SUMMARY AND CONCLUSION
The present study was carried out to understand the chronic toxicity of carbendazim in the spermatogenic as well as androgenic compartments of the testis of rats.

90 days old adult male Wistar rats (*Rattus norvegicus*) were exposed to carbendazim dissolved in corn oil at a dose of 25mg/kg body weight orally, for 48 days.

The concentration of carbendazim in the serum and testicular tissue was increased.

Reproductive toxicity of carbendazim was attested by morphological and ultrastructural changes.

Morphological changes include the reduction in epididymal sperm count, sperm motility, viability, seminiferous tubule and lumen diameters and increase in the incidence of sperm abnormalities.

Ultrastructural studies revealed the continuous loss of germ cells, sloughing of Sertoli cells, damaged Sertoli-Sertoli junctions/blood-testis barrier, Sertoli cell-only-syndrome, Sertoli cell fibrosis, cytoplasmic vacuolation, premature release and degeneration of pachytene spermatocytes and round spermatids, death of germ cells through necrosis, presence of cell debris, lipid droplets, dispersed, hypertrophied Leydig cells, elongated nucleus, swelling of mitochondria and endoplasmic reticulum and collapse of cristae.
The unaltered levels of serum gonadotrophins and prolactin indicated that the pituitary-hypothalamic function was not affected by carbendazim. However, the disruption in testicular function was indicated by reduced serum titres of testosterone and estradiol.

Carbendazim can directly interfere with the function of Leydig cells, as indicated by suppressed output of testosterone, activities of steroidogenic enzymes such as 3β-HSD and 17β-HSD.

In order to understand the biochemical mechanism underlying the reproductive toxicity of carbendazim, Leydig cellular lipid peroxidation, ROS (H₂O₂, ·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 carbendazim.

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

Carbendazim induced changes in lipid profiles indicates the alteration in Leydig cellular structure and function. The reduction in the levels of total lipid, total cholesterol, total glyceride glycerol, and total phospholipid, free cholesterol and esterified cholesterol was due to the lipid peroxidative damage caused by carbendazim.
To test the ameliorative effect of antioxidant vitamin E, a group of rats were given vitamin E at the dose of 20mg/kg body weight along with carbendazim.

Co-administration of vitamin E with carbendazim resulted in complete prevention of the deleterious effect of carbendazim in testis, epididymis, seminal vesicles and ventral prostate weights. Testis showed normal seminiferous tubules with intact seminiferous epithelium, spacious lumen and normal Sertoli, germ and Leydig cells. Co-administration of vitamin E with carbendazim protected Leydig cells against lipid peroxidation by increasing enzymatic and non-enzymatic antioxidants.

To test whether the selected dose of vitamin E has any effect on the normal structure and function of testis, a group of rats were given vitamin E alone (20 mg/kg body weight). Interestingly, in none of the parameters studied, vitamin E exerted any adverse effects. These findings indicate that vitamin E does not intervene with normal testicular structure and function.

To test the reversibility of carbendazim-induced reproductive toxicity, a group of animals exposed to a dose of 25mg/kg body weight was withdrawn of carbendazim treatment and maintained in a carbendazim-exposure-free condition for a further period of 48 days.

Normal reproductive function (sperm count, caput and cauda sperm concentration, motility, viability, testicular structure and function), oxidative balance and lipid metabolism in the testicular
Leydig cells of rats withdrawn of carbendazim treated rats suggest that carbendazim-induced reproductive toxicity is transient and reversible.

In conclusion, chronic low dose treatment of carbendazim is capable of inducing reproductive toxicity through increased oxidative stress, but is transient and reversible upon withdrawal of treatment. Further, vitamin E an antioxidant by itself quenches the oxidative stress and protects the male reproductive organs from the onslaught of oxidative stress.