Effects of iron-tanning acid nanoparticles on hepatocarcinogenesis in rats

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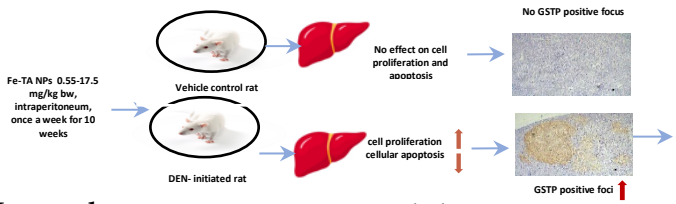
Abstract: Metal-polyphenol nanoparticles have been proposed as a tool for combined therapy in cancer diagnosis and treatment. Iron-tannic acid nanoparticles (Fe-TA NPs) are reported to have anti-proliferative effect via enhanced autophagic death of liver cancer cells. Furthermore, Fe-TA NPs provide MRI signal in both liver cancer cells and preneoplastic rat livers. Our previous studies demonstrated that Fe-TA NPs were not mutagenic and clastogenic in both mutated bacterial and animal models. The lethal dose at 50% (LD_{50}) of Fe-TA NPs via intraperitoneum was greater than 55 mg/kg body weight (bw) in rats evaluated by acute toxicity test. The 28-day repeated dose toxicity studies in both sexes of rats in the doses ranging from 0.22-5.5 mg/kg bw via intraperitoneum every 3 days for 10 times did not alter the level of standard blood parameters and pathological changes. This study investigated the effect of Fe-TA NPs on hepatocarcinogenesis in rats. Medium-term carcinogenicity test was conducted in 3 various doses of Fe-TA NPs, ranging from 0.55-17.5 mg/kg bw, via intraperitoneum weekly for 10 times. It was found that Fe-TA NPs did not induce the formation of preneoplastic lesions, glutathione S-transferase placental form (GST-P) positive foci. However, Fe-TA NPs at the dose of 1.75 mg/kg bw enhanced both number and size of GST-P positive foci in diethylnitrosamine-induced rats indicating non-genotoxic carcinogenicity. It increased the number of proliferating cell nuclear antigen positive hepatocytes but decreased the number of apoptotic cells in rat livers. In conclusion, the relationship between Fe-TA NPs and hepatocarcinogenicity might be in a fashion of inverted U-shape regulated by the balance of cell proliferation and apoptosis in the liver.

Graphical abstract:



Keywords: Hepatocarcinogenesis, Diethylnitrosamine, Iron, Tannic acid, Nanoparticle

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