Protective effects of *Corchorus olitorius* and *Butea monosperma* against Arsenic induced aberrant methylation and mitochondrial DNA damage in wistar rat model

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**A B S T R A C T**

Millions of people around the world are chronically exposed to Arsenic (As) through food and drinking water. Studies revealed that Arsenic is genotoxic and causes damage to DNA. In this study, we evaluated *Corchorus olitorius* and *Butea monosperma* for their alleviative properties against Arsenic induced genotoxicity in vivo using Wistar Rat model. Arsenic exposed rats were given *C. olitorius* leaf powder and *B. monosperma* flower powder as supplementation with normal food. Methylation status of p53 promoter was measured using Methylation Sensitive Restriction Endonuclease PCR (MSRE-PCR) assay and mitochondrial DNA (mtDNA) copy number as well as occurrence of a common deletion in mtDNA in liver and kidney tissue was determined through quantitative realtime PCR (qPCR). Arsenic exposed rats after supplementation showed relatively less severe effects of toxicity evident by significantly higher amount of (p<0.05) mtDNA copy number and reduced occurrence of deletion containing mtDNA as well as lower levels of methylation in p53 gene promoter. Histopathological analysis revealed less severe histopathological changes of liver and kidney and normal liver and kidney function parameters in supplemented rats. So, the protective properties of *B. monosperma* and *C. olitorius* against Arsenic toxicity is evident in molecular level.

**1. Introduction**

Arsenic (As) is a ubiquitous toxic metalloid present in the environment all over the world in organic and inorganic form [1]. It is one of the most epidemiologically important toxicant affecting millions of people around the world [2]. Beside severe skin pigmentation and keratosis, Arsenic causes respiratory disease, peripheral neuropathy, liver fibrosis, edema of legs, anemia and cancers. Chronic exposure to Arsenic especially through drinking water and food is associated with a number of different cancers (e.g., skin, bladder, liver and urinary tract) [3,4].

Arsenic is a proven carcinogen [5]. Though the exact mechanism is still not apparent it is understood that As is a potent genotoxic substance. It has the ability to directly affect the genetic material in numerous ways [6]. The genotoxic effects of Arsenic include induction of oxidative stress and DNA damage, inhibition of DNA repair enzymes, tumor promotion, cell proliferation, chromosomal aberrations (CA), signal transduction, [7] inhibition of DNA ligase [8], interference with tubulin polymerization in the mitotic spindle [9] and influencing telomere length through the stimulation of telomerase reverse transcriptase [10]. Also, exposure to heavy metal pollutants can influence neuro-developmental disorders such as Autism spectrum disorder (ASD) through various mechanisms [11]. Reports found association between the levels of heavy metals such as Arsenic, lead etc. in hair and severity of ASD symptoms [12]. In addition, prolonged inhalation of heavy metal polluted particulate matter (PM 2.5) can cause respiratory dysfunction and aggravated symptoms in respiratory viral infections such as influenza and COVID-19 [13]. Recent reports also suggest that Arsenic is an epi-mutagen [14]. That is Arsenic is capable of changing the methylation pattern of a single

**Abbreviations:** As, Arsenic; MtDNA, Mitochondrial DNA; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; ROS, Reactive oxygen species; MSRE-PCR, Methylation sensitive restriction enzyme digestion Polymerase Chain Reaction; qPCR, Quantitative Polymerase Chain Reaction; HG-AAS, Hydride Generation - Atomic Absorption Spectroscopy.

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gene to even whole genome [15]. Epigenetic changes are closely related with various diseases such as cancer [16], neurodegenerative diseases [17] and cardiovascular diseases [18].

Despite being a very concerning problem worldwide there is no dependable and safe treatment for arsenic toxicity [19]. Currently, Arsenic toxicity is treated with Sulhydryl containing chelating agents like 2,3-dimercaptopropane-1-sulfonate, Meso-2,3-dimercaptosuccinic acid etc. [20]. These are prescribed in combination with natural antioxidants like vitamin C and E. But most of these chelating agents have severe side effects and are toxic in nature [21]. At this context, medicinal plants attracted much attention lately; largely due to the antioxidative properties of many plant derivatives. The free radical scavenging property of plant derivatives can reduce the oxidative damage induced by Arsenic [22].

