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Evaluation of the Effect of Secnidazole on the Relative Weight of the Testis and Epididymis of Male Wistar Rats

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ABSTRACT

Reproductive toxicity is a phenomenon caused by exposure to hazardous chemical substances which interfere or cause detrimental changes in the reproductive system and such substances are called reprotoxic substances. It includes adverse effects on sexual function and fertility in adult male's reproductive system, as well as developmental toxicity in the offspring. The effect of secnidazole on the relative weight of the testis and epididymis of male Wistar rats were evaluated. Forty adult male Wistar rats weighing 150-200g were used for this study. They were allowed to acclimatize to the laboratory environment for two weeks before the commencement of the experiment. Rats in group 1 received 2 ml/kg of distilled water only, group 2 rats received 14.3 mg/kg of secnidazole (low dosage) for 8 weeks; group 3 rats received 28.6 mg/kg of secnidazole (normal dosage) for 8 weeks; group 4 rats received 57.2 mg/kg secnidazole (high dosage) for 8 weeks; Rats in groups 5, 6 and 7 received 14.3 mg/kg, 28.6 mg/kg, 57.2 mg/kg of secnidazole respectively for 8 weeks and they were allowed to recover from treatment for another 8 weeks. There was no significant difference in body weight of rats between the drug-treated and the control (p=0.1981, F=1.7929) and after recovery (p= 09477, F= 0.11864). There was no significant difference in the relative weight of the testis rats between the drug-treated and the control after treatment (p=0.1527, F=2.0357) and after recovery (p = 0.4337, F= 0.9640). There was no significant difference in the relative epididymal weight of the rats between the drug-treated and the control (p=0.1527, F=2.0316) and after recovery (p= 0.3227, F = 1.2561). The absence of a significant change in the relative testicular weight suggests that when compared to its counterpart in the nitro-imidazole drugs, secnidazole may not induce its toxicity through permeation of the blood-testis barrier.
Keywords: Secnidazole, relative weight, testis, epididymis and Wistar rats

INTRODUCTION

Male reproductive toxicity is also associated with derangement in the structures and functions of the male reproductive system such as sperm parameters, abnormal hormonal secretion and abnormal testicular and epididymal functions. It also induces altered variables indicative of oxidative stress like glutathione (GSH) depletion. Infertility has become an ominous problem in Africa on the average, about 10% of all couples face difficulty in starting a family and this creates a feeling of great personal failure [1]. Many factors both extrinsic and environmental factors including the increased use of antibiotics and anti-effective drugs have been implicated as potential causes of male infertility. Studies have shown that antimicrobial combination therapy such as metronidazole, quinolones, tetracycline, ketoconazole, fluconazole and other imidazole group of antibiotic drugs are among the most prescribed classes of drugs in medicine. There is a high possibility that some of the couples presenting with history of infertility or inability to conceive may be due to these groups of drugs [2].

Nitro-imidazole, an antimicrobial drug is among the most clinically prescribed classes of drugs for couples presenting with infertility in the clinics. However, these classes of drug have been shown to possess mutagenic activities in bacterial assay and reproductive toxicity including inhibition of spermatogenesis in rats [2]. Studies have also shown that some nitro-imidazole class of drugs such as metronidazole and ketoconazole may have being responsible for some reproductive toxicity which causes inhibition of spermatogenesis in rats earlier reported by [3].

Secnidazole is one of the representatives of nitro-imidazole group of drugs. It is highly effective and differs from other compounds in this group by a prolonged serum half-life of about 17-29 hours [4]. The prescription of secnidazole have increased due to its pharmacological advantages in treatment of adults and children with intestinal amoebiasis, urinary tract infection (UTI), pelvic inflammatory disease (PID) and vaginal infections mostly of mild or moderate severity [4].

Secnidazole is an anti-biotic with distinct pharmacological properties that are different from other imidazole group of drugs, giving it a relative pharmacological advantage. The frequency of prescription of secnidazole has increased tremendously in recent years due to its pharmacological advantages [4].

