic activity by altering the expression inflammatory cytokines, reducing urinary hydroxyproline, glucosamine, and histology showed that it restored the structural architecture of bones.^[12] Several active bioactive constituents are associated with black teas which are theaflavins, EGCG, EGC, ECG, and EC. Theaflavin, one of the major constituent of black tea, is said to be associated with antitumorogenic activity by inhibiting proteasome activity of tumor.^[13,14] Anticancer activity is also exhibited by catechin and EC another bioactive ingredient.^[15] Catechins and theaflavin are also associated antioxidant and free radical scavenging activity, antimicrobial, apoptogenic activity, anti-ischemic activity, and anti-inflammatory activity.^[16,17]

Despite the increasing demand for tea/active constituents, few studies have reported their safety. Tea being the most widely drunk beverage, and despite having numerous beneficial role toward health and disease, its safety evaluation during pregnancy and prenatal, postnatal developmental period needs to be monitored. Very few studies have been reported regarding tea extract consumption and its effect during pregnancy in animal models.^[18] Pu-erh black tea a highly fermented version of black tea is associated with the development of fetal toxicity at a high concentration.^[5,19] In the present study, an attempt has been made to assess the effect of varying doses of BTE in pregnant and lactating rat model and to evaluate its actions on their pups through different biochemical, serum parameters, histology, and biomorphometric analysis.

MATERIALS AND METHODS

Chemicals

Calcium kit (LABKIT, Spain), Creatinine kit (LABKIT, Spain), Di sodium hydrogen phosphate (SRL, India), Eosin (Sigma, USA), Formaldehyde solution 37%–41% w/v (Merck, India), Glacial Acetic Acid, Hematoxylin (Merck, Germany), interleukin 1 alpha (IL-1 α) rat ELISA kit, interleukin 1 beta (IL-1 β) rat ELISA kit, interleukin 6 (IL-6) rat ELISA kit, IL-10 rat ELISA kit (RayBiotech, USA), Magnesium kit (LABKIT, Spain), Methanol (Merck, India), Multistrix SG Reagent Strips for Urinalysis (Siemens, India), Paraffin wax 56–58°C (Merck, India), Picric Acid (Merck, India), Salt mixture H. M. W.(SRL, India), Sodium chloride (SRL, India), Sodium di hydrogen phosphate (SRL, India), tumor necrosis factor alpha (TNF- α) rat ELISA kit (RayBiotech, USA), Urea kit (BEACON), and Xylene (Merck, India) were used.

Animals

Male (150 \pm 10 g) and female (120 \pm 10 g) Wistar albino rats collected from the enlisted supplier of CPCSEA, India. They were housed in polypropylene cages (421 mm \times 290 mm \times 190 mm) at control temperature (25 \pm 2°), with light conditions (12 h light and dark cycle) and relative humidity (65% \pm 5%). The animals were provided with pellet diet (Ashirwad Industries, Chandigarh, India), green vegetables, gram, and water *ad libitum*. All animals for this experiment were kept in CPCSEA approved animal house of Maulana Azad College, Kolkata, West Bengal, India (vide F. No. – 25/250/2012-AWD, dated 26.2.2014), and experiments described in this study were done by following the

guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animal (CPCSEA), Government of India.

Collection of black tea

Fresh black tea (C. T. C., Assam) was purchased from M/S. Subodh Brothers Pvt. Ltd., Kolkata - 700 012, India.

Preparation of black tea extract and treatment schedule

Tea leaves were added to boiling water and kept covered for 5 min, filtered, and cooled down to 40°C.^[12] This was expressed as BTE. BTE was expressed in terms of dry weight. Freshly prepared BTE was administered orally to the pregnant mother throughout their prenatal (21 days) and postnatal periods of time (21 days).

Experimental design

The pregnant rats were selected by pairing a proestrous female overnight with two male rats of proven fertility and determining the vaginal sperm count on the following day (9:00–9:30 a. m.) using an improved Neubauer hemocytometer. Rats with vaginal sperm counts $>45 \times 10^6$ /ml were selected and considered as at day 0 of pregnancy. Three groups of animals were selected for this study. Group 1 was the control group where pregnant female rats were treated with saline. Group 2 was pregnant female rats treated with BTE (50 mg BTE/kg body weight/day, p.o.), and group 3 was pregnant female rats treated with BTE (100 mg BTE/kg body weight/day, p.o.). Both the doses of BTE were administered in the pregnant mother throughout their prenatal (21 days) and postnatal periods of time (21 days). All three groups of rats were provided with pellet diet, green vegetables, gram, and drinking water *ad libitum*.

