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ORIGINAL ARTICLE

Designing polymeric microparticulate drug delivery system for hydrophobic drug quercetin

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Abstract The aim of this study was to investigate pharmaceutical potentialities of a polymeric microparticulate drug delivery system for modulating the drug profile of poorly water-soluble quercetin. In this research work two cost effective polymers sodium alginate and chitosan were used for entrapping the model drug quercetin through ionic cross linking method. In vitro drug release, swelling index, drug entrapment efficiency, Fourier Transforms Infrared Spectroscopy (FTIR), Scanning Electron Microscopy (SEM), X-ray Diffraction (XRD) and Differential Scanning Calorimetric (DSC) studies were also done for physicochemical characterization of the formulations. Swelling index and drug release study were done at a pH of 1.2, 6.8 and 7.4 to evaluate the GI mimetic action which entails that the swelling and release of the all the Formulation1 (F1), Formulation2 (F2) and Formulation3 (F3) at pH 1.2 were minimal confirming the prevention of drug release in the acidic environment of stomach. Comparatively more sustained release was seen from the formulations F2 & F3 at pH 6.8 and pH 7.4 after 7 h of drug release profiling. Drug entrapment efficiency of the formulations shows in F1 (D:C:A = 2:5:30) was approximately 70% whereas the increase in chitosan concentration in F2 (D:C:A = 2:10:30) has shown an entrapment efficiency of 81%. But the comparative further increase of chitosan concentration in F3 (D:C:A = 2:15:30) has shown a entrapment of 80% which is not having any remarkable difference from F2. The FTIR analysis of drug, polymers and the formulations indicated the compatibility of the drug with the polymers. The smoothness of microspheres in F2 & F3 was confirmed by Scanning Electron Microscopy (SEM). However F1 microsphere has shown more irregular shape comparatively. The DSC studies indicated the absence of drug-polymer interaction in the microspheres. Our

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XRD studies have revealed that when pure drug exhibits crystalline structure with less dissolution profile, formulated microparticles can help us to obtain amorphous form of the same drug that is likely to have more dissolution property. The findings of the study suggest that the microsphere formulations were a promising carrier for quercetin delivery and can be considered as a favorable oral controlled release dosage form for hydrophobic drug quercetin.

1. Introduction

Researchers have treasured the potential benefits of micro technology in providing vast improvements in drug delivery. The method by which a drug is delivered can have a noteworthy effect on its efficacy. One of the most attractive areas of research in drug delivery today is the design of micro-particulate systems that are able to deliver drugs to the right place, at appropriate times and at the right dosage. Recently, the idea of using microparticles made from natural biodegradable polymers to deliver drugs has provoked great interests. Among them, keeping the cost effectiveness in mind two polymers have been used alginate and chitosan which are very promising and have been widely subjugated in pharmaceutical industry for controlling drug release as revealed from the previous article of Hamidi et al., 2008.

Gombotz and Wee (1998), Smidsrod and Skjakbraek (1990) and Murata et al. (2007) have reported that alginate can be used as mucoadhesive, biodegradable and has prospective for numerous pharmaceutical and biomedical applications such as drug delivery system and cell encapsulation. Chitosan, a linear polysaccharide consisting of glucosamine and *N*-acetyl glucosamine units, is biocompatible, biodegradable, and nontoxic in the application of peroral delivery of drugs as reported by Kotze et al. (1999) and Shi et al. (2008).

The drug Quercetin has been extensively investigated for its antioxidant, antitumor, hepatoprotective activity by the previous researchers like Inal and Kahraman (2000), Hertog et al. (1992), Kanadaswami et al. (2005). But at the same time it has been noticed in spite of having so many therapeutic effect oral administration of quercetin has been limited by its poor bioavailability which can be evidenced from the work of Davis et al., 2000. Several attempts were made for increasing the bioavailability of the quercetin by different researchers including the complexation with cyclodextrin and liposome as seen in the work of Jessy and Sneha (2012). Nevertheless, the use of cyclodextrin is associated with a risk of nephrotoxicity and employing liposome might incur stability problems during storage as supported by the work of Frijlink et al. (1990). However no attempts have been made for increasing the oral bioavailability of quercetin by incorporating the drug in the matrix of biopolymers like chitosan and sodium alginate which on the other hand promises the drug delivery to a higher intestinal pH in which the drug is soluble enough.

It is therefore clear that a safe, stable, and efficient delivery method in increasing the solubility of quercetin is warranted. In the present research work quercetin microparticulate system has been prepared by a simple ionic cross linking technology with sodium alginate and chitosan as carriers and also the effect of the chitosan concentration on drug release profile has been evaluated. Physicochemical characterization of the formulations has been done by in vitro drug swelling index study, Scanning Electron Microscopy (SEM), differential scanning calorimetry (DSC), powder X-ray Diffraction (XRD), Fourier transform infrared spectroscopy (FT-IR).

2. Experimental

2.1. Materials

Chitosan, 75–85% deacetylated, intermediate viscosity (Brookfield, 1% solution in acetic acid) 20–300 cP, sodium alginate and quercetin were purchased from Sigma Aldrich, India. The other entire reagent used was of analytical grade.

2.2. Preparation of quercetin microparticles

The formulations were made according to the described method of the previous researcher Wittaya-areekul et al. (2006). Briefly all the chitosan solutions (0.5%, 1% and 1.5%w/v) were prepared by dissolving chitosan in a solution of 1% acetic acid followed by the addition of 4% calcium chloride. The whole solution was homogenized at 500 r.p.m for 1 h. The sodium alginate solution at a concentration of 3% (w/v) was prepared. After complete mixing of sodium alginate quercetin was added in the concentration of 0.2% (w/v). The sodium alginate-drug solution was then dropped to the chitosan–calcium chloride solution through a 0.45 mm syringe needle at a dropping rate of 1.0 ml/min. The microparticles were allowed to harden for 2 h before washing them and were then dried at room temperature.

2.3. Microparticles characterization

2.3.1. Determination of Drug Entrapment Efficiency (DEE)

The quercetin content was determined by dissolving 100 mg of microparticles in phosphate buffer of pH 7.4 under sonication (Front line sonicator FS600) for 30 min until the microparticles were completely dissolved. After that the samples were filtered and analyzed spectrophotometrically (Thermo Spectronic, UK) at 370 nm.

The encapsulation efficiency was calculated using the following formula.

$$\text{Drug entrapment efficiency } (\%) = (\text{calculated drug concentration} / \text{theoretical drug concentration}) \times 100$$

2.3.2. In vitro release studies

Drug release profiles from alginate/chitosan microparticles containing quercetin with an accurately weighed amount of