Conclusions and hypothesis

1. This study provides evidences for intragonadal role of locally produced estradiol in the testis of mice.
2. This study suggests involvement of estradiol mediated ERα-NO pathway in regulation of testicular spermatogenesis in mice.
3. Evidences from present study suggest that estradiol modulates steroidogenesis and germ cell survival in the testis of mice during reproductively active period whereas in old age decreased estradiol concentration causes increased nitric oxide which in turn decreases testicular steroidogenesis and germ cell apoptosis.
4. The tamoxifen-induced decreased estrogenic effect may be responsible for increased production of i-NOS and nitric oxide which may be responsible for increased germ cell apoptosis and impaired spermatogenesis.
5. The tamoxifen treatment in vitro caused inhibitory effect on testicular testosterone and estradiol synthesis.
6. The tamoxifen treatment in vivo showed stimulatory effect on testosterone because of indirect effect of tamoxifen on gonadotropin release.
7. The mice treated with Letrozole suppresses spermatogenesis by reducing insulin sensitivity and glucose transport in the testis, but significantly increased testosterone synthesis by promoting gonadotrophin release by negative feedback effect of decreased estradiol.
8. The present study revealed the importance of Genistein, a phytoestrogen, as an important therapeutic agent for the treatment of diabetes-induced testicular dysfunction.
Avenues for future investigation

1. Future studies are required for understanding the interaction between testosterone and estrogen and how these hormones affect multiple physiological functions in men.

2. Extensive study is required to determine the mechanism by which decline in estradiol during aging and diabetic condition lead to reproductive dysfunction in men.

3. Further research is required on the use of selective estrogen receptor modulators (SERM) and aromatase inhibitors (AIs) in improving hypogonadal conditions in order to fully establish their use in the treatment of male infertility.

4. Whether decline in testicular activities during aging occur as a result of decreased production of estrogen or increased synthesis of nitric oxide require further confirmation.

5. Role of estrogen in male accessory sex gland is not completely understood.

6. Further research is required in order to confirm the role of phytoestrogen in improving the reproductive dysfunction in diabetic male, and hence to provide effective therapeutic opportunities for diabetic men.