Urine strip analysis

Qualitative test of urinary glucose, bilirubin, ketone (acetoacetic acid), specific gravity, blood, pH, protein, and urobilinogen was assessed using reagent strips for urinalysis (Siemens, India). First fresh urine was collected in a clean, dry container and was mixed well. The urine was applied to different color blocks on strips and was matched with the chart present on the bottle label at the time specified and observations were recorded.^[20] Urine strip analysis was done from urine of mother of three different groups at the end of lactation period following manufacturer's instructions.

Urinary marker analysis

Urine was obtained (after 12 h) from all three groups of animals during prenatal period of pregnant rats on day 0, day 7, day 14, and day 20. Quantity of urinary markers such as calcium, magnesium, urea, and creatinine was obtained by performing Arsenezo III, Calmagite-EGTA, Jaffe, and UV GLDH biochemical assays, respectively, following manufacturer's instructions of biochemical kits (LABKIT, Spain).

Histopathological examination

For morphological observation by light microscopy, the kidneys from mothers of all experimental groups were collected at the end of postnatal period. The tissues were fixed in 10% neutral buffered formalin for 24 h. Tissues were then dehydrated in graded (50%–100%) ethanol followed by clearing in xylene. Paraffin (56°C–58°C) embedding was done at 58°C \pm 1°C for 4 h, followed by paraffin block preparation. Tissue sections of 5 μ m were cut using a rotary microtome (Weswox model MT-1090, India). Xylene was used to deparaffinize the paraffin sections, then counterstained with hematoxylin-eosin, and was mounted in DPX with a coverslip. Histological changes were observed with a bright field

microscope (Motic, Germany), and photographs were captured using Motic Images Plus 2.0 software (Motic, Hong Kong).

Measurement of cytokines

Blood was collected from retro-orbital plexus from mothers of three different groups on day 0, day 20, and day 42. The level of cytokines such as IL-1 α , IL-1 β , IL-6, IL-10, and TNF- α from serum were analysed by enzyme-linked immunosorbent assay following the manufacturer's instruction of ELISA kits (RayBiotech, USA).^[21]

Biomorphometric analysis of pups

Biomorphometric parameters such as body weight, cranial length, cranial diameter, neck diameter, tail length, and craniosacral length was measured using digital balance and caliper on day 0, day 10, and day 21 from pups of three different groups of rats during lactation period. Male-female ratio of pups, day of ear opening, eye opening, and appearance of fine fur was also noted during lactation period from all three groups of animals.^[22] Comparative of whole length of pups of three different groups were taken on day 0, day 10, and day 21 of lactation.

Statistical analysis

The data generated on various parameters were subjected to statistical analysis for reporting group means and standard deviation (mean \pm standard deviation) with significance between the controls and the treated groups ($n = 6$ in all experiments, except the biomorphometric analysis of pup where $n = 18$). Collected data were subjected to one-way analysis of variance and Tukey test considering $P < 0.05$ was considered as statistically significant. SPSS 17.0 software (IBM Corporation, United States) was used for statistical analysis.

RESULTS

Effect of black tea extract on urine strip analysis

BTE (50 mg and 100 mg/kg body weight/day, p.o.) increased the level of protein, ketone, and bilirubin in urine as compared with control group. The urine pH and specific gravity were within the normal range [Figure 1].

Effect of black tea extract on urinary markers

BTE (50 mg/kg body weight/day, p.o.)-treated rats showed no significant ($P < 0.05$) changes in urinary Ca²⁺, magnesium, creatinine,

and urea levels on day 0, day 7, day 14, and day 20 as compared with control group. BTE (100 mg/kg body weight/day, p.o.)-treated rats showed significantly increased ($P < 0.05$) urinary Ca²⁺ level on day 20; significantly decreased ($P < 0.05$) creatinine level found on day 7, 14, and 20, whereas the urea level was found to be decreased on day 14 and 20 as compared with control group [Figure 2].

