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Pathological effects of diethyl nitrosamine (DEN) on testes of wistar albino rats

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Abstract
Diethyl nitrosamine (DEN) is considered a potent hepatotoxin that can induce cell death in various tissues. In this study, pathological effects of DEN on testes of rats was studied. Wistar albino rats were treated with DEN for 120 days and changes in the testes were recorded. Testes showed hypoplasia to complete atrophy with oligospermia to aspermia indicating the toxic effects of DEN on testes.

Keywords: Testes, diethyl nitrosamine, rat

Introduction
Diethyl nitrosamine/ N Nitrosodiethylamine (DEN) is a synthetic, volatile, clear yellow oil soluble in water, lipids and other organic solvents and like other N-nitroso compounds, sensitive to light, which leads to its photodegradation otherwise stable at room temperature in aqueous solution. Many studies prove DEN as a potent hepatocarcinogen whereas no study has been done to prove its effect on reproductive organs. Hence this study aims to focus on adverse effects of DEN on testicular tissue.

Materials and Methods
Animals: Wistar albino male rats (n=12) weighing 150±10 g purchased from Tamil Nadu Veterinary and Animal Sciences University, Chennai, were used in this study. They were housed in polypropylene cages with 12 h light and dark cycle. Animals were fed standard pellet feed and water *ad libitum*. All animal experiments were performed in accordance with the strict guidelines prescribed by the Institutional Animal Ethical Committee (IAEC) and after getting necessary approval (Approval Lr. No. 370/DFBS/IAEC/2021, dated: 16.08.2021).

Chemicals: N-Nitrosodiethylamine (DEN) (Sigma Catalogue No. N0258, ISOPAC, 1 g) was obtained from M/s. Sigma Aldrich Inc., St. Louis, MO, USA and stored at room temperature.

Experimental design: Rats were divided into two groups with six animals in each group. Control group (Sham control), DEN group (0.01% in drinking water every day for 17 weeks). On 120th day, rats were euthanised by CO_2 asphyxiation and lesions were observed.

Histopathology: Testes was collected for histopathology in 10% neutral buffered formalin and processed and stained by H&E stains according to the standard protocol [2].

Results and Discussion
Clinically, DEN induced rats showed piloerection, dullness, emaciation, rough haircoat and bleeding through natural orifices such as mouth and nasal cavity, oedema and haemorrhages at pressure points in paws and extremities were observed. Grossly, both testes in all animals were greatly reduced indicating atrophy (Fig. 1). The most remarkable histopathological change in testicular tissue was hyperplasia of epididymis (Fig. 2), aspermia to oligospermia (Fig. 3), degeneration of all germinal layers, single layer of spermatogonial cells in DEN treated rats. These changes might be caused due to the activation of reactive intermediates through hydroxylation by cytochrome P450 enzymes, resulting in reactive intermediates, which in turn cause the formation of methylated macromolecules, like N7-methylguanine and O6-methylguanine in DNA and these DNA modifications either directly leading to base mispairing or giving rise to apurinic sites that lead to guanine to thymine transformation ultimately leading to tissue damage [3].

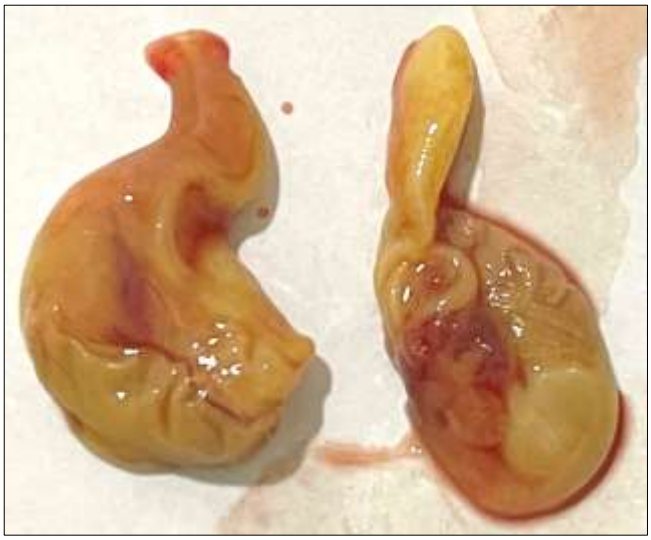

Fig 1: Testicular degeneration in rats treated with DEN on 120th day

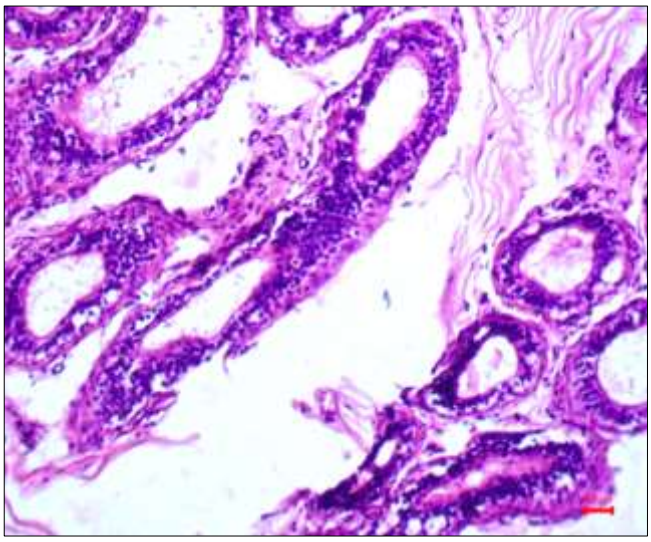

Fig 2: Rat- Testes- DEN- 120d- HP- Hyperplasia of epididymis- H&E Bar=20µm

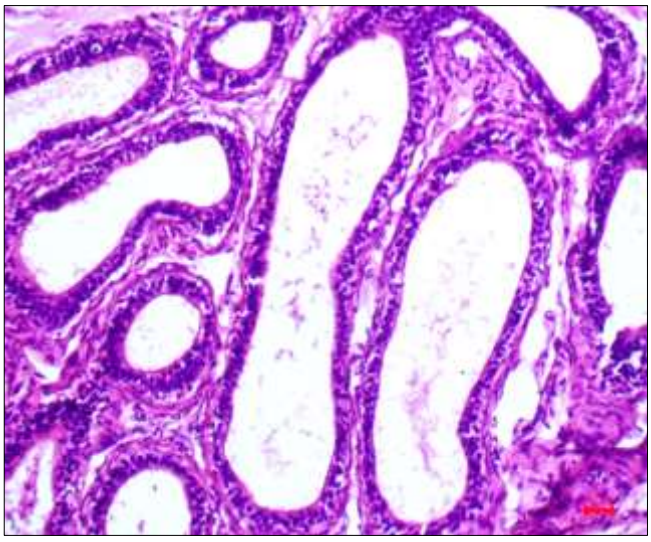

Fig 3: Rat- Testes- DEN- 120d- HP- Aspermia - H&E Bar=20 µm

Conclusion

Based on the results of the study, DEN is found to cause severe testicular degeneration causing decreased libido and reproduction failure apart from carcinogenesis.

References

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