Corchorus olitorius otherwise known as ‘Tossa’ jute contains antioxidants such as carotenoids, flavonoids and vitamin C and antitumor agents such as phytol and monogalactosyl-diacylglycerol [23]. Studies also provided evidence of C. olitorius reducing oxidative damage in rat renal and hepatic tissue due to Arsenic [24].

Butea monosperma is another medicinal plant used in folk medicine alike C. olitorius. According to Ayurvedic medicine and modern studies every part of B. monosperma contains medicinal properties. These include anti-oxidative, anti-inflammatory, anti-diarrheal, bactericidal and fungicidal properties [25]. Studies also reported that B. monosperma flower contains butein, butin, butrin, isobutrin, coreospin etc., all of which have anti-oxidative attribute [26]. Therefore, evidences suggest that traditional herbal medicines such as B. monosperma and C. olitorius can potentially produce a protective effect against Arsenic and reduce its toxic effects, although this remains to be fully determined.

Drinking water is the most common route of exposure to Arsenic. But Arsenic exposure may also be through food, especially rice, via soil/toxic effects, although this remains to be fully determined. The average weight of the rats was 167.35gm and the rats were provided with sufficient laboratory rodent pellet diet and water. Then the rats were divided into four groups randomly placing five rats in each group. Group I, the control group received normal diet (pellet feed), Group II received normal diet mixed with Arsenic contaminated rice, Group III and IV was fed with Arsenic contaminated rice with C. olitorius leaf powder and B. monosperma flower powder mixed pellet feed supplementation in their diet respectively for 150 days for simulating sub-chronic exposure. All the experiments were carried out according to the institutional and national guidelines.

2. Collection of blood and tissue samples

The experimental animals were sacrificed on the 150th day after fasting them overnight. Blood was collected in K$_3$EDTA tubes for each rat and centrifuged at 1500xg for 15 min. After centrifugation blood plasma was collected in pre labeled microcentrifuge tubes and stored at −80 °C. Liver and kidney from sacrificed rats were removed carefully and after washing the organs with PBS a section was immersed in 10 % formalin solution for histology and the rest of the organs were immersed in absolute ethanol and preserved in an ultra-low temperature freezer (−86 °C) for molecular analysis and Arsenic measurement.

2.4. Biochemical assay

Liver and kidney function tests were performed by measuring liver enzymes (AST, ALT) and urea level in serum respectively. These tests were performed with commercially available kits from Human GmbH using CHEM-5v3 analyzer (Erba, Mannheim, Germany) following manufacturer’s instruction.

2.5. Histopathology

Preserved liver and kidney tissues were cut in longitudinal and transverse pieces and passed through ascending series of ethanol washes. Then the samples were cleared with toluene and embedded in paraffin. 4µM sections of the paraffin embedded tissues were fixed on a glass slide after staining with hematoxyline and eosin and observed under light microscope.

2.6. Arsenic measurement in tissue

The concentration of As in different organs (liver, kidney) was determined using FI-HG-AAS method. From each organ, 0.25gm sample was weighed and taken in beaker. The samples were digested with a mixture of HClO$_4$+HNO$_3$ solution (ratio 1:3 v/v) at 130 °C. After removal of HNO$_3$ by evaporation, the digested samples were diluted with deionized water up to 100 mL. The concentrations of As in digested samples were measured at 193.7 nm wave length and 10 mA current using Atomic Absorption Spectrophotometer equipped with As lamp. Vapor generation accessory (VGA) was used to produce hydride vapors
2.7. DNA extraction

DNA from cryopreserved rat liver and kidney tissues were extracted following standard phenol-chloroform method [34]. After ethanol precipitation DNA was resuspended in nuclease free water. DNA was quantified and checked for purity in a NanoDrop 2000 (Thermo Fisher Scientific, Waltham, Massachusetts, U.S.) and stored in −20 °C freezer.

2.8. Methylation of TP53 promoter region

Methylation Sensitive Restriction Endonuclease PCR (MSRE-PCR) technique was used to quantify the methylation level in the promoter region of the tumor suppressor gene TP53 following a previously described technique [35]. The extracted DNA from liver and kidney tissue of the rats from each group were digested with a methylation sensitive restriction endonuclease BstUI. BstUI enzyme recognizes a CpG site 5′-CGG-3′ within the 85bp basal promoter region of TP53. Methylation of the internal cytosine blocks cleavage. Thus the number of hypermethylation bands are showing varied intensity corresponding to the level of point methylation.

