Optimization of the effectiveness and cytocompatibility of -Nigella sativa as a co-treatment for reducing methotrexate related adverse effects

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Abstract:

Methotrexate (MTX) is mainly used as antimetabolite agents in cancer therapy. It causes serious side effects such as nephrotoxicity, hepatotoxicity, and anemia. Nigella sativa (NS) is a medicinal herb that has protective effects against the MTX-related side effects. The study aimed to determine the optimal concentration of the combination of NS-MTX mixture to improve the antitumor effects of MTX and reduce its related adverse effects. In this study, in vitro evaluation of anti-tumor and anti-angiogenic activities of NS, MTX, or their mixture in different concentrations using liver hepatocellular carcinoma and endothelial cells were performed. The protective effects of NS on normal hepatic and kidney cells against the risks of MTX treatment was also tested in vitro. Moreover, for in vivo evaluation, male Wistar rats were treated with MTX or a combination of MTX and NS. Hematological and serological, biochemical, functional, and histopathological studies were performed. The results showed that the low concentration of NS enhanced the anti-tumor and anti-angiogenic effects of MTX. Moreover, it had protective effects on normal hepatic and kidney cells against toxicity induced by MTX treatments. The in vivo results showed significant improvements in the blood condition and liver functional parameters in MTX-intoxicated rats after treating with NS. NS reduced the oxidative stress indices in both kidney and liver tissues. The histopathological examinations showed that NS reduced degenerative changes and necrosis in both kidney and liver. These results suggested that NS in low concentration could improve the efficacy and the safety of MTX treatment.

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