Tukey test showed significant change in mean differences ($|q|$) between Gr. 1 and G.3 in urinary Ca²⁺ level ($|q|=0.026, P = 0.037$) on day 20; in urinary creatinine level on day 7 ($|q|=0.950, P = 0.001$), on day 14 ($|q|=0.989, P = 0.016$), and on day 20 ($|q|=1.072, P < 0.001$); and in urinary urea level on day 14 ($|q|=0.779, P = 0.022$) and day 20 ($|q|=0.479, P = 0.034$). Significant mean difference between Gr. 2 and Gr. 3 was only found in urinary creatinine level on day 20 ($|q|=0.500, P = 0.044$).

Effect of black tea extract on kidney histology

BTE (50 mg/kg body weight/day, p.o.)-treated rat kidney showed decreased glomerular space as compared with control group. In BTE (100 mg/kg body weight/day, p.o.)-treated rat kidney, vacuolization, glomerular necrosis, and disintegration were observed as compared with control rat kidney [Figure 3].

Effect of black tea extract on serum cytokines level

BTE (50 mg/kg body weight/day, p.o.)-treated rats showed TNF- α get increased significantly ($P < 0.05$) and the level of IL-6, IL-10 decreased significantly ($P < 0.05$) on day 20, whereas IL-10 decreased significantly ($P < 0.05$) on day 42 as compared with control group. BTE (100 mg/kg body weight/day, p.o.)-treated rats showed that IL-1 α , IL-1 β , and TNF- α increased significantly ($P < 0.05$) and IL-6 and IL-10 get decreased significantly ($P < 0.05$) on day 20, whereas TNF- α was increased and IL-10 decreased significantly ($P < 0.05$) on day 42 as compared with control group [Figure 4].

Tukey test showed significant change in mean differences ($|q|$) between Gr. 1 and G.2 in the level of TNF- α ($|q|=0.250, P < 0.01$), IL-6 ($|q|=0.327, P < 0.01$), and IL-10 ($|q|=0.742, P < 0.01$) on day 20 and in the level of IL-10 ($|q|=0.639, P < 0.01$) on day 42. Significant differences were found between Gr. 1 and G.3 in the level of IL-1 α ($|q|=0.277, P < 0.01$), IL-1 β ($|q|=0.829, P < 0.01$), TNF- α ($|q|=0.335, P < 0.01$), IL-6 ($|q|=0.402, P < 0.01$), and IL-10 ($|q|=0.817, P < 0.01$) on day 20 and in the level of TNF- α ($|q|=0.196, P < 0.01$) and IL-10 ($|q|=0.985, P < 0.01$) on day 42. Significant mean difference between Gr. 2 and Gr. 3 was found in the level of IL-1 α ($|q|=0.219, P < 0.01$), IL-1 β ($|q|=0.86, P < 0.01$) and in the level of TNF- α ($|q|=0.14, P = 0.041$) and IL-10 ($|q|=0.346, P < 0.01$) on day 42.

Effect of black tea extract on biomorphometric parameters

Pups from BTE (50 mg/kg body weight/day, p.o.)-treated mothers showed no significant change ($P < 0.05$) in body weight, cranial length, cranial diameter, tail length, neck width, and craniosacral length on day 0; significantly decreased ($P < 0.05$) body weight, tail length, and craniosacral length on day 10, whereas body weight, cranial length, cranial diameter, neck width, tail length, and craniosacral length significantly decreased ($P < 0.05$) on day 21 during lactation period compared to pups of control rats. Pups of BTE (100 mg/kg body weight/day, p.o.)-treated mothers showed significantly decreased ($P < 0.05$) in body weight, cranial length, neck width, and craniosacral length on day 0; significantly decreased ($P < 0.05$) body weight, cranial length, cranial diameter, tail length, neck width, and craniosacral length on day 10 and day 21 during lactation period compared to pups of control rats [Figure 5 and Table 1].

