8. Summary

The current investigation shows that arsenic treatment clearly induced hepatic tissue degeneration. Metabolites of arsenic can impair cell division via tubulin and other hyposkeleton structure disruption (Kligerman et al., 2005). Hepatic necrosis and lobular structural disintegration shown in the present study is justified by the present result. Similarly, damages in the renal structure and nephritic damages are evident in this study. This disintegration is distinctly protected by the present BBE supplementation schedule. Methylated As (III) compounds are more genotoxic than methylated arsenicals in its (V) state. MMA (III) and DMA (III) are the final genotoxic forms of arsenic and they are regarded as the clastogenic compound. Report reveals that intracellular levels of arsenic metabolites are regulated by folate and B_{12} (Kligerman et al., 2003). The oxidation of more toxic DMA (III) to less toxic DMA (V) requires some strong oxidant like H_2O_2. The present result of XO-inhibition suggests the possible lower production, thus unavailability of H_2O_2 which could have been involved to metabolize more toxic As (III) to less toxic As (V) state. In addition, the urate, product of the XO-catalyzed reactions might have played as a reliable antioxidant role. One earlier report on rat model suggests that arsenic-induced DNA damage can be prevented by uric acid treatment (Gurr et al., 1998). DNA damage has been suggested to induce apoptotic tissue damage (Vermeulen et al., 2005). The urate, regarded as a longevity enhancer (Cutler, 1984; Glantzounis et al., 2005) has been recognized as a pro-oxidant/antioxidant (Glantzounis et al., 2005). Lowering of antioxidant capacity in some hypouremic condition may promote diseases like multiple sclerosis and others (Toncev, 2006). In this study, a significant decrease in uric acid and the increase in free radicals like MDA and other lipid peroxides level may be linked to the aging promoting ability of arsenic (Zhang et al., 2003). One early investigation indicates that arsenic treatment can deplete

serum uric acid in rats (Jauge and Del-Razo 1985). Report reveals that blocking of molybdenum (Mo) centre of xanthine oxidase by arsenic minimize O_2 reduction to form H_2O_2 at the time of catalysis of hypoxanthine to xanthine and xanthine to uric acid (Aposhian et al., 2003). Thus, oxidation of arsenicals from its (III) to (V) state is also similarly important, like the methylation-associated detoxification of this compound. Lactoperoxidase (LPO) is a member of a large group of mammalian heme peroxidises that include myeloperoxidase (MPO), eosinophil peroxidise (EPO), and thyroid peroxidase (TPO) (Sharma et al., 2013). LPO is predominant in lung tissue. In an attempt to investigate the possible protective and therapeutic effect against arsenic induced rat tissue damage are conferred by antioxidative mechanism and attenuation of pro-inflammatory. This potent organism might be a natural choice against arsenic and several other toxicities. Our studies on arsenic-exposed human can correlate carcinogenesis with DNA-damage. In an attempt to investigate the possible protective and therapeutic effect against arsenic induced hepatotoxicity, the extract of *Bellamya bengalensis* was tested in arsenic intoxicated rat model. The time- and dose-dependent effect of arsenic toxicity was also tested in *Bellamya bengalensis.* Sodium-meta-arsenite $NaAsO_2$ (0.6 ppm/100g b.w./day for 28 days, as earlier reported) was treated alone or in combination with the *Bellamya bengalensis* water extract (BBE, 100mg/100g b.w.) to rat and compared with vehicle treated control. In other experiment, the *Bellamya bengalensis* was exposed to high concentration of $NaAsO_2$ contaminated water (5 to 20 ppm for 1 to 9 days) in laboratory condition and their DNA quality was evaluated in relation to its possible oxidative threat. Any concentration of arsenic was incapable to initiate a significant DNA damage in *B. bengalensis*. Lipid peroxidation was increased in arsenic exposed *Bellamya* after longer duration of its exposure. Increase in reduced antioxidant like non-protein-soluble thiol (NPSH) is concordant with the decrease in

lipid peroxidation and DNA stability in this organism. In rat experiment, the BBE supplementation strongly prevented arsenic-induced oxidative, necrotic and apoptotic damages to liver tissue/DNA by strengthening antioxidant systems, which has been shown in hepatic DNA-fragmentation, Mitochondrial membrane potential, comet-assay, histo-architecture (haematoxylin/eosin), alkaline-phosphatase, serum-glutamate-pyruvate-transaminase and lactate-dehydrogenase (tissue-degeneration-marker) results. Moreover, an arsenic-induced increase in pro-inflammatory cytokine TNF-α was restored terminating an acute-phase reaction. Only arsenic exposure decreased hepatic superoxide-dismutase (SOD) in-vivo and in-vitro (H_2O_2/ arsenite redox-stress to dialyzed and concentrated, 6-8kd cut-off millipore liver cytosolic SOD), catalase, xanthine-oxidase, lactoperoxidase activities and the level of NPSH with a concomitant increase in malondialdehyde resulting in mutagenic DNA-breakage and apoptotic liver damage which has been decisively restrained in *B. bengalensis* extract. The current investigation shown strong evidence on the hepato-protective and medicinal efficiencies of BBE against oxidative stress induced by arsenic. In the present study, a significant restoration of LPO is observed in mainly lung and moderately in liver tissues in the BBE supplemented group. This suggests the effective drainage of free radicals, which might be helpful in tissue/ DNA protection.