Thymoquinone-loaded nonostructured lipid carriers : preparation, gastroprotection, in vitro toxicity, and pharmacokinetic properties after extravascular administration

ABSTRACT

Background: Nanostructured lipid carriers (NLCs), composed of solid and liquid lipids, and surfactants are potentially good colloidal drug carriers. Thymoquinone is the main bioactive compound of Nigella sativa. In this study, the preparation, gastroprotective effects, and pharmacokinetic (PK) properties of thymoquinone (TQ)-loaded NLCs (TQNLCs) were evaluated. Method: TQNLCs were prepared using hydrogenated palm oil (Softisan® 154), olive oil, and phosphatidylcholine for the lipid phase and sorbitol, polysorbate 80, thimerosal, and double distilled water for the liquid lipid material. A morphological assessment of TQNLCs was performed using various methods. Analysis of the ulcer index, hydrogen concentration, mucus content, and biochemical and histochemical studies confirmed that the loading of TQ into the NLCs significantly improved the gastroprotective activity of this natural compound against the formation of ethanol-induced ulcers. The safety of TQNLC was tested on WRL68 liver normal cells with cisplatin as a positive control. Results: The average diameter of the TQNLCs was 75 ± 2.4 nm. The particles had negative zeta potential values of −31 ± 0.1 mV and a single melting peak of 55.85°C. Immunohistochemical methods revealed that TQNLCs inhibited the formation of ethanol-induced ulcers through the modulation of heat shock protein-70 (Hsp70). Acute hepatotoxic effects of the TQNLCs were not observed in rats or normal human liver cells (WRL-68). After validation, PK studies in rabbits showed that the PK properties of TQ were improved and indicated that the drug behaves linearly. The Tmax, Cmax, and elimination half-life of TQ were found to be 3.96 ± 0.19 hours, 4811.33 ± 55.52 ng/mL, and 4.4933 ± 0.015 hours, respectively, indicating that TQ is suitable for extravascular administration. Conclusion: NLCs could be a promising vehicle for the oral delivery of TQ and improve its gastroprotective properties.

Keyword: Lipid based nanoparticles; Black seed oil; Gastric ulcer