14.0. Summary

The outcome of experiment-1 indicates that isolated CCPS from bitter gourd (*Momordica charantia*) consists of D-galactose and D-methyl galacturonate with a molar ratio of 1:4. Fourier-transform infrared spectroscopy (FTIR) study of CCPS and sodium arsenite (As^{III})-CCPS association specified a possible chelating property of CCPS in presence of binding site of hydroxyl group (-OH) which interact and chelate with metal. Presence of negatively charged galacturonate residues in CCPS structure provide better potential action for cation chelation.

Experiment-2 helps to understand that sodium arsenite at the dose of 0.6 and 0.8 ppm more or less similar toxic than that of 0.2 and 0.4 ppm when liver slices were incubated in presence of this metalloid. The bioactive of pectic polysaccharide (CCPS) and curcumin were used to mitigate the hepatocellular oxidative stress against 0.6 ppm dose of sodium arsenite in an *in-vitro* model that used rat hepatic slices for short duration (3 and 6 hrs). CCPS and curcumin directly interact with the arsenic and H_2O_2due to its chelating property. Acquired data pointed out that CCPS and curcumin alone or its combination mode are helpful in restoring arsenic mediated generation of hepatic oxidative stress (MDA and CD) by inducing antioxidant enzymatic activity (SOD, catalase and peroxidase).

Experiment 3 was intended to find out, the critical dose of curcumin in the amelioration of arsenic mediated female reproductive disorders. At the dose of 20 mg/ kg BW curcumin exhibited effective protection of the uterine and ovarian disorders than that of the dose 15 mg/ kg BW against the 10 mg/Kg BW of sodium arsenite. The utero-ovarian deterioration and alteration of oxidative stress markers, gonadotrophins, estradiol level were corrected by the co-administration of critical dose of curcumin.

Experiment 4 confirmed the critical dose of CCPS that need to neutralize the arsenic induced malfunction. The doses of 2.0 mg and 2.5 mg CCPS reflected better protection than that of the dose of 1.5 mg /Kg BW when 10 mg/Kg BW of sodium arsenite dose were given to the rats. The co-treatment of CCPS following arsenication re-established the baseline functioning of the antioxidant enzyme systems followed by diminishing the lipid peroxidation products and finally, improved ovarian steroidogenesis and estradiol levels.

Experiment-5 elucidates that curcumin and CCPS exerts its protective effects against the arsenic mediated ailments of female reproductive organ. Treatments with curcumin and CCPS attenuated the uterine oxidative stress and thereby improved antioxidant defense. The combination of curcumin and CCPS on arsenicated rats counteracted a remarkable and supportive effect on the elevated necrosis biomarkers. Different inflammatory markers were suppressed in arsenicated rats by these flavonoid and polysaccharide. Moreover, the level of serum gonadotrophins, Hcy, and estradiol were restored by the addition of curcumin and CCPS. Curcumin and CCPS structure have chelating properties that could help in trapping of arsenic. Arsenic detoxification process may be executed by the potential involve of SAM pool in the removal of arsenic that ultimately increases by the bio-availability and maintenance of the circulating level of B_{12}, folate and Hcy.

From experiment-6 it has been explored that CCPS has curative effects on arsenic induced female repro-toxicity. CCPS treatment reinstated oxidative induced liver and kidney injury via the modification of antioxidant redox signaling pathway in arsenic fed rats. CCPS significantly mitigated arsenic induced uterine and ovarian lipid peroxidation, and reactive oxygen species (ROS) generation by the restoration of superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx) activities and expression. CCPS post-treatment improved ovarian steroidogenesis along with a restoration of normal tissue histoarchitecture in arsenic fed rats by regulating the estradiol receptor alpha-1. Additionally, inhibition of NF-κB

pathway in arsenic fed rats was observed due to CCPS that finally results in the downregulation of the inflammatory and pro-inflammatory cytokines. Up-regulation of uterine pro-apoptotic/ apoptotic proteins poly ADP ribose polymerase (PARP), caspase-3, phospho p53, proliferating cell nuclear antigen (PCNA), and Bax followed by downregulation of Bcl-2 and protein Kinase B (AKT) signaling pathway along with uterine tissue regeneration were prominent in exposed rats. Dietary CCPS, maintained normal weight of the pregnant rats and was helpful in successful delivery of pups without any death and contributes in improving the rate of female fertility. CCPS has galacturonate acid residue hydroxyl group and these groups are useful in chelating arsenic by the modulation of B_{12} and Hcy in SAM pool.

From experiment 7 it has been explored that encapsulated curcumin chitosan nanoparticles (ECNPs) could be used as potential as a drug delivery system. The encapsulated curcumin in nanoparticles introduced a new way to improve the drug targeting for the treatment of reproductive disorders in arsenic-challenged rats. Present study however, focuses a high potential activity of curcumin-loaded chitosan nanoparticles. It may be speculated that due to its nano-size (8-40 nm) with high stability protects the arsenic induced female repro-toxicity by curative mode.

Experiment-8 it has been explored that encapsulated curcumin in chitosan nanoparticles (ECNPs) has curative effects on arsenic induced female repro-toxicity. Two critical dose 1.0 mg and 1.5 mg ECNPs per Kg BW is more significantly effective than that of 0.5 mg ECNPs dose when 10 mg/Kg BW of sodium arsenite dose were given to the rats. Our results confirmed that arsenic could possibly interact with hydroxyl group of ECNPs structure results in the formation of aggregation ECNPs. Addition of ECNPs in arsenicated rats inhibited ROS production and was counteracted by these nano-chelating agent reversed the action of uterine oxidative stress markers, improved antioxidant status and ovarian steroidogenesis expression.

This above formulation however, gives a new curative action for preventing the arsenic toxicity.