Evaluation of Antifertility Potential of Ketoconazole and Assessment of its Reversible Effect on Concomitant Treatment with Metformin and Hydroxytyrosol in Rats

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Abstract:
Fifty percent of pregnancies worldwide are unintended despite numerous contraceptive methods available to women. The only male contraceptive methods, vasectomy and condoms, are used by 10% and 16% of couples, respectively. To fix the combinational therapeutical dose the toxicological assessment was done and found to be non-toxic at maximum of 20mg/kg dose level. In the in-vivo pharmacological studies, we tested the toxic effect of Ketoconazole alone and its normalization effect in the formulated ketoconazole and Metformin with Hydroxytyrosol 20mg/ml suspension (KMH) at 5, 10, 20 mg/kg. P.o. on the epididymal spermatozoa.

The adult male rats were exposed to KMH for 14 days. The rats (n=6) were grouped as normal control group which received 2% CMC alone as vehicle. Second group of animals served as positive control treated with only ketoconazole as male infertility agent. Third group of rats were administered with KMH for 14days and left untreated for further period of 14 days. Ketoconazole treatment resulted in a significant decrease in the epididymal sperm count, motility and viability and increased incidence of sperm abnormalities. However, the toxic effect of ketoconazole was reversible in the KMH group.

Thus, the present investigation suggests that the chronic treatment of ketoconazole is capable of inducing male infertility and supplementation with metformin and Hydroxytyrosol combinational therapy significantly helps in regaining the mating behavior, number of spermatozoa in the cauda epididymis, motility of spermatozoa, weights of testes, epididymides, vas deferens and prostate were normalized. The microanatomical architecture of male reproductive organs, mating behavior and F1 litter size and other biochemical parameters in this group confirms the reversal effect of fertility with normal reproductive character in the male rats.

Conclusion: Based on the results obtained in this study, it can be concluded that this combination of drugs at the dose level used can be used to induct safe and reversible male infertility.