

Liver targeted delivery of quercetin in hepatocellular carcinoma by phytosterol containing solid lipid nanoparticles

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Background and Aims: Quercetin is a potential chemotherapeutic drug with many biological activities. However, the insolubility of quercetin seriously limits its clinical use. Sterols can make fluent bilayer with high cellular penetration. Therefore due to lack of any report on their use in solid lipid nanoparticles (SLN) and their ability to accumulate in the liver, the aim of this study was to design sterol containing SLNs of quercetin with possible higher cellular penetration for targeting hepatocellular carcinoma cells.

Methods: 23 different formulations of quercetin-loaded SLNs (QT-SLNs) were prepared using three variables including: lipid type (cholesterol, stigmasterol and stigmastanol), drug and lipid content in a surface response D-Optimal design by emulsification solvent evaporation method. The particle size and zeta potential were measured by Malvern Nanosizer. Transmission electron microscopy (TEM) was used to study the morphology of QT-SLNs and their fluidity was studied by DSC analysis. Drug loading capacity (DL%) was determined spectrophotometrically. The drug release test was studied by dialysis method and release efficiency (RE%) was calculated. Cytotoxicity of SLNs was determined by MTT assay on HepG-2 cells and cellular uptake by flow cytometry.

Results: SLNs prepared by 20 mg stigmastanol and 10 mg quercetin showed the optimum results from physicochemical point of view. These SLNs with particle size of 121.86 nm, drug release efficiency of 63.92%, drug loading percent of 99.87% and zeta potential of -16.6 mV showed good stability and were used for cell culture studies. The QT-SLNs showed spherical shape in TEM. Cytotoxicity tests on HepG-2 cells showed promising results for enhanced cytotoxicity of quercetin.

Conclusions: QT-SLNs which prepared by phytosterols have more fluidity and can effectively accumulate in hepatocellular carcinoma cells. Thus they might be useful for liver targeting of quercetin.

Keywords: Quercetin; Phytosterol; Lipid nanoparticles; Hepatocellular carcinoma