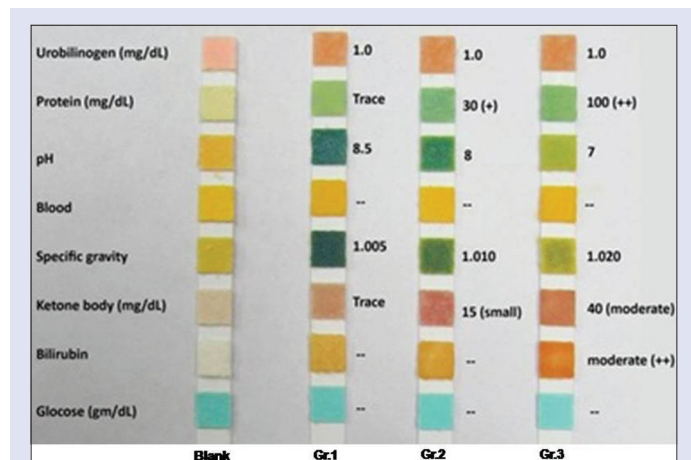


Figure 1: Urine strip analysis from urine of mothers at the end of lactation (on day 42). Gr. 1: control group, Gr. 2: pregnant female rats treated with black tea extract (50 mg black tea extract/kg body weight/day, p.o.), Gr. 3: pregnant female rats treated with black tea extract (100 mg black tea extract/kg body weight/day, p.o.)

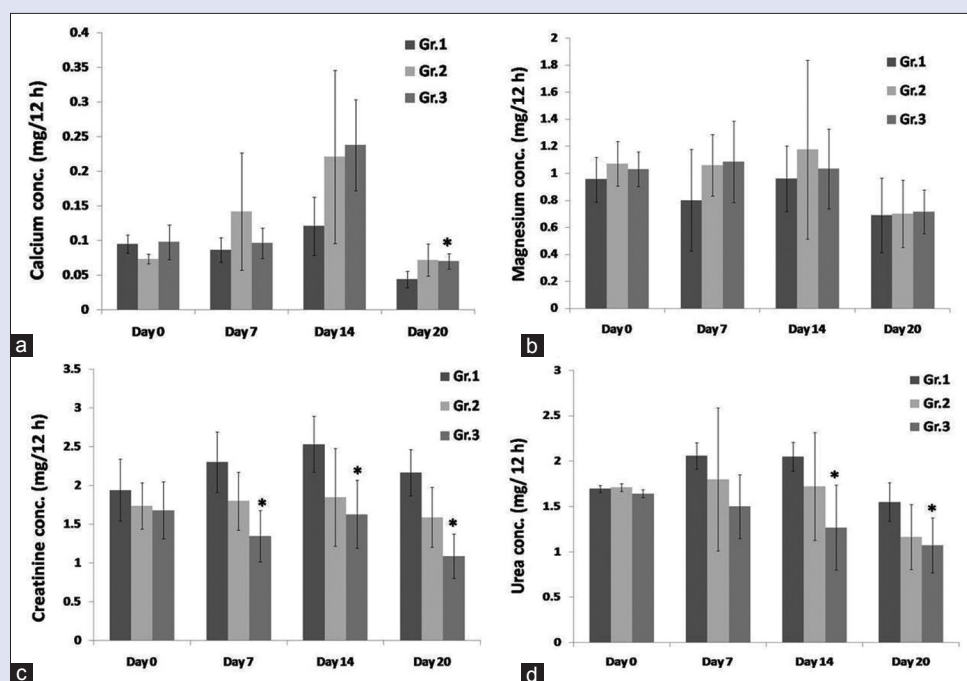


Figure 2: Effect of urinary markers after treatment with black tea extract in pregnant Wistar rat model. (a) Concentration of calcium, (b) Concentration of magnesium, (c) Concentration of creatinine, and (d) Concentration of urea were expressed mg/12 h. Data represent the mean \pm standard deviation ($n = 6$). * $P < 0.05$ when compared to control group 1 animals. Gr. 1: control group, Gr. 2: pregnant female rats treated with black tea extract (50 mg black tea extract/kg body weight/day, p.o.), Gr. 3: pregnant female rats treated with black tea extract (100 mg black tea extract/kg body weight/day, p.o.)

