Chitosan Dextran Microparticles as the Potential Carrier for Colon Specific Delivery of 5- Fluorouracil

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Abstract

Introduction: Colorectal cancer is one of the most commonly diagnosed cancers in the world. The main and classic treatment of this cancer is 5-fluorouracil (5-Fu) that its cytotoxicity and low systemic absorption restricted its therapeutic efficacy. To overcome these problems, mucoadhesive and colonic microbially degradable formulations based on chitosan and dextran sulphate hydrogels could be effective.

Methods and Results: 5-Fu loaded hydrogel microparticles were formed via polyelectrolyte complexation technique using chitosan and dextran sulphate solutions. It was optimized by a systematic multi-objective optimization approach in terms of the particle size and loading efficiency of the resulting microparticles. Under this condition, the molecular weight of chitosan and 5-Fu concentration are the two factors which significantly influence the particle size and loading efficiency, respectively. Then the optimized microparticles were prepared and were characterized based on particle size, zeta potential, drug loading and drug release behavior. Finally the cytotoxicity of optimized microparticles was assessed by MTT assay (SW742 cell line) compare to free drug solution. Therefore, spherical particles of 51.33±0.95 µm mean diameter and a narrow size distribution were obtained under optimal conditions. The zeta potential, loading efficiency and loading capacity of optimized microparticles were 18.1±0.87mv, 26.96±0.38 and 13.12±0.65%, respectively. The *in vitro* drug release profile was fitted on Higuchi model and the cytotoxicity MTT results indicated the higher cytotoxicity of studied formulation on cells compare to free drug. The hydrogel microparticles were further lyophilized to prepare the enteric coated tablets and all tests endorsed that the coating process was suited.

Conclusions:

The designed formulations have provided appropriate properties and offer a potential mean for colon specific delivery of 5-Fu via oral administration.

Key words: 5-fluorouracil, Colon delivery, colorectal cancer, Drug release, Hydrogel.

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