Summary of the Thesis
The present study was carried out to understand the biochemical mechanism underlying the reproductive toxicity of chromium in males.

90 days old adult male Wistar rats (*Rattus norvegicus*) were exposed to different doses of hexavalent chromium (50, 100, 200, 400 and 800 ppm, as potassium dichromate) through drinking water for 30 days.

The concentration of chromium in the serum and testicular tissue increased linearly in a dose dependent manner.

Reproductive toxicity of chromium was attested by the dose dependent reduction in epididymal sperm count and forward motility.

Reproductive toxicity of chromium was ascertained by the disrupted spermatogenic process as indicated by a significant reduction in the number of spermatogonia, spermatocytes, and round and elongated spermatids.

Disruption of pituitary-testicular axis was indicated by reduced plasma titres of FSH, LH, testosterone, and estradiol.

Chromium toxicity brought down the number of Leydig and Sertoli cells, which was accompanied by diminished function of these cell types, as indicated by decreased concentration of testosterone and ABP, respectively, in the TIF.
In order to understand the biochemical mechanism underlying the reproductive toxicity of chromium, testicular lipid peroxidation, ROS (H$_2$O$_2$, *OH), and non-enzymatic (Vitamin A, C, & E and GSH) and enzymatic (SOD, CAT, GPx, GR, γ-GT, GST, G6PDH) antioxidants were quantified in rats exposed to chromium.

A dose dependent decrease in the activities of enzymatic and non-enzymatic antioxidants was observed in animals given various doses of chromium. This was accompanied by an increase in the production of reactive oxygen species like hydrogen peroxide and hydroxyl radical, and lipid peroxidation.

Chromium-induced oxygen toxicity was induced by enhanced ROS production with a concomitant reduction in antioxidant defense system.

To test the reversibility of chromium-induced reproductive toxicity, one set of experimental animals exposed to the maximal effective dose of chromium (400 ppm) was withdrawn of chromium treatment and maintained in a chromium-exposure-free condition for a further period of 30 days.

Normal reproductive function (sperm count and forward motility, testicular structure and function) and oxidative balance in the testicular tissue of rats withdrawn of chromium treated rats suggest that chromium-induced reproductive toxicity is transient and reversible.
To test the prophylactic effect of antioxidant vitamins, another set of rats given the maximal effective dose i.e. 400 ppm chromium were given simultaneous supplementation of vitamin C or E along with chromium.

Administration of different doses of either vitamin C or E prevented chromium induced reproductive dysfunctions and maintained normal testicular structure and functions. From these experiments, it is concluded that chromium-induced reproductive toxicity which is accompanied by an oxygen stress in the testis, can be prevented by simultaneous supplementation of vitamin C or E.

The data from studies with isolated testicular cells *in vitro* show that chromium can directly interfere with the function of Leydig and Sertoli cells, as indicated by suppressed output of testosterone and ABP, respectively. These adverse effects of chromium on Leydig cell and Sertoli cell *in vitro* were prevented by the addition of either vitamin C or E to the culture medium.

Taken together, the data from the present investigation indicates that chromium induces reproductive toxicity in male rats by inducing oxygen toxicity in the testis, which is reversible under chromium-exposure-free conditions and can be prevented by simultaneous administration of antioxidant vitamins. Chromium can directly interfere with Leydig and Sertoli cell functions.

In conclusion, the present study, for the first time provide evidence for the involvement of testicular ROS and antioxidant system in mediating the transient/reversible reproductive toxicity of chromium in male rats. The study also underscores the quenching effect of antioxidant vitamin C or E on testicular toxicity of chromium.