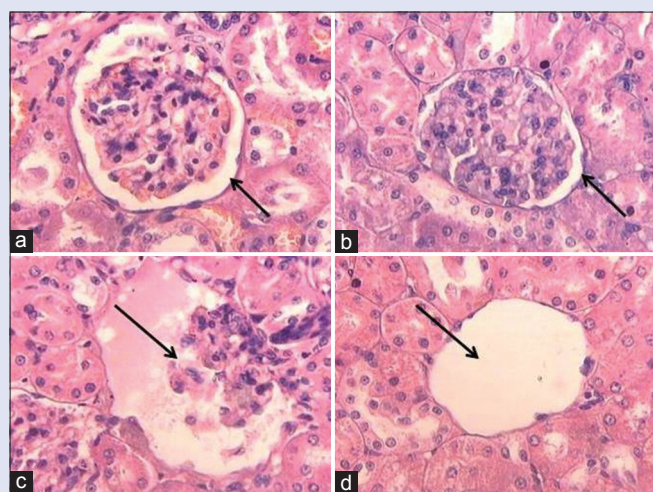


Figure 3: Microscopic study of sagittal sections of the kidney ($\times 400$). Histological sections of kidney were stained with haematoxylin and eosin. (a) In Group 1 Control rats arrow shows proper capsular space, (b) In Group 2 pregnant female rats treated with black tea extract (50 mg black tea extract/kg body weight/day, p.o.) capsular space decreases significantly, (c and d) In Group 3 pregnant female rats treated with black tea extract (100 mg black tea extract/kg body weight/day, p.o.), arrow indicating degradation of glomerulus and no glomerulus in Bowman's capsule

Table 1: Effect of black tea extract on physical parameters by biomorphometric analysis of pups

Physical parameters	Group 1 pups	Group 2 pups	Group 3 pups
Physical parameters of day-0 pups			
Body weight (g)	5.39 \pm 0.34	5.15 \pm 0.39	4.78 \pm 0.32*
Cranial length (mm)	15.37 \pm 0.28	15.35 \pm 0.32	14.83 \pm 0.24*
Cranial diameter (mm)	10.06 \pm 0.17	10.07 \pm 0.14	9.93 \pm 0.22
Tail length (mm)	16.02 \pm 0.55	15.88 \pm 0.42	15.76 \pm 0.49
Neck width (mm)	8.69 \pm 0.24	8.65 \pm 0.22	7.90 \pm 0.24*
Craniosacral length (mm)	48.54 \pm 0.95	47.36 \pm 0.96	46.96 \pm 0.82*
Physical parameters of day-10 pups			
Body weight (g)	13.02 \pm 0.42	12.36 \pm 0.28*	11.10 \pm 0.75*
Cranial length (mm)	22.99 \pm 0.38	22.55 \pm 0.42	20.82 \pm 0.41*
Cranial diameter (mm)	14.98 \pm 0.34	14.87 \pm 0.42	13.48 \pm 0.34*
Tail length (mm)	34.34 \pm 0.68	33.28 \pm 0.34*	32.44 \pm 0.57*
Neck width (mm)	13.35 \pm 0.31	13.23 \pm 0.36	12.30 \pm 0.41*
Craniosacral length (mm)	76.99 \pm 1.12	74.05 \pm 1.35*	69.94 \pm 1.36*
Physical parameters of day-21 pups			
Body weight (g)	29.37 \pm 2.12	24.77 \pm 1.78*	21.12 \pm 1.21*
Cranial length (mm)	34.11 \pm 0.85	32.79 \pm 0.78*	30.71 \pm 0.79*
Cranial diameter (mm)	18.82 \pm 0.78	18.64 \pm 0.76	15.96 \pm 0.84*
Tail length (mm)	59.98 \pm 1.31	55.77 \pm 1.23*	48.33 \pm 1.15*
Neck width (mm)	16.46 \pm 0.59	15.72 \pm 0.65*	14.84 \pm 0.54*
Craniosacral length (mm)	106.11 \pm 3.12	96.44 \pm 3.68*	81.41 \pm 2.92*

Data represent the mean \pm SD ($n=18$). * $P < 0.05$ when compared to control group 1 animals. Group 1: Control group; Group 2: Pups of female rats treated with BTE (50 mg BTE/kg body weight/day, p.o.); Group 3: Pups of female rats treated with BTE (100 mg BTE/kg body weight/day, p.o.). BTE: Black tea extract; SD: Standard deviation