The specific objective of the study is to

(a) investigate the effect of secnidazole on the relative weight of the testis and epididymis of male Wistar rats

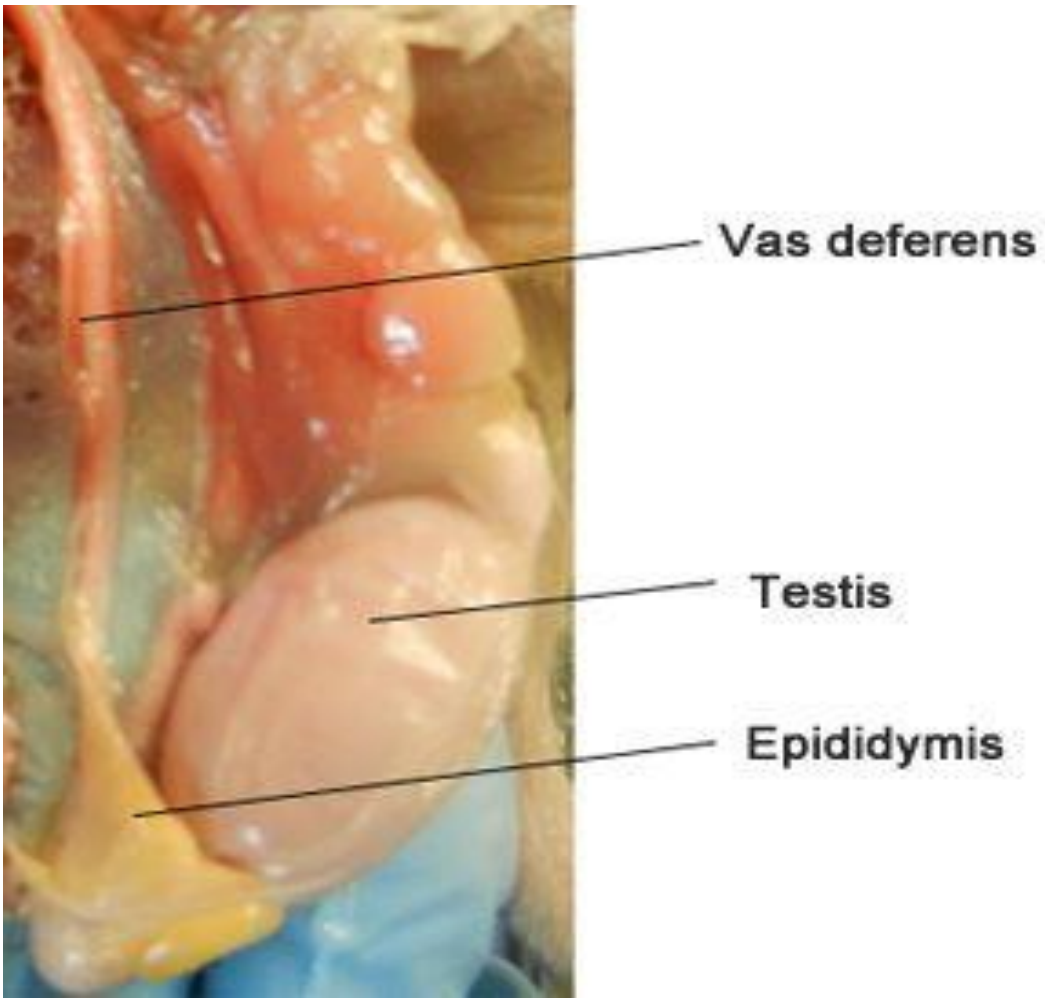

Figure 1: Structures of male Testis in Rats [3]

METHODOLGY

Animals

Forty adult male Wistar rats weighing 150-200g were used for this study. The animals were obtained from the Animal House, College of Health Science, Obafemi Awolowo University, Ile-Ife, Nigeria. The rats were housed in the Animal House, Faculty of Basic Medical Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria. The rats were kept in cages under normal environmental conditions and given free access to standard pellet diet and water. They were allowed to acclimatize to the laboratory environment for two weeks before the commencement of the experiment.

