-Indomethacin Sustained Release Pellets Prepared by Extrusion Spheronization

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Abstract:

Gastrointestinal side effects may interrupt essential therapy with indomethacin, a non-steroidal anti-inflammatory drug. Formulation of this drug into sustained release multiparticulate form may reduce some of these side effects by avoiding contact of drug crystals with gastrointestinal mucosa at high concentrations, as may happen with immediate release dosage forms. Indomethacin (IM) sustained release pellets containing 5 or 10% w/w of the drug were prepared using an extrusion-spheronization technique. Different concentrations of hydrophilic polymers, polyethylene glycol 4000 (PEG