DISCUSSION

Several researches had been done for the past few decades to established whether black tea consumption has a positive or negative impact on health.^[23] Tea is associated with several beneficial effects on health, and

so far, all of the reports that are available established tea as one of the most promising antioxidant, but the safety level should not be neglected

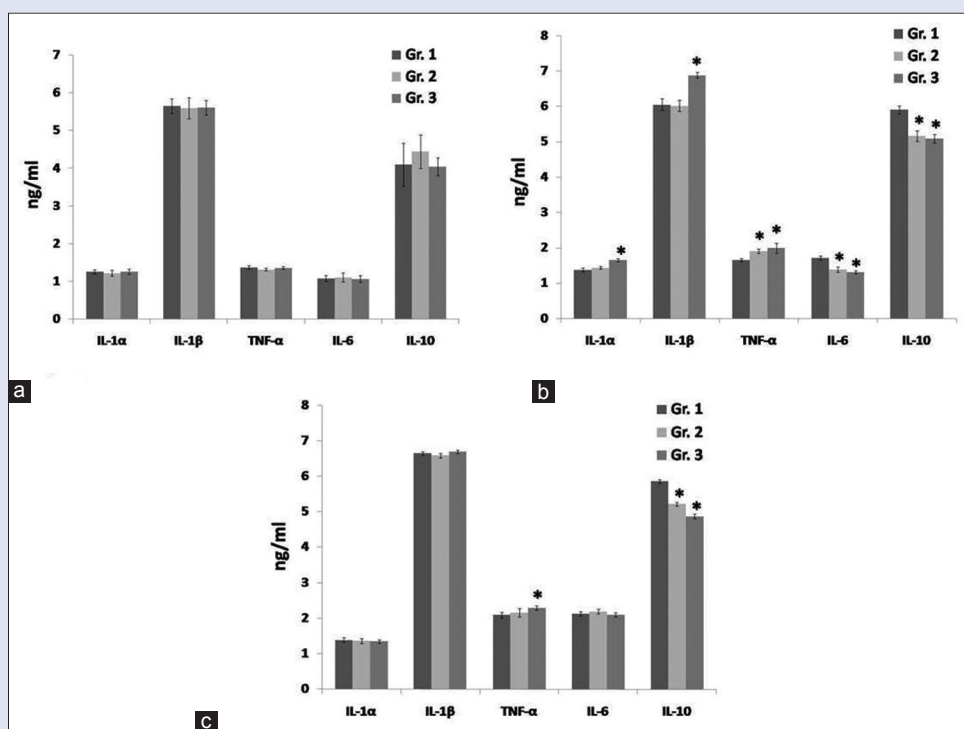


Figure 4: Effect on cytokines of serum after treatment with black tea extract in pregnant and lactating rat. (a) On day 0, (b) on day 20 and (c) on day 42. Data represent the mean \pm standard deviation ($n = 6$). * $P < 0.05$ when compared to control group 1 animals. Gr. 1: control group, Gr. 2: pregnant female rats treated with black tea extract (50 mg black tea extract/kg body weight/day, p.o.), Gr. 3: pregnant female rats treated with black tea extract (100 mg black tea extract/kg body weight/day, p.o.)

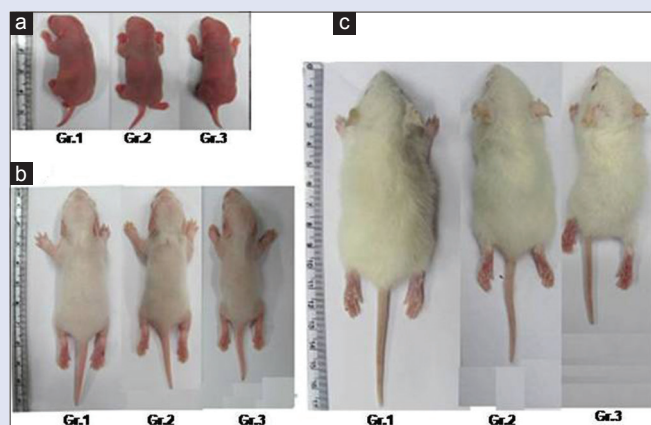


Figure 5: Comparative of length of pups of Group 1, Group 2, and Group 3 on different periods of lactation. Gr. 1: control group, Gr. 2: pregnant female rats treated with black tea extract (50 mg black tea extract/kg body weight/day, p.o.), Gr. 3: pregnant female rats treated with black tea extract (100 mg black tea extract/kg body weight/day, p.o.). (a) Pups of day 0, (b) Pups of day 10, (c) Pups of day 21

