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ORIGINAL MANUSCRIPT

Novel interpenetrating polymeric network based microbeads for delivery of poorly water soluble drug

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Abstract

A well-designed drug delivery platform improves the pharmacological properties of therapeutics. Here, we report a biodegradable interpenetrating polymer network (IPN) microbeads delivery technology developed by crosslinking a polymer blend of poly(-vinyl alcohol), xanthan gum, and sodium alginate to enhance the solubility of poorly soluble drugs. The microbeads effectively improve the solubility of a model BCS Class IV drug, norfloxacin, known for its low solubility and low permeability. Differential scanning calorimetry, powdered X-ray diffractometry, and FT-IR data showed that the IPN microbeads solubilised and encapsulated the drug within the network. We found over 83% encapsulation efficiency for norfloxacin and this efficiency increases with the concentration of polymer. Ex vivo experiments using caprine intestine revealed that the IPN microbeads adhered to the intestinal epithelium, a mucoadhesive behaviour that could be beneficial to the drug pharmacokinetics while in vitro experiments in phosphate buffer show that the IPN enables significant drug release. We believe that these IPN microbeadsare an excellent drug delivery system to solubilise norfloxacin, ensure adhesion to the intestinal wall, thereby localising the drug release to enhance bioavailability of poorly soluble drugs.

Keywords Interpenetrating polymer network (IPN) · Drug delivery · BCS class drug · Ex-vivo · Bioavailability

Introduction

The oral route of administration remains the most convenient to deliver drugs [1]. However, low bioavailability due to poor drug transport through the intestinal epithelium as well as poor target and degradation due to the harsh biochemical and physiological conditions of the gastrointestinal tract limit utilization of the oral route. A well-designed drug delivery system can overcome some of these challenges by improving bioavailability and eventually enhancing the therapeutic efficacy [2, 3]. Microbeads are emerging as multiparticulatedrug delivery systemwith the potential to effectively deliver drugs orally [4–6], therefore, are an alternative to conventional oral dosage forms [7]. Spherical microbeads are comparatively easy to prepare, especially usingstarch, gum, chitosan, and alginate. Typical of multiparticulate delivery systems, microbeads can be engineered into controlled or sustained drug release technology to improve bioavailability, reduce adverse effects, prolong drug action, and ensure reproducible and predictable pharmacokinetic and pharmacodynamic responses [8]. Depending on need, it may be necessary to formulate beads into long-acting dosage form to effectively and precisely target biological site [9–11].

Designing microbeads involves combining two or more polymers. An interpenetrating networked (IPN) microbeads [12], for example, is a composite of two or more polymers that do not necessarily crosslink but in the presence of another chemical entity form a crosslinked network. Recently, considerable attention is focused on engineering hydrophilic polymers-derived IPN multiparticulate systems [13–18] into

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