Drugs

Secnidazole was procured by May & Baker Company, Sangto-Otta, Ogun State, Nigeria.

Ethical Clearance

Ethical clearance for this study was obtained from the Health Research Ethics Committee (HREC) of the Institute of Public Health, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Osun State Nigeria. (HREC Assigned Number: IPHOAU/12/1624).

Experimental Design

GROUPS	NUMBER OF RATS	TREATMENTS	NUMBER OF DAYS
GROUP A1 **A2**	5 5	2mls of distilled Water (control)	8 Weeks treated 8 Weeks Recovery
GROUP B	5	14.3mg secnidazole (low dose)	8 Weeks
GROUP C	5	28.6mg secnidazole (medium dose)	8 Weeks
GROUP D	5	57.2mg secnidazole (high dose)	8 Weeks
GROUP E	5	14.3mg secnidazole (low dose)+ Recovery	8 Weeks treated + 8 Weeks Recovery
GROUP F	5	28.6mg secnidazole (medium dose) + Recovery	8 Weeks treated + 8 Weeks Recovery
GROUP G	5	57.2mg secnidazole (high dose)+Recovery	8 Weeks treated + 8 Weeks Recovery

Secnidazole Drug Administration

Rats in group 1 received 2 ml/kg of distilled water only, group 2 rats received 14.3 mg/kg of secnidazole (low dosage) for 8 weeks; group 3 rats received 28.6 mg/kg of secnidazole (normal dosage) for 8 weeks; group 4 rats received 57.2 mg/kg secnidazole (high dosage) for 8 weeks; Rats in group 5, 6 and 7 received 14.3 mg/kg, 28.6 mg/kg, 57.2 mg/kg of secnidazole respectively for 8 weeks and they were allowed to recover from treatment for another 8 weeks.

Stock Solution Preparation

A stock solution of 500mg was prepared in 20mls of distilled water and from this a dosage of 2mls/kg was administered. All administration was done orally with the aid of an oral cannula.

Animal Groupings and Administration

Thirty five male rats were grouped into 7 groups containing 5rats each.

Group A1 (n=5) were given distilled water (2ml/kg) which was the vehicle used to dissolve the drug.

A2 (n=5) were given distilled water and allowed to recover for another 8 weeks

Group B (**n** = 5) received 14.3mg/kg of secnidazole (low dosage) for 8 weeks only [5].

Group C (**n** = 5) Received 28.6mg/kg of secnidazole (medium dosage) for 8 weeks only [5].

Group D (**n** = 5) Received 57.2mg/kg of secnidazole (high dosage) for 8 weeks only [5].

Group E (**n** = 5) Received 14.3mg/kg of secnidazole (low dosage) for 8 weeks once daily and allowed to recover for another 8 weeks [5].

Group F (**n** = 5) Received 28.6mg/kg of secnidazole (medium dosage) for 8 weeks once daily and allowed to recover for another 8 weeks [5].

Group G (**n** = 5) Received 57.2mg/kg of secnidazole (high dosage) for 8 weeks once daily and allowed to recover for another 8 weeks [5]. All administrations were done orally with the aid of an oral cannula.

Mode of Sacrifice and Organ Collection

After eight weeks of administration of secnidazole, the rats were sacrificed by cervical dislocation. Their blood was collected through cardiac puncture. The testis and epididymis were harvested and weighed using digital weighing scale. The right testis of each rat was immediately fixed in Bouin's fluid for histological processing. The semen for sperm parameters was obtained from the caudal epididymis and their sperm parameters were assessed under the microscope. The same sacrificial procedure was repeated for rats in the recovery groups.

