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ACCEPTED MANUSCRIPT

Sunitinib induces hepatocyte mitochondrial damage and apoptosis in mice

Short title: Sunitinib and liver function in mice

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Highlights

- Sunitinib (7.5 mg/kg) for 14 days causes hepatocellular injury in mice
- Hepatocellular injury can be explained by hepatocyte apoptosis and necrosis
- Hepatocellular injury is a consequence of repetitive direct mitochondrial damage

Abstract

Reports concerning hepatic mitochondrial toxicity of sunitinib are conflicting. We therefore decided to conduct a toxicological study in mice. After having determined the highest dose that did not affect nutrient ingestion and body weight, we treated mice orally with sunitinib (7.5 mg/kg/day) for 2 weeks. At the end of treatment, peak sunitinib plasma

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