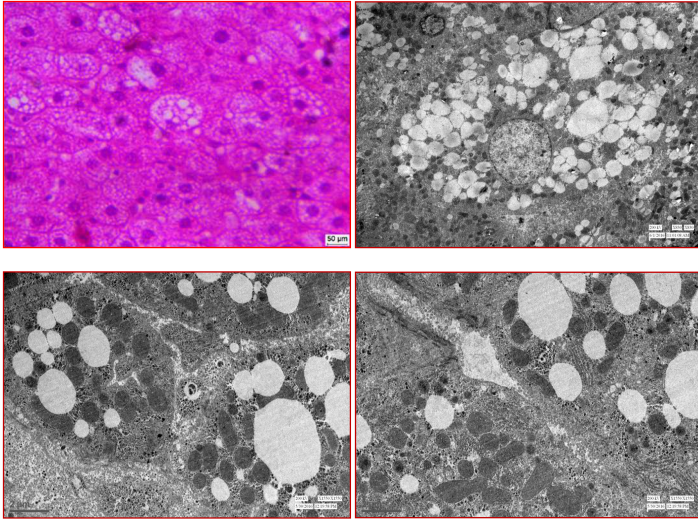


A Handbook on Hepatotoxicity



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Chapter 12

Diethylnitrosamine induced Hepatotoxicity and Hepatocarcinogenesis

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When it was found that diethylnitrosamine (DEN) might be one of the causal agents that generate liver damage in males, the N-nitroso compounds' potential for cancer was first brought to the public's notice (Vesselinovitch and Mihailovich, 1983). A single oral or parental dose of DEN (20 to 40 mg/kg body weight) causes severe liver necrosis in rats, mice, rabbits, guinea pigs, and dogs, which was experimentally verified by Heath and Magee in 1962. In this groundbreaking discovery, it was further demonstrated that the liver lesion that results in DEN-poisoned mice is distinguished by a distinct boundary between the completely damaged parenchyma and regions of the liver cells that appear unharmed (Katoch and Patial, 2021). Extension of these studies subsequently revealed that the chronic application of DEN in rats resulted in a very high incidence of malignant hepatic tumours. The scientists concluded that DEN, because of its chemical and physical features, may be of fundamental importance for the exploration and analysis of hepatic carcinogenesis, even if the particular path mechanism that caused hepatic tumorigenesis was not understood at the time. Many other N-nitroso compounds, notably diethylnitrosamine (figure-1), have been linked to hepatotoxic and