when consumed at a high level. The proposed study was an attempt to explore the toxicity of BTE in pregnant female rats and pups at high dose. This study showed, for the first time, that consumption of high dose of BTE is hazardous to pregnancy outcome. BTE induced nephrotoxicity such as decreased glomerular space, vacuolization, glomerular necrosis and disintegration, changes in urinary parameters such as calcium, creatinine, and urea in prenatal period and also showed proteinuria and ketonuria in postnatal period. BTE also increased the proinflammatory

cytokines (IL-1 β , TNF- α) and decreased the anti-inflammatory cytokine (IL-10) in mothers during prenatal period (on day 20).

Preeclampsia is a disease of late pregnancy characterized by increased maternal blood pressure, proteinuria, increase in proinflammatory cytokine, and decrease in anti-inflammatory cytokine.^[24,25] In the study, possibly a Preeclampsia like events may occur with BTE also as evident by the significant altered level of different proinflammatory cytokines (IL-1 β and TNF- α) and decreased level in anti-inflammatory cytokines (IL-10). Proteinuria was also evident in rats treated with BTE could support this view. A case-control study was carried out among nulliparous pregnant women in Quebec between January 2003 and March 2006.^[26] A total number of 92 women with preeclampsia and 245 controls were analyzed using a structured study questionnaire. Univariate analysis and multivariate regression were performed to examine the association between tea consumption and preeclampsia. The crude odd ratio and adjusted odd ratio for persistent tea consumption in preeclampsia and severe preeclampsia showed persistent tea drinking during pregnancy may be associated with an increased risk of preeclampsia.

Ratnasooriya and Fernando worked out on the effect of Sri Lankan black tea (high grown dust grade no. 1) on pregnancy and observed no significant changes in pregnancy outcome in terms of quantal pregnancy, number of uterine implants, number of viable implants, implantation index, preimplantation loss, postimplantation loss, gestation index, number of pups born, litter index, live birth index, viability index, length of the implants/fetus, gestation length, cranial length, cranial diameter, and tail length of pups during prenatal period and time taken to open eyes, eruption of incisors, and appearance of fur during postnatal period of rats.^[22] In our study, biomorphometric parameters such as cranial length, cranial diameter, neck width, cranosacral length, and tail length showed BTE retards the growth of pups, but no significant changes

were found in terms of time taken to open eyes, eruption of incisors, and appearance of fur. Chu *et al.* worked out detailed pharmacokinetic studies through compartmental model of green tea catechin (GTC) in rat maternal plasma, placenta, and fetus. It was found that catechin concentration in maternal plasma was 10 times higher in comparison with placenta and 50–100 times higher in fetus. This increased value of C_{max} in fetus may act as *in utero* antioxidant protection.^[27] Isbrucker *et al.* showed that the EGCG a principal component of green tea has a crucial role in the fetal development but no adverse effects on reproduction or fertility. The growth rate of offspring was reduced, and pup loss was slightly increased using the highest dose.^[18] In a study, pu-erh black tea a highly fermented version of black tea is associated with the development of fetal toxicity at a high concentration.^[28] Fan and Chan reported EGCG induces embryonic toxicity in mouse blastocysts through apoptosis.^[19] Although in another study there were no heat-sterilized GTCs-H related fetal malformations or developmental variations.^[29] These findings also supported the proposed findings. The animal results are also applicable to human. The high dose of black tea during pregnancy may be harmful to pregnancy condition. Further studies are warranted to establish the BTE-induced physiological changes during pregnancy and development of embryos.

CONCLUSION

High dose of BTE induced nephrotoxicity at the end of postnatal period and retarded the normal growth of pups. BTE also induced preeclampsia-like symptoms characterized by increased proinflammatory cytokines level, decreased anti-inflammatory cytokine level, proteinuria. Hence, the BTE produced toxicity in both mothers and pups in prenatal as well as postnatal periods

Transparency document

The transparency document associated with this article can be found in the online version.

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Conflicts of interest

There are no conflicts of interest.

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