2.9. mtDNA copy number and deletion analysis

mtDNA copy number and frequency of deletion in rat liver and kidney tissue was carried out following a method reported by Nicklas et al. [36]. For the quantification of mtDNA copy number and frequency of deletion, separate reactions were set up with 2x AddProbe qPCR Mastermix (ADDBIO Inc. Korea), 7.5 μM of d-Loop specific primer (Fwd 5′- GGT TCT TAC TTC AGC ATC A-3′, Rev 5′- GAT TAG ACC GTG CAT CAT CGA GAT-3′) or Deletion specific primer (Fwd 5′- AAG GAC GAA CCT GAG CCC TAA TA-3′, Rev 5′- CGA AGT AGA TGA TCC GTA TGC TGT A-3′), 100 nM of each specific probe (D-loop- 56FAM- TTG GTT CAT /ZEN/ CGT CCA TCT GCT CCC CTT A-3IABkFQ, Deletion-56FAM- TCA CTT TAA /ZEN/ TCG CCA CAT CGA TAA CTG CGT T -3IABkFQ) and 50 ng of genomic DNA. The reactions were carried out in 25 μl volume. The PCR profile was 95 °C for 10 min followed by 45 cycles of denaturation at 95 °C for 15 s and hybridization and elongation at 60 °C for 30 s. Fluorescence was detected in the last step in a QuantStudio 3 system (Applied Biosystems, USA). Rat b-actin gene (Fwd 5′-GGG ATG TTT GCT CCA ACC AA-3′, Rev 5′- GGG CTT TTG ACT CAA GGA TTT AA-3′) was used as the internal control to calculate the relative copy number of mtDNA and relative frequency of deletion in mtDNA using the 2−ΔΔCt method.

2.10. Statistical analysis

Statistical analysis was performed with SPSS for Windows V.24. All data were analyzed by using one-way analysis of variance (ANOVA) followed by Duncan’s Multiple Range Test (DMART) with a p-value <0.05 considered to be statistically significant. All the values are expressed as mean ± SEM.

3. Results

3.1. Changes in morphology, food and water intake

All the activities were found normal in both control and arsenic-treated groups. No mortality was observed in any of the groups during the period of study. The albino rats of Group II developed ‘Chromodacryorrhea’ around their eyes after 80 days of Arsenic exposure. The food and water intake and body weight of the animals were monitored regularly although the study period. Change in body weight is used as an indicator for checking the animal health status. We observed significant (P < 0.05) changes in food and water intake after arsenic exposure. After treatment with C. olitorius and B. monosperma food and water intake both improved significantly (P < 0.05) (Table 1). The mean initial body weight of Group I (Normal diet for 150 days), Group-II (As cont. rice for 150 days), Group-III (As cont. rice plus 4% C. olitorius for 150 days), Group-IV (As cont. rice plus 4% B. monosperma for 150 days) were 166.1 ± 2.46 gm, 163.78 ± 3.08 gm, 160.56 ± 3.12 gm, 163.18 ± 3.66 respectively. After 150 days study, the mean final body weight was 205.7 ± 3.60 gm, 183.9 ± 2.61 gm, 197.14 ± 3.49 gm, 205.48 ± 3.47 gm respectively. The mean final body weight of Group-II significantly (P < 0.05) decreased compared to Group-I. On the other hand, the mean final body weight of Group-III and Group-IV significantly (p < 0.05) increased compared to Group-II.

Table 1

| Effect of C. olitorius and B. monosperma on daily food and water consumption of albino rats. Group II rats consumed significantly (p < 0.05) less food and water compared to control group. Whereas, in Group III and IV food and water consumption increased significantly (p < 0.05) after C. olitorius and B. monosperma treatment compared to arsenic exposed rats of group II.
| Groups | Food Intake (gm/rat/day) | Water Intake (ml/rat/day) |
|--------|-------------------------|--------------------------|
| Group-I (Control) | 17.17 ± 0.62 | 13.30 ± 0.20 |
| Group-II (As cont. rice) | 11.98 ± 0.35 | 7.23 ± 0.27 |
| Group-III (As + C. olitorius) | 17.99 ± 0.35 | 13.20 ± 0.46 |
| Group-IV (As + B. monosperma) | 21.08 ± 0.40 | 12.76 ± 0.32 |

Table 1: Effect of C. olitorius and B. monosperma on daily food and water consumption of albino rats. Group II rats consumed significantly (p < 0.05) less food and water compared to control group. Whereas, in Group III and IV food and water consumption increased significantly (p < 0.05) after C. olitorius and B. monosperma treatment compared to arsenic exposed rats of group II.

