Chapter – 12

Summary and Conclusion
Summary of the study

Alcohol induced sterility
- Alcohol is a testicular toxin
- Induces apoptosis of spermatogenic cells

Stress induced sterility
- Affects the Hypothalamo-Hypophyseal-Gonadal axis
- Decreases the testosterone production and spermatogenesis

Diabetes induced sterility
- Free radicals produced by Streptozotocin, causes oxidative stress in testes
- Affects the Hypothalamo-Hypophyseal-Gonadal axis

C. circinalis L and I. suffruticosum Ging
- Presence of flavonoids, tanins & alkaloids (Antioxidant activity)

- Alkaloids possibly might have triggered the production of testosterone hormone
- Flavonoids might have acted by resisting the effect of sterility
- Tannins possibly might have inhibited oxidation by acting as an antioxidant

- Increase in number of spermatogenic cells
- Increase in volume and weight of testes
- Increase in number of spermatogenic cells and increase in its nuclear diameter
- Increase in number of normal spermatozoa
- Increased sperm count

- Increase in sexual behaviour
- Increase in number of Leydig cells which secretes testosterone hormone

- Fertility of all the sterile rats has restituted back to normal
- Both C. circinalis and I. suffruticosum had improved the fertility
- I. suffruticosum was proved to be more effective when compared to C. circinalis
12. CONCLUSION:

12.1. Phytochemical screening and antioxidant activity of C. circinalis and I. suffruticosum:

The phytoconstituents such as terpenoids, flavonoids, glycosides, phytosterols, amino acids and alkaloids were found to be present in both the herbs. The GCMS analysis showed 16 bioactive phytoconstituents in C. circinalis and 18 bioactive constituents in I. suffruticosum. The phytoconstituents and secondary metabolites were known to have some medicinal and physiological activity. The fertility effect of both the herbs might have been possibly due to the phytosterols, alkaloids and flavonoids. These phytoconstituents were metabolized and converted to phytosteroids, which results in the androgenic activity of the male rats. The antioxidant analysis of both the herbs showed that I. suffruticosum has more free radical scavenging activity when compared to C. circinalis. The I. suffruticosum was much more effective in restituting the fertility effect in sterility induced male rats when compared to C. circinalis possibly due to the presence of flavonoids and various antioxidants. Further the research will be carried out in future for isolating the specific phytoconstituents responsible for fertility effect.

12.2. Acute and subacute toxicity study of C. circinalis and I. suffruticosum:

The haematological, biochemical and histological findings of the acute and sub-acute toxicity tests suggests that the C. circinalis and I. suffruticosum is practically non-toxic when administered orally for an extended period at therapeutic doses. The acute toxicity study shows that the lethal dose of both C. circinalis and I. suffruticosum were determined to be higher than 2000 mg/kg and also regarded as safe within the dose. The sub-acute toxicity study reveals that the ethanolic extract of C. circinalis and I. suffruticosum when given orally at concentration of 1000 mg/kg body weight, will not exhibit any toxicological effect and proved to be safe until 1000 mg/kg.

12.3. Effect of C. circinalis and I. suffruticosum in fertility of young male Wistar rats:

Cycas Circinalis and Ionidium Suffruticosum both have fertility effect, when compared to that of synthetic hormones and were found to be having almost an equal effect for I. Suffruticosum than that of C. Circinalis on the young male Wistar rats. Since the synthetic hormonal preparations have grave side effects, it's better to go with herbal aphrodisiac for better results, without any side effects. Even though herbs (Cc and Is) may take a long period to show their effect in improving the fertility, drastic side effects can be prevented by avoiding synthetic hormonal preparations. The C. circinalis and I. suffruticosum administration has shown significant positive results in improving various fertility parameters and sexual behaviour involved in maintaining maleness. The herbs
were found to increase the testosterone hormone level which in turn induces the production of good quality and increased quantity of spermatozoa and thus there was an increase in sperm count. The Hypothalamo-Pituitary-Gonadal axis might have been induced by the phytoconstituents of Cc and Is, which in turn possibly stimulated the Leydig cells to synthesize testosterone hormone within normal limits.

