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RESEARCH ARTICLE

Diclofenac Sodium-Loaded Eudragit® Microspheres: Optimization Using Statistical Experimental Design

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Abstract
Purpose In this study, polymeric microspheres containing diclofenac sodium were prepared by single emulsion (oil-in-water) solvent evaporation method and evaluated for their size, morphology, encapsulation efficiency, drug loading, and in vitro drug release.
Methods Two nonbiodegradable polymers, Eudragit® RS100 and RL100 were used in combination. Microspheres were prepared by varying the amount of polyvinyl alcohol as a surfactant (0.05, 0.125, and 2.0 %, *w*/*v*) to the external phase; varying the amount of polymer (1:1, 2:1, and 3:1, *w*/*w*) to the drug by employing 3^2 full factorial design using the Design Expert (Version 8.0.7.1). The drug polymer interactions were investigated by Fourier transform infrared spectroscopy (FTIR) and X-ray powder diffractometry (XRPD). Imaging of particles was performed by field emission scanning electron microscopy.
Results Graphical and mathematical analysis of the design showed a quadratic model was significant for the responses. Low magnitude of error and significant values of R^2 proves the high prognostic ability of the RSM. Encapsulation efficiency of microspheres (41.13 to 65.33 %) increases with an increase in surfactant concentration but decreases with an increase in polymer concentration. The microspheres were found to be discrete, spherical with smooth surface. The absence of drug polymer interactions was confirmed by FTIR spectroscopy. XRPD revealed the dispersion of drug within microspheres formulation. The Perfect pH-independent release profile was achieved from Eudragit® microspheres by anomalous transport mechanism.
Conclusions In conclusion, Eudragit® microspheres containing diclofenac sodium can be successfully prepared, and seem to be promising for sustained release application.

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Keywords Diclofenac sodium · Biocompatible polymers · Response surface methodology · Encapsulation · Design and optimization

Introduction

Musculoskeletal disorders are characterized by local inflammatory processes and are treated with nonsteroidal anti-inflammatory drugs (NSAIDs). Diclofenac sodium (DS; sodium(*O*-((2,6-dichlorophenyl)-amino)-phenyl)-acetate) is a NSAID that appears to be promising and most commonly used drug in the treatment of inflammatory processes because its potential anti-inflammatory and analgesic activity. DS is useful in the inflammatory disorders especially in rheumatoid arthritis, osteoarthritis, dental pain, and ankylosing spondylitis. A major disadvantage of DS therapy is the potential for upper gastrointestinal (GI) effects, increases a risk of ulcer bleeding resulting in an increase in rates of hospitalization or death from a GI complication [1–7]. With an increased use of NSAIDs comes an increased pressure to develop the new drug delivery strategies that will achieve the highest healing effect of DS with minimal GI events. For that purpose, sustained release formulation of DS is essential, and sustained release microspheres might be beneficial in overcoming the GI side effects of the conventional dosage forms thereby improving patient compliance.

Biodegradable and biocompatible microspheres are popularly investigated drug delivery system for therapeutic drugs. Administration of medication via such system is advantageous because microspheres can be tailored for desired release profiles. They are capable of providing the controlled release of the encapsulated drug for longer duration [8–11]. Solvent evaporation and organic phase separation techniques are widely used in pharmaceutical industries for the preparation of microspheres [8, 9, 12–14]. Eudragit RS 100 and RL 100 are water insoluble, pH independent polymers having 5 and 10 % functional quaternary ammonium groups and capable of limited swelling. Thus these polymers appear to be a good