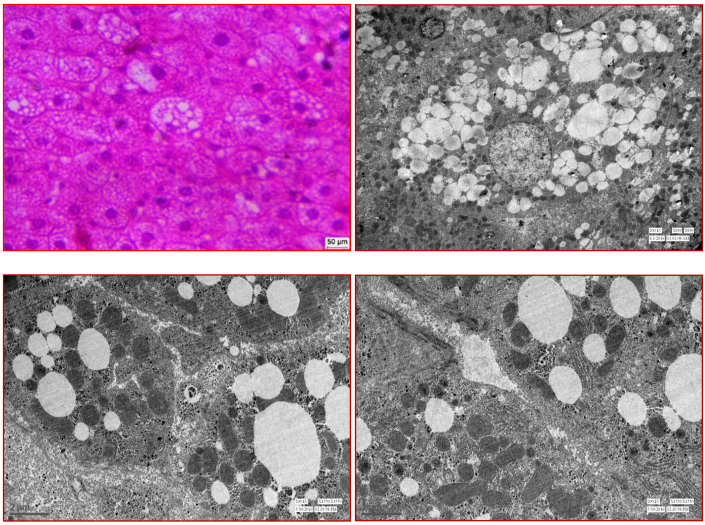
A Handbook on

Hepatotoxicity



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α-Naphthylisothiocyanate induced Hepatotoxicity

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α-Naphthyl isothiocyanate (ANIT) is a hepatotoxicant that has been used primarily as a tool to study the pathogenesis of chemical-induced cholestasis, particularly drug-induced cholestasis. Its mechanisms of cholestasis involve impairment of bile salt transporter expression, disruption of hepatic tight junction and, lately, biliary obstruction due to desquamation of the epithelial cells of the bile duct. ANIT also causes death of hepatocytes and cholangiocytes by necrosis and apoptosis, both by direct toxic action and, indirectly, through the generation of an intense inflammation associated with the infiltration of neutrophils around the hepatocytes and bile ducts; this inflammatory state leads to the production of reactive oxygen species (ROS), thus inducing oxidative stress which can also cause death of hepatocytes and cholangiocytes, with the subsequent formation of obstructive cellular debris. Many of these alterations are similar to that occurring in obstructive cholangiopathies such as primary sclerosing cholangitis and this is why ANIT-induced cholestasis has been used as an experimental model to mimic this disease.