In the present study, the effects of ELAP and Andrographolide on male reproductive health in rats were studied. Exposure to graded doses of ELAP or Andrographolide did not affect the body weight gain. The weights of liver and kidneys were not significantly changed in rats administered with low and medium doses of ELAP when compared to the control rats indicating that the metabolic activity in these organs is not affected. In contrast, rats administrated with high dose of ELAP and Andrographolide resulted in a significant decrease in the body weights and indices of liver and kidney, whereas the relative weight of brain is comparable among all groups of rats indicating that the selected doses and time schedule of treatment may not be effective to induce neurotoxicity. A significant decrease was observed in the weights of accessory sex organs such as seminal vesicles and penis were observed in rats administered with medium, high doses of ELAP and Andrographolide, suggesting that these reproductive organs are the vulnerable targets of toxicity. A significant decrease was also observed in the weights of testes in all the experimental rats except in the rats administered with low dose of ELAP when compared to controls. Since the relative weights of testis decreased in all the experimental rats, in the present study, the author delved in to analyze the testicular (daily) sperm production, sperm reserves in epididymis and the quality of mature sperm in rats administered with graded doses of ELAP and Andrographolide, which were used as important markers for the determination of male fertility.

Significant decrease in daily sperm production, sperm reserves, sperm motility, sperm viability and deterioration in sperm membrane integrity (HOS test) was observed in rats administered with graded doses of ELAP and Andrographolide when compared to the control rats. The data clearly indicates that ELAP and Andrographolide affect both sperm production and maturation. Since growth and functioning of accessory sex organs and secondary sexual characters, production and maturation of sperm is under
the control of androgens, the author ventured on determining the steroidogenesis and testosterone levels in circulation in control and experimental rats.

As demonstrated above, administration of graded doses of ELAP and Andrographolide is clearly associated with suppressed steroidogenesis and abnormal spermatogenesis in rats. Therefore, the author investigated whether testes from experimental rats had any change in the number of spermatocytes and spermatids when compared with testes from control animals, using histological characteristics. Histological observations of the transverse section of testis of the control rats have showed that seminiferous tubules contain all stages of spermatogenesis and interstitial cells. The transverse section of testis of experimental rats has showed a decrease in the number of spermatocytes, spermatids and sperm in the lumen of seminiferous tubules. The deterioration in the testicular architecture of rats administered with graded doses of ELAP or Andrographolide is generally ascribed to insufficient availability of testosterone or may be due to increased oxidative damage.

The results in the preceding chapter clearly indicated that administration of graded doses of ELAP or Andrographolide induced oxidative stress in the testes of experimental rats. It is well established that imbalance in pro-oxidant and antioxidant status leads to several sperm abnormalities including infertility (Makker et al., 2009). Excess generation of ROS, results in lipid peroxidation which can cause damage to sperm and other cytoplasmic organelle membrane structures through peroxidation of lipids, proteins and nucleotides resulting in production of inferior sperm quality (Aitken et al., 1989; Armstrong et al., 1999; Agarwal and Allamaneni, 2004) and leading to infertility (Aitken and Baker, 2006).

The final reproductive endpoint that was tested was the male’s ability to sire offspring in a fixed time period. Fertility related studies provide valuable information
about reproductive behavior and attitude and will help to analyze the relationship, if any, with testicular sperm quantity and quality and/or sexual desire of the animal. Observations that all males in experimental groups sired pups, but with reduced number, indicate that treatment used in this study was effective in inducing suppressed fertility in males. The presence of copulatory plugs or presence of sperm in vaginal washings in females mated with the experimental males suggests that sexual behavior is not compromised, whereas additional observations of fewer pups per litter and higher pre- and post-implantation loss in females mated with experimental males suggest compromised sperm fertility. In conclusion, the present study provides compelling evidence of altered reproductive functions, including levels of testosterone, density, motility and viability of sperm and fertility in adult rats administered with graded doses of ELAP or Andrographolide. The decreased serum testosterone levels might be responsible for the decreased sperm density and poor sperm quality in rats. The lower testosterone level observed in rats administered with graded doses of ELAP and Andrographolide alone probably resulted from an effect directly on Leydig cells. The inferior sperm quality and low sperm density might be responsible for suppressed reproductive performance in the male rats.
Conclusions

1. Administration of graded doses of *A. paniculata* extract or Andrographolide reduced the weights of reproductive organs indicating that they are the vulnerable targets for physical or chemical toxicity. In addition, administration of high dose of *A. paniculata* and Andrographolide resulted in reduction in the weights of liver and kidney.

2. Administration of graded doses of *A. paniculata* extract or Andrographolide decreased the daily sperm production, sperm reserves, motile and viable sperm and HOS tail coiled sperm, indicating spermato-toxic effects of *A. paniculata* and Andrographolide.

3. Administration of graded doses of *A. Paniculata extract* or Andrographolide induced lipid peroxidation levels as evidenced by elevated tissue MDA levels, with a significant decrease in the SOD and catalase activity levels in the testes and epididymis, indicating the disturbance in pro- and anti-oxidant machinery in these tissues.

6. Many histological alterations are observed in the testis of rats administered with graded doses of *A. Paniculata extract* or Andrographolide, which includes large lumen with reduced sperm tails, few degenerating spermatocytes and empty lumen devoid of sperm indicating deterioration in testicular architecture.

7. A decrease in fertility index, number of implantations and live pups and increases in pre- and post-implantation loss observed in rats mated with males administered with graded doses of *A. paniculata* extract or Andrographolide indicates suppressed fertility out in experimental rats.

8. The significant finding of the present study is that administration of graded doses of *A. paniculata* extract or Andrographolide potentiated the reproductive toxicity in rats. The suppression in steroidogenesis, spermatogenesis and fertility was observed in the experimental rats.