13.0. Conclusion

Arsenic is one of the most fatal toxicants for the living beings. Its exposure in humans mainly comes via drinking water that results in creating a sweltering health condition worldwide. Exposure to arsenic is a burning problem for a large population in India and other parts of the world. The main targets of arsenic toxicity are skin and different metabolic organs. Arsenic is known to develop male and female reproductive functional discrepancies. Female infertility is one of the major outcome of consuming arsenic contaminated drinking water. Uterine arsenic exposure impairs thymic development in children and subsequently enhances the morbidity via immune-suppressive activity. Several approaches of treatment strategy at experimental levels are being executed in managing arsenic induced health disorders. Although the chelating agents e.g. BAL and DMSA are commonly used as conventional therapeutic agents to treat arsenic affected patients. Very often metal chelation therapy is compromised with several side effects and drawbacks along with exerting its efficacy with low therapeutic index and unsafe administration. Moreover, there is a controversy regarding the continuation of long term treatment by painful intramuscular injection of these chelators as these increase the risk of redistribution of arsenic into the brain. Despite many years of research, we are still far from an appropriate treatment of arsenicosis. So, the problem is unresolved. Hence, an attempt was given through our present investigation to develop easily available effective bio-ingredients from natural resources with antioxidant or chelating property and least toxic effects against arsenic mediated female reproductive disorders. This study is intended to emphasize the effects of curcumin, Pectic polysaccharide (CCPS) from *Momordica charantia* and encapsulated curcumin chitosan nanoparticles (ECNPs) on arsenic-induced ovarian and uterine disorders since arsenic intoxication is one of the most important illness behind female infertility.

The pure form of these above biomolecules was administered or supplemented at different stages to the arsenic challenged experimental animal. The protective and curative roles of curcumin, CCPS and ECNPs have been executed to establish its therapeutic effect on arsenic mediated repro-toxicity. Wistar female rats were used for the tratment strategy. We selected 20 mg, 2.0 mg and 1.0 mg per Kg body weight respectively for application of curcumin, CCPS and ECNPs respectively against 10 mg sodium arsenite per Kg BW. Extracted CCPS from *Momordica charantia* has possible capability to interact with sodium arsenite via involvement of the active sites of the hydroxyl groups on the surface of polysaccharide.

Spherical particles sizes of ECNPs were ranging from 8-40 nm have high stability in biological system and also have possible ability to interact with sodium arsenite via the connection of hydroxide groups of curcumin and ammonium groups of chitosan. Curcumin, CCPS and ECNPs treatment scavenges the ROS production in uterus, ovary and liver caused by arsenic. Treatment with these biomolecules has better antioxidant and chelating activity which contributes distinct protective and curative effects against the arsenic induced alteration of uterine and ovarian oxidative stress. Curcumin, CCPS and ECNPs treatment significantly attenuated the arsenic mediated oxidative stress and lipid peroxidation level in uterus and ovary. The serum levels of LH, FSH and estradiol were maintained towards normalcy accompanied with the restoration of estradiol receptor-1 stability that finally inducing the steroidogenic activities in rat when treatment with curcumin, CCPS and ECNPs were given to arsenic treated rats. H-E staining confirms the restoration of uterine and ovarian histomorphology in response to the addition of curcumin and CCPS in arsenicated rats. CCPS and curcumin have excellent anti-inflammatory properties. These regulate the inflammatory marker NF-κB and pro-inflammatory cytokines TNF-α and IL-6 during the mitigation of arsenic induced toxicity. In this study it is confirmed that up-regulation of uterine apoptotic markers (caspase-3, Bax), p53, PCNA, PARP and down-regulation of Bcl_2,

AKT in arsenic-exposed rats could be definitely restored by the addition of CCPS treatment by the involvement of the different intrinsic and extrinsic pathways. CCPS treatment additionally induces gene expression of NF-κB, TNF-α, Bax and p53. However, oral CCPS contributes in attenuating above apoptotic expressional changes in arsenicated rats. Ultimately dietary CCPS ensured successful outcome of fertility in female rats with the delivery of healthy pups in arsenic treated rats.

Though, these bioactive molecules treatment against arsenic toxicity may directly or indirectly remove this deterious effect of arsenic toxicity from the body involving of S-adenosine methionine (SAM) pool in *in-vivo*-manner. In addition *in-vitro* experiment is also supportive of possible direct action on of these polyphenols and polysaccharides against arsenite. Our study reveals that curcumin, CCPS and ECNPs treatment on the rat models could possibly use for the human beings, especially for the female reproductive organs. This work will aid to prime the work on human for the expansion of potent nutraceuticals against arsenic mediated infertility.