Determination of Relative Organ Weight

Relative weight of the testis were calculated at sacrifice as follows:

Relative organ weight =

$$\frac{\text{Organ Weight}}{\text{Body weight at sacrifice}} \times 100$$

Percentage body weight changes were calculated using the formula below;

$$PW = \frac{\text{(Final Body Weight-Initial Body weight)}}{\text{Initial Body Weight}} \times 100$$

Statistical Analysis:

Data were analyzed by using one-way analysis of variance (ANOVA) followed by Students Neuman-Keuls (SNK) and Turkey test for multiple comparisons. Results were expressed as mean ± S.E.M., $p < 0.05$ was taken as accepted level of significant difference.

RESULTS

Effect of secnidazole on change in body weight of male Wistar rats

There was no significant difference in body weight of rats between the drug-treated and the control (p=0.1981, F=1.7929) and after recovery (p= 09477, F= 0.11864). (Fig 1)

Effect of secnidazole on the relative weight of the testis of male Wistar rats

There was no significant difference in the relative weight of the testis rats between the drug-treated and the control after treatment (p=0.1527, F=2.0357) and after recovery (p = 0.4337, F= 0.9640). (Fig 2)

Effect of Secnidazole on relative epididymal weight

There was no significant difference in the relative epididymal weight of the rats between the drug-treated and the control (p=0.1527, F=2.0316) and after recovery (p= 0.3227, F = 1.2561). (Fig 3)

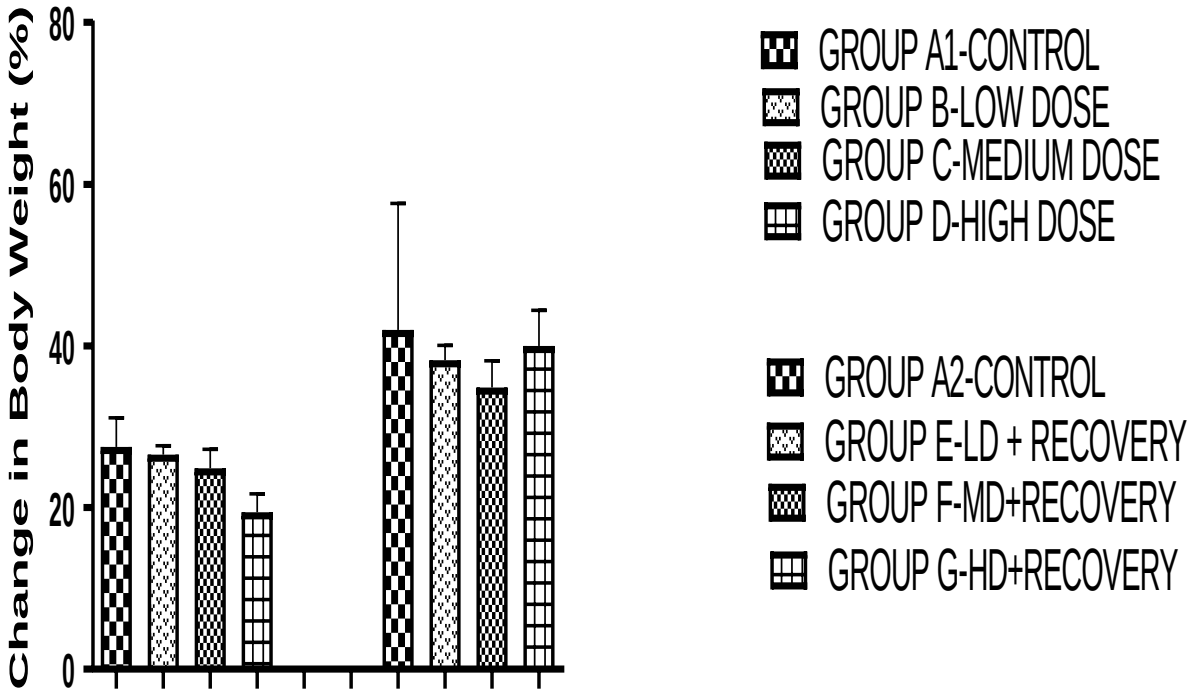

Figure 1: Effect of secnidazole on change in body weight
Graph showing the effects of secnidazole on change in body weight of the male Wistar rats
Results are presented as Mean ± SEM, n = 5 ($p < 0.05$)