Here, values are expressed as MEAN ± SEM;
3.2. Arsenic deposition in rat liver and kidney

Arsenic accumulation in the rat organ samples were determined through FI-HG-AAS analysis. Fig. 2 is showing the mean ± SEM values of arsenic deposition in liver and kidney tissues of the three experimental groups exposed to arsenic. In control rats (Group I) mean Arsenic accumulation in liver and kidney was 0.44 ± 0.15 μg/gm and 0.46 ± 0.04 μg/gm respectively. After Arsenic exposure overall arsenic accumulation was significantly higher in kidney than liver in all groups. Arsenic contaminated rice fed rats (Group II) had 33.872 μg/gm accumulated arsenic in kidney and 12.97 μg/gm accumulated arsenic in liver on average. However, rats of group III (C. olitorius leaf powder) and IV (B. monosperma flower powder) which received supplementation with arsenic contaminated rice had significantly less arsenic accumulation in both liver (5.27 μg/gm in GIII and 5.44 μg/gm in GIV) and kidney (18.34 μg/gm in GIII and 21.89 μg/gm in GIV) tissue compared to group II (no supplementation).

To further investigate the extent of protective capabilities of Corchorus olitorius and Butea monosperma histopathological analysis of liver and kidney tissue was done. The tissue samples from group II (only arsenic contaminated rice) exhibited severe changes in the histostucture (Fig. 2b). We observed necrosis and degenerative changes of varied severity in hepatocytes and central veins including sinusoidal dilation, venous congestion, increased lymphatic cell population, free nuclei and fatty degeneration. Similar degenerative changes were also seen in kidney tissue samples (Fig. 2f). Moderate to severe glomerulonephritis, coagulative and liquefactive necrosis along with epithelial damage and loss of nuclei was seen. Minor alterations in histostucture with mild degenerative changes in liver and kidney was observed in groups III and IV which received Corchorus olitorius (Fig. 2c, g) and Butea monosperma (Fig. 2d, h) supplementation respectively. The organ weight to body weight ratio was calculated to determine hypertrophy of organs in study animals. We observed mild liver hypertrophy in group II animals (Arsenic exposed) when compared to control rats (Group I) where the liver weight to body weight ratio was 3.13 ± 0.03 and 3.82 ± 0.09 in Group I and Group II respectively. In treatment groups the liver weight to body weight ratio was 2.97 ± 0.07 (Group IV-As + C. olitorius) and 2.89 ± 0.09 (Group III-As + B. monosperma). Kidney weight to body weight ratio was 0.29 ± 0.01, 0.37 ± 0.01, 0.31 ± 0.01, 0.29 ± 0.01 respectively in Group I, II, III and IV. However, none of these changes were statistically significant (p>0.05).

The evidence of Arsenic induced damage was also clear from the biochemical assays. As the data on Table 2 represents the Arsenic exposed rats had abnormal liver function due to significantly increased level of liver enzymes (AST and ALT) compared to control group of rats. These enzymes work as markers for liver abnormalities. Arsenic exposed rats also suffered from kidney abnormalities having significantly higher levels of serum urea. However, all the markers were maintained nearly within the normal levels with C. olitorius leaf powder and B. monosperma flower powder supplementation showing significant difference from arsenic exposed group of rats. In our study we did not find any significant difference in serum urea level between the treatment groups.

3.3. Methylation in the p53 promoter region

Methylation status of a CpG site within the 85bp basal promoter region of rat TP53 gene was analyzed in liver and kidney tissue of rats from experimental groups. The semi-quantitative analysis revealed control group of rats had about 10 % methylation at the CpG site (both in liver and kidney) but arsenic exposed rats had significantly higher percentage of methylated CpG (25.5 % in liver and 17 % in kidney) at the specific site of the p53 promoter (Fig. 4). However, after B. monosperma flower powder and C. olitorious leaf powder supplementation despite arsenic exposure rats showed significantly lower site-specific methylation both in liver (12.55 % in GIII and 17.8 % in GIV) and kidney (12.6 % in GIII and 13.4 % in GIV) tissue. On the other hand, the mean percentage of methylation was higher in kidney than liver of arsenic exposed rats. Although DNA hypermethylation may precede histological changes but in this study no significant correlation was seen between hypermethylation of p53 promoter and degree of histological damage both in liver and kidney tissue.

