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Cytological and Histological Studies on the Hepatotoxic Effects of Sorafenib (Nexavar) in Albino Rats

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Background: Sorafenib (Nexavar) is an oral inhibitor of multi-kinase proteins approved in 2005 for treatment of metastatic advanced hepatocellular carcinoma. It causes many metabolic side effects, including diarrhea, hypertension, hand-foot skin reaction, and fatigue. This study aims to detect the histopathological, histochemical and DNA contents changes of the rat's liver under Nexavar treatment. **Methods:** The rats were divided into 3 groups. • Group 1: Served as control (rats were orally administrated with ml of normal saline for a month. • Group 2: Rats of this group were treated with the multikinase inhibitor Sorafenib (60 mg/kg body weight/day) for 15 days by gavage. • Group 3: Rats of this group were treated with the multikinase inhibitor Sorafenib (60 mg/kg body weight/day) for 30 days by gavage. Animals were sacrificed and specimens from the liver were processed for histopathological, histochemical; by estimation of total carbohydrates and total protein contents; and cytological studies by estimation of DNA contents at the different stages of the cell cycle by the flow cytometer analysis. **Results:** In treated animals, there were histopathological and histochemical alterations, as a destruction of the normal hepatic architecture, swollen hepatocytes with vacuolar degenerated cytoplasm. Some hepatocytes showed mild to severe signs of injury such as swelling of their nuclei. Karyolysis of other hepatocytes are encountered. Severe reduction in the glycogen and proteins contents of the hepatocytes was observed by using PAS and bromophenol blue staining techniques. Moreover, the results showed that Nexavar causes apoptosis by 15.41% and 13.72% in both groups 2 and 3, respectively. Liver genotoxicity induced by Nexavar for 15 and 30 days decreases the G1 cells constitute to 5.08% and 6.50% and increases the S-phase cells constitute to 19.17% and 20.28%, respectively. Moreover, the G2 cells increases to 2.32% and 2.45, about half of the last amount is aneuploidy cells. **Conclusion:** Nexavar treatment showed mild to moderate hepatotoxic effects and induces many histological, histochemical and cytological changes causing liver damage.