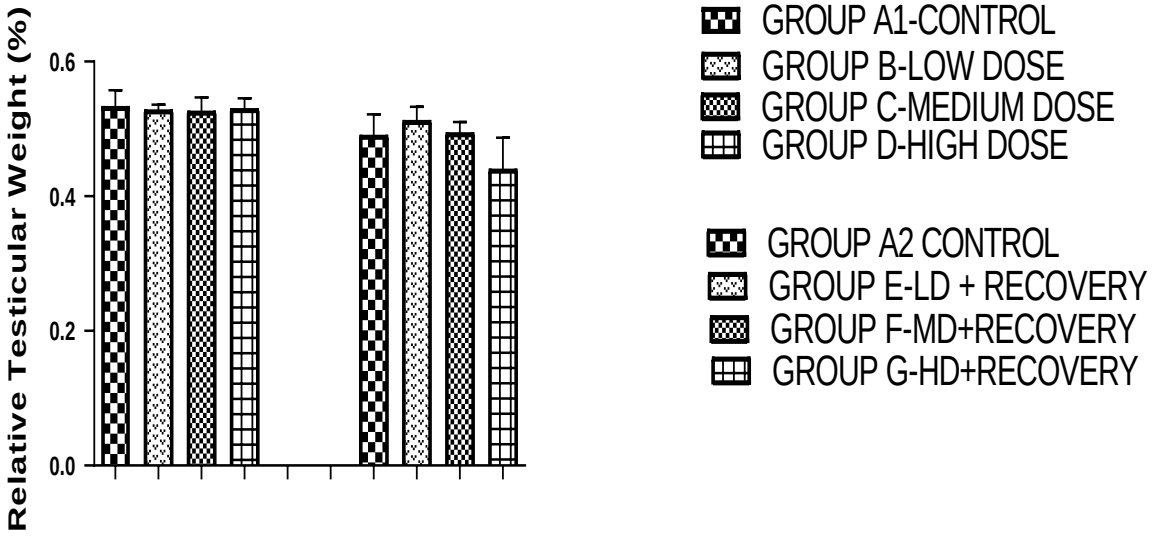

Figure 2: Effect of secnidazole on the relative weight of the testis
Graph showing the effect of secnidazole on the relative weight of the testis
Results are presented as Mean ± SEM, n = 5 ($p < 0.05$)