3.4. mtDNA copy number

The basic mechanism of arsenic induced toxicity is oxidative stress [37]. Therefore, mitochondria are the key target of arsenic induced oxidative damage. To ascertain the mitochondrial damage after arsenic exposure in liver and kidney tissue mtDNA number were measured through qPCR. The relative number of mtDNA in liver and kidney tissue of rats from experimental groups are shown in Fig. 5. The relative number of mtDNA was significantly (p < 0.05) lower in group II (72 % and 57 % of normal value in liver and kidney respectively) when compared to group I. Conversely, B. monosperma and C. olitorius helped to retain higher level of mtDNA despite arsenic exposure both in liver (79 % and 86 % of normal value in GIII and GIV respectively) and kidney (76 % and 70 % of normal value GIII and GIV respectively). Both the plants showed good nephroprotective activity but showed lesser potential in retaining hepatic mtDNA after arsenic exposure. C. olitorius supplementation in GIII did not have significant effect on liver tissue.

3.5. Relative frequency of deletion in mtDNA

Similar results (Fig. 6) were also found in case of deletion in mtDNAs. Deletions in mtDNA is seen as a marker of excessive oxidative stress and may cause mitochondrial dysfunction [38]. Arsenic exposure caused drastic increase in deletion containing mtDNA population in liver tissue (4.2-fold) compared to control rats. In kidney tissue however this increase in deleted mtDNA population was also significant (2.2-fold) but not as marked as in liver tissue. The nephroprotective potential of B. monosperma and C. olitorius was also evident in preserving mtDNA as the group of rats receiving supplementation retained near normal level (1.46-fold and 1.3-fold more than normal in GIII and GIV respectively) of deleted mtDNA population. This difference was significant (p<0.05) compared to the arsenic exposed group. However, we observed contrasting result in liver tissue as neither plant supplementation produced significant difference between the arsenic exposed rats and treated rats.

4. Discussion

In our previous studies we have shown that C. olitorius [39] and B. monosperma [40] can alleviate the altered histological and
hepato-biochemical parameters caused by rice induced arsenic toxicity. In this study, we aimed to investigate the genotoxic effects of arsenic contaminated rice in rat model and assess the protective effects of *Butea monosperma* and *Corchorus olitorius* two plant species used in traditional herbal medicine, against arsenic induced toxicity. Arsenic is known to cause both hypo and hypermethylation either in the promoter region or in whole genome [15]. We observed significantly increased methylation in p53 promoter of the Arsenic exposed rats of Group II (As containing rice for 150 days) both in liver and kidney tissues (Fig. 4). Similar results confirming hypermethylated p53 promoter were observed in other studies [41,42]. In other experiments, it was suggested that promoter regions of tumor suppressor genes are target of oxidative stress induced aberrant methylations [43]. As methylated promoters of tumor suppressor genes are frequently reported in malignant tissues, the findings of our study suggest that prolonged Arsenic exposure may result into malignant transformation in liver and kidney tissues.

Arsenic toxicity can cause mitochondrial dysfunction, mtDNA depletion and occurrence of deletions in mtDNA [38]. In our study we observed significant decrease in relative mtDNA copy number in arsenic exposed rat liver and kidney tissues (Fig. 5). There are different factors which could affect the number of mitochondrial DNA such as cellular

