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Review

Models of hepatotoxicity and the underlying cellular, biochemical and immunological mechanism(s): A critical discussion

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ABSTRACT

Liver is a primary organ involved in biotransformation of food and drugs. Hepatic diseases are a major worldwide problem. Hepatic disorders are mainly caused by toxic chemicals (alcohol), xenobiotics (carbon tetrachloride, chlorinated hydrocarbons and gases CO_2 and O_2) anticancer (azathioprine, doxorubicin, cisplatin), immunosuppressant (cyclosporine), analgesic anti-inflammatory (paracetamol, thioacetamide), anti-tubercular (isoniazid, rifampicin) drugs, biologicals (Bacillus-Calmette–Guerin vaccine), radiations (gamma radiations), heavy metals (cadmium, arsenic), mycotoxin (aflatoxin), galactosamine, lipopolysaccharides, etc. Various risk factors for hepatic injury include concomitant hepatic diseases, age, gender, alcoholism, nutrition and genetic polymorphisms of cytochrome P_{450} enzymes have also been emphasized.

The present review enumerates various in vivo animal models and in vitro methods of hepatic injury using diverse toxicants, their probable metabolic pathways, and numerous biochemical changes viz. serum biomarkers enzymes, liver function, oxidative stress associated events like free radicals formation, lipid peroxidation, enzyme antioxidants and participation of cytokines (tumour necrosis factor-α, transforming growth factor-β, tumour necrosis factor-related apoptosis inducing ligand), and other biomolecules (Fas and C-jun N-terminal kinase) are also discussed. The underlying cellular, molecular, immunological, and biochemical mechanism(s) of action responsible for liver damage (toxicity) are also been discussed. This review should be immensely useful for researchers especially for phytochemists, pharmacologists and toxicologists working on hepatotoxicity, hepatotoxic chemicals and drugs, hepatoprotective agents and drug research organizations involved especially in phytopharmaceuticals and other natural products.

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