12.4. Effect of *C. circinalis* and *I. suffruticosum* in fertility of senile male Wistar rats:

The gonadal function declines with age. In male there is progressive atrophy of the sperm producing elements of the testes resulting in diminished spermatogenesis. *I. suffruticosum* (Is) and *C. circinalis* (Cc) has proved to be having a great efficacy in improving the fertility parameters and sexual behaviour of senile rats. The androgenic effects of the herbs were responsible for increased testosterone hormone secretion which in turn increased the size of the seminiferous tubules, induced spermtogenesis and thus raised the sperm count. The testosterone infused positive control showed increased fertility parameters when compared to Cc and Is infused rats. The Is was more effective than Cc in improving the fertility of senile rats.

12.5. Effect of *C. circinalis* and *I. suffruticosum* in fertility of alcohol induced sterility of male Wistar rats:

The *I. suffruticosum* was found to be more effective in restituting the fertility of sterile male Wistar rats. The phytoconstituents such as alkaloids of *C. Circinalis* and *L. Suffruticosum* might have possibly triggered the production of testosterone which was proved by the increased testosterone hormone level in Cc and Is infused group of rats, flavonoids might have acted by resisting the effect of alcohol on gonads which was proved by the restitution of fertility back to normal in sterile rats, tannins might have inhibited oxidation by acting as an antioxidant. The free radicals are harmful byproducts of many normal metabolic processes. To prevent the damage it must be quickly converted into other non-toxic substances. The antioxidants of the natural herbs inhibit the oxidation and prevent the production of free radicals. This study has given us a definite hope about the efficacy of the drug. *I. suffruticosum* was found to be more effective than *C. circinalis* in alcohol induced sterile rats.

12.6. Effect of *C. circinalis* and *I. suffruticosum* in fertility of stress induced sterility of male Wistar rats:

*Cycas Circinalis* and *Ionidium Suffruticosum* has some important phytoconstituents such as alkaloids, flavonoids, terpenoids and phytosterols which might have been beneficial in promoting male sexual behavior in normal rats as well as stress induced sexual dysfunction. Possibly, the active phytoconstituents may produce these effects probably mediated through
Hypothalamo-hypophyseal-adrenocortical axis by regulating abnormality of limbic system through androgen modulating property of phytosteroids, and antistress activity of alkaloids and their protective effect on accessory sexual organs. The *I.suffruticosum* was more effective in regaining the fertility in stress induced rats than the synthetic testosterone hormone and *C.circinalis* administered male rats.

12.7. Effect of *C.circinalis* and *I.suffruticosum* in fertility of diabetes induced sterility of male Wistar rats:

*C.circinalis* (Cc) and *I.suffruticosum* (Is) has antioxidant properties, which may be possibly due to the high level of alkaloids and flavonoids found in these herbs. Alkaloids were used as precursors in the manufacture of steroidal drugs. Flavonoids are functional as disease resistant; Is also contains tannins that inhibit oxidation. The alkaloids might have triggered the production of testosterone, flavonoids might have acted by resisting the effect of diabetes and tannins might have been possibly inhibited oxidation by acting as an antioxidant. These potent properties of Cc and Is may have likely influenced the regenerative effects of testicular tissue observed in the groups, given extracts of Cc and Is. The fertility effect was regained back to normal in diabetic sterile rats by infusion of Cc and Is, out of which Is was found to be more effective in improving the fertility parameters than Cc. The hypolipidemic activity was done earlier by other researchers and the anitdiabetic effects of the herbs were also done as a pilot study in Wistar rats by us and published separately. Furthur the hypoglycemic effect of the herbs (Cc and Is) will be carried out in future in Wistar rats.

The phytoconstituent specificity of the herbs has to be further studied with more parameters with the aids of advanced technology. Furthur the study will be carried out in future to find out the exact mode of action of these herbs (Cc and Is) at cellular levels. In day today practice of Indian system of medicine both the above herbs were given to infertile males, which proved to be more effective in improving the fertility parameters, but the scientific justification for the improvement of fertility has not yet been done till date. After stabilizing the exact mechanism of action of the herbs, the study will be carried out in humans after obtaining the appropriate human ethical clearance.