Development of a Colon-Targeted Grape Seed Extract-Based Nanomedicine for Ulcerative Colitis

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Abstract

Polymeric nanoparticles present a hopeful strategy for localized-site delivery of herbal phytoconstituents in the management of colon disorders such as ulcerative colitis. Grape seed extracts (GSEs) are a rich source of phytoconstituents with a famous anti-inflammatory activity against ulcerative colitis. However, their clinical utilization is limited due to poor water solubility and absence of targetability towards ulcerative colitis lesions. This study aims to improve the selectivity and efficiency of hydrophobic GSEs by loading them in colon-targeted polymeric nanoparticles (NPs). Herein, The GSEs loaded NPs were synthesized using flash nanoprecipitation method, optimized using various theoretical amounts and polymeric base, and thoroughly characterized. The study found that encapsulating 4 mg of Obeidi grape seed extract (OB) in Eudragit S100 -poly (ethylene glycol)-poly(lactide-co-glycolide) (ES100-PEG-PLGA) NPs coated with hyaluronic acid (HA) for colon targeting showed high loading efficiency, stability, targetability, and sustained release at colonic pH. The cellular uptake and cellular reactive oxygen species (ROS) assays in murine macrophages showed that HA-coated OB NPs had higher cellular internalization and ROS suppression activity in comparison with nontargeted NPs and free extract. The in vivo studies on dextran sulfate sodium (DSS) - induced colitis murine model showed that 20 mg/Kg/day of HA-OB NPs significantly decreased disease activity index (DAI) scores and exhibited normal histological appearance in comparison with the colitis group, but no significant effect could be found on pro-inflammatory cytokines and colon length shortening. Overall, the results highlight the promising potential of GSEs within HA-targeted ES100-PEG-PLGA NPs as a dosage form for UC targeting and treatment.

Keywords: DSS-induced ulcerative colitis, Grape Seed Extracts, polymeric nanoparticles, colon-targeted delivery.