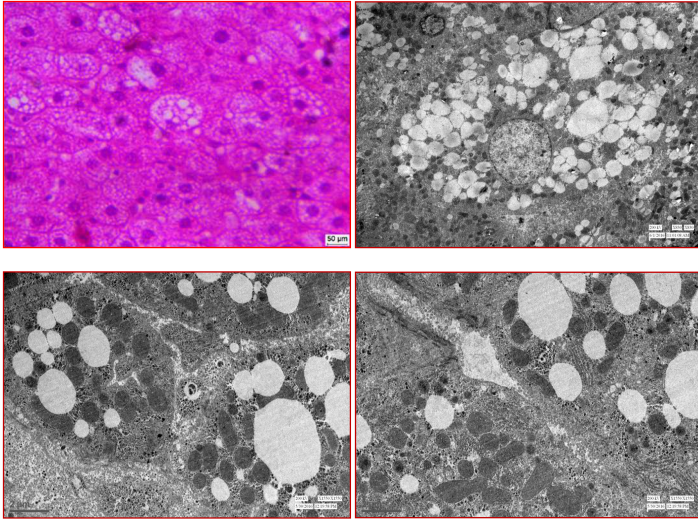


A Handbook on Hepatotoxicity



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Chapter 2

Biochemical and Physiological Pattern of Hepatotoxicity

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Liver is the largest organ in body that filters and processes blood. It metabolizes nutrients, detoxifies harmful substances, makes blood clotting proteins, and performs many other vital functions. The cells in the liver contain proteins called enzymes that drive various chemical reactions. Liver is often the target organ for chemically induced injuries. Several factors contribute to the liver's susceptibility for induction of hepatotoxicity. Most xenobiotics enter into body through mouth and reach to gastrointestinal tract and, after absorption, are transported by hepatic portal vein to liver. Thus, liver is the first organ perfused by chemicals that are absorbed in the gut and is exposed to the highest concentrations of xenobiotics. High concentration of xenobiotic metabolizing enzymes is present in liver for detoxification of xenobiotics. There is primarily cytochrome P450-dependent monooxygenase system. During bio-transformations of xenobiotics, many oxidative reactions produce reactive metabolites that can induce lesions within the liver. Centrilobular region of liver is the main site of damage. Hepatocytes in this localization have the highest concentration of cytochrome P450s