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THE HISTOPATHOLOGICAL, IMMUNOHISTOCHEMICAL AND ULTRASTRUCTURAL ALTERATIONS FOLLOWING ADMINISTRATION OF *NIGELLA SATIVA* IN RATS HEPATOCELLULAR CARCINOMA

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Abstract

Hepatocellular carcinoma (HCC) is the 3rd greatest cause of carcinoma-related deaths. In the present study, the Nigella sativa was used as a pharmaceutical agent in the hepatocarcinogenesis of rats which induced by Diethyl nitrosamine (DEN). Four groups of animals were used and fed ad libitum. The 1st group was a control; the 2nd was fed ad libitum and given 0.2 g/rat/day orally in a watery suspension till the time of sacrifice. The 3rd group was intraperitoneally injected with a single dose of DEN 150 mg k-1 b.wt. The 4th group was intraperitoneally injected with DEN and after one week, the each rat was given *Nigella sativa* as in group 2 at dose 0.2 g/rat/day. The results of the present study observed that Nigella sativa treated rats showed normal liver histology, immunohistochemistry as seen as in normal liver of control rats, but DEN injected group produced a variety of lesions ranging from severe inflammatory reaction to liver carcinogenesis compared to the control group. PCNA and P53 expression were significant nuclear positive staining in DEN group ($p<0.0001$). In the ultrastructural level, the most striking feature in the DEN-injected rats was the appearance of hepatocyte with abnormal nucleus elongated and spherical mitochondria, dilated extracellular spaces, elongated and spherical mitochondria (polymorphism), aggregation of glycogen particles and lipid vacuoles. Rats treated with diethyl nitrosamine and protected with *Nigella sativa* extract, showed hepatocytes with normal nuclei, large number of mitochondria and well developed RER indicating liver regeneration; extensive RER reflected the activity of the cell to produce high amount of proteins needed for normal differentiation. These results showed that supplementation of diet with *Nigella sativa* has a protective effect against DEN-induced, inflammatory response and carcinogenesis in rat liver. So, the present study suggested that using *Nigella sativa* is the useful therapeutic agents in hepatocarcinogenesis in rats.

Keywords: Hepatocellular carcinoma, Nigella sativa, P53, PCNA, Ultrastructure