Cadmium is a toxic heavy metal with a long history of detrimental effects which adversely affects the reproductive system. Sexual dysfunctions are common in the general population exposed to toxic elements like heavy metals. It is observed that cadmium exposure may inhibit the testicular macrophage functions and reproductive functions. The testis though recognized as an immuneprivileged organ, the presence of a number of immunocompetent cells like macrophages, neutrophils and monocytes within the testicular interstitial compartment give evidence of testicular immune response. Testicular macrophages are the largest population of immune cells in the rodent testes. Exposure to cadmium chloride *in vivo* and *in vitro* is known to inhibit the testicular macrophage functions. But the extent of effect or the mechanism thereof is not well elucidated.

The present study examined the extent of immunomodulatory effect in murine testes after *in vivo* and *in vitro* exposure to cadmium. To elucidate the immunomodulatory effects of cadmium *in vivo*, experimental animals were divided into two groups: Control (isotonic saline) and treated (0.35 mg/kg b.w of cadmium chloride) intraperitoneally for 15 days. For *in vitro* exposure a dose of 10 ng/ml concentration of cadmium was optimized. Cell function studies such as morphological alteration, phagocytosis, chemotactic migration, intracellular killing mechanism, DNA fragmentation, enzyme activity (nitric oxide, myeloperoxidase synthase, lysozyme release, alkaline phosphatase release) and proinflammatory cytokines (TNF-α and IL-6 release ) assays as well as anti-inflammatory cytokine response (TGF-β) were performed in testicular macrophages isolated from cadmium-treated and control group of adult male Swiss albino mice.
The present study also investigates the extent of immunomodulatory effects in lieu with semenological alterations in the immunoprivileged organ-testes, after exposure to cadmium (*in vivo*) in male Swiss albino mice. Among the semenological parameters, sperm count, sperm motility, sperm morphology and the testosterone level in the epididymal semen samples from both groups were determined. The concentration of fructose in the experimental groups was measured to determine the proper functioning of the seminal vesicle. Oxidative stress was also estimated from lipid peroxidation (LPO) level for which the level of malondialdehyde (MDA is a marker of LPO) concentration was determined. The activity of antioxidant enzymes superoxide dismutase (SOD) and the catalase (CAT) activities in testes of control and cadmium treated were determined.

The *in vitro* study shows morphological alteration in cadmium treated (*in vitro*) group along with DNA damage as compared to control. It also indicates an impairment of the microbicidal capacity due to suppressed phagocytosis, chemotactic migration and intracellular killing consorted to a reduction of inflammatory response. This is due to decrease of both reactive nitrogen and oxygen species in the phagocytic niche of macrophages in the presence of cadmium ions. It was observed that the myeloperoxidase enzyme release is also lowered with a concomitant decrease of nitric oxide release due to cadmium treatment. The present work shows that cadmium is responsible for a significant alteration, degenerative changes and reduced cell function in testicular macrophages probably by increasing oxidative damage. Such oxidative stress also causes a parallel dysfunction of the semenological parameters. The cytokines TNF-α, IL-6 and TGF-β show significant alteration and can be correlated with the semenological dysfunction, loss of immuneprivilege and immunesuppression. Macrophage population is known to influence the function of the
neighboring Leydig cells. Thus, the effect of cadmium exposure on testicular macrophages not only portray a potent mechanism of immunesuppression as well as reproductive toxicity, but also give clues to occurrence of an immune induced infertility in mice.