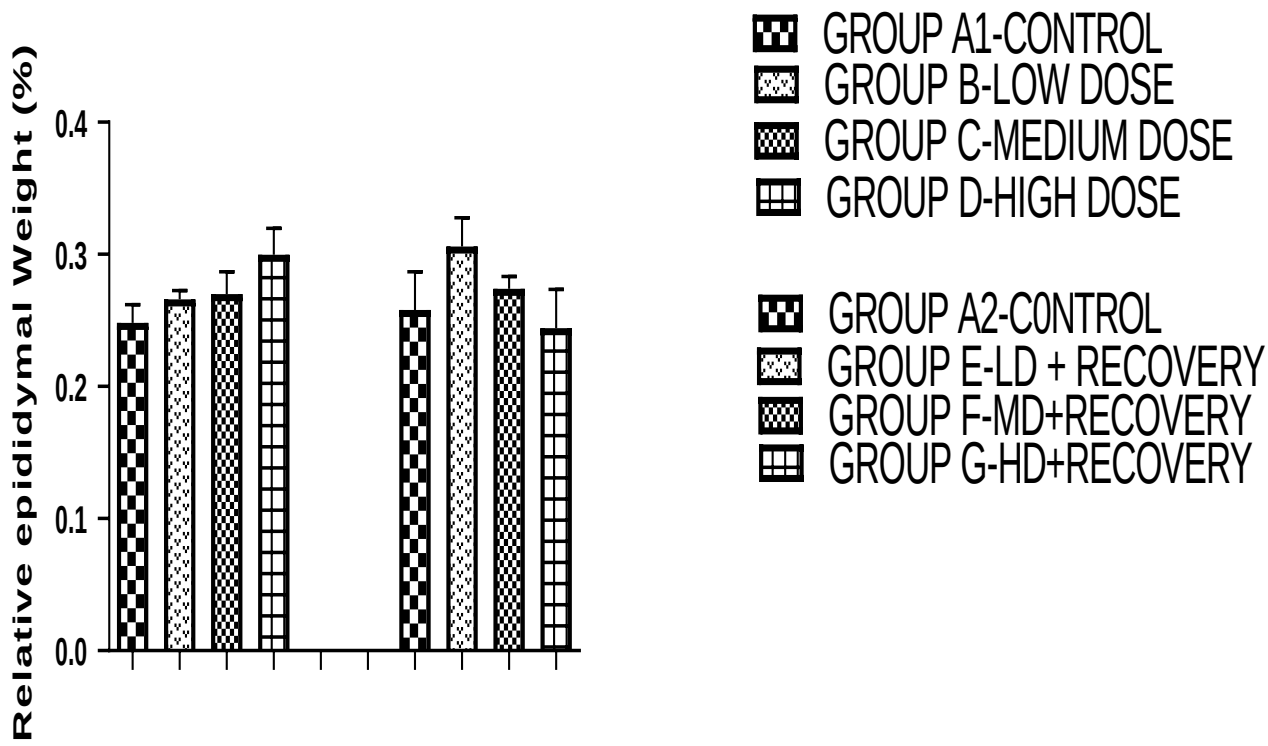

Figure 3: Effect of Secnidazole on relative epididymal weight
Graph showing the effect of Secnidazole on relative epididymal weight
Results are presented as Mean ± SEM, n = 5 ($p < 0.05$)

DISCUSSION

This study assessed the toxicity potential of secnidazole on body weights, relative testicular weight and relative epididymal weight in Wistar Rats. Three doses were administered orally. The lowest dose was 14.3mg/kg and it was a sub therapeutic dose; 28.6mg/kg represented the average daily recommended dose; and 57.2mg/kg was the maximum daily dose. There was no significant change in body weight of the rats in the treated groups when compared with the control following treatment and even after recovery. This may be due to the fact that secnidazole inhibits intestinal absorption thereby preventing lipid deposition (which may promote weight gain). [6] reported a significant reduction in body weight when treated with 200mg/kg and 400mg/kg of metronidazole (a member of nitro imidazole group) for eight weeks. There was no significant difference in the relative testicular weight between the drug treated groups and recovery groups. The existence of blood-testis barrier surrounding the seminiferous tubules in the mammalian testis has been document in literature [7]. The absence of a significant change in the relative testicular weight suggests that when compared to its counterpart in the nitro-imidazole drugs, secnidazole may not induce its toxicity through permeation of the blood-testis barrier. Also, it has been found that ordinazole a group of nitro-imidazole drug cause of no significant change in relative testicular weight of male Wistar rats when treated with 400mg/kg/day for four weeks [8]. Also, there was no significant difference in the relative epididymal weight between the drug treated rats and the control and after recovery. This suggests that the blood epididymis barrier restricted the permeability of epididymal tissues to secnidazole. However, [9,10,11,12]

reported a significant change in the relative epididymal weight when treated with metronidazole a group of nitro-imidazole drug treated with 400mg/kg and 500mg/kg for eight weeks.

CONCLUSION

This study concluded that the absence of a significant change in the relative testicular weight suggests that when compared to its counterpart in the nitro-imidazole drugs, secnidazole may not induce its toxicity through permeation of the blood-testis barrier.

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