![fig. 3. Photomicrograph of liver and kidney tissue cross section of experimental groups. Features are indicated with arrow. Cross section of liver tissue of (a) control group showing normal histostructure (H&E 20x), (b) arsenic exposed group showing necrosis and mononuclear cell infiltration in liver tissue (H&E 40x), (c) group III (As+ *C. olitorius* leaf powder) showing mild congestion and edema (H&E 40x) and (d) Group IV (As+ *B. monosperma* flower powder) showing portal duct and mild necrosis (H&E 40x). Kidney tissue cross section of (e) control group depicting normal histostructure (H&E 200x), (f) arsenic treated group showing total tubular epithelium necrosis with hemorrhage, mononuclear cell infiltration (H&E 400x) besides (g) group III (As+ *C. olitorius* leaf powder) and (h) Group IV (As+ *B. monosperma* flower powder) showing near normal kidney structure with mild proximal tubular necrosis, mononuclear cell infiltration and mild hemorrhage (H&E 400x).]
C. olitorius arsenic exposure in group II compared to control rats. After treatment with methylation in liver and kidney tissue of wistar albino rats. After arsenic arsenic decreases the expression of DNA polymerase polymerase and repair enzymes [38]. Recent reports suggesting that ROS level, mitochondrial dysfunction and reduced expression of DNA polymerase promoter could be the potential reason behind depletion of mtDNA [44,45]. The findings of our study certainly agree with these explanations. We also observed significantly increased number of deletion containing mtDNA (Fig. 6). Truncated expression and activity of mtDNA replicating enzymes might cause ROS level, mitochondrial dysfunction and reduced expression of DNA polymerase polymerase and repair enzymes [38]. Recent reports suggesting that ROS level, mitochondrial dysfunction and reduced expression of DNA polymerase promoter could be the potential reason behind depletion of mtDNA [44,45]. The findings of our study certainly agree with these explanations. We also observed significantly increased number of deletion containing mtDNA (Fig. 6). Truncated expression and activity of mtDNA replicating enzymes might cause

**Table 2**

| Parameters | Group-I (Control) | Group-II (Arsenic) | Group-III (Arsenic + C. olitorius) | Group-IV (Arsenic + B. monosperma) |
|------------|------------------|--------------------|----------------------------------|------------------------------------|
| AST        | 60.6 ± 3.61      | 99.4 ± 3.5         | 67.6 ± 2.5                       | 70.00 ± 4.35                      |
| ALT        | 80.0 ± 2.98      | 122.4 ± 6.87       | 108.4 ± 5.57                     | 97.2 ± 5.45                       |
| Urea       | 49.4 ± 2.08      | 64.4 ± 1.8         | 52.0 ± 1.61                      | 59.2 ± 1.77                       |

Values are expressed as mean ± SEM.

**Fig. 4.** Effect of Corchorus olitorius and Butea monosperma on p53 promoter methylation in liver and kidney tissue of wistar albino rats. After arsenic exposure Arsenic exposed group is showing significantly increased methylation in liver and kidney tissue compared to control group. Both treatment groups, Group III (As + C. olitorius) and IV (As + B. monosperma) showing significantly (p < 0.05) reduced methylation compared to non-treatment arsenic exposed group II both in liver and kidney tissue. Each bar represents the mean ± S.E.M.

**Fig. 5.** Relative number of mtDNA copy in rat liver kidney tissue. Relative mtDNA count increased significantly (p < 0.05) in liver and kidney tissue in Group III (Arsenic + Corchorus) and IV (Arsenic + Butea) except in liver tissue of group III. Arsenic exposed group II had significantly (p < 0.05) decreased mtDNA count both in liver and kidney compared to control rats. Each bar represents the mean ± S.E.M.

**Fig. 6.** Relative frequency of mtDNA with common deletion in rat liver and kidney tissue. Group II (Arsenic) is showing significant (p < 0.05) increase in the number of deleted mtDNA after Arsenic exposure compared to control group. Group III (Arsenic + Corchorus) and IV (Arsenic + Butea) is showing significant (p < 0.05) decrease in deleted mtDNA population after treatment in kidney tissue. However, the changes were not significant (p > 0.05) in liver tissue, both in group III (Arsenic + Corchorus) and IV (Arsenic + Butea). Data expressed as mean ± S.E.M.
prevention of lipid peroxidation by chelating Arsenic induced ROS. Heavy burden of ROS due to Arsenic can impair the activity of anti-oxidative enzymes such as super oxide dismutase (SOD) [54]. Thus C. olitorius may provide protection from the oxidative damage by inhibiting lipid peroxidation with phytophenolic compounds to prevent mitochondrial damage and preventing the ensuing damaging effects.

Similarly, rats of Group IV (B. monosperma flower powder for 150 days) showed lower p53 promoter methylation along with significant retention of mtDNA in both liver and kidney after B. monosperma flower power supplementation in their feed. Even after Arsenic exposure the retention of mtDNA in both liver and kidney after

Author Statement

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Declaration of Competing Interest

The authors declare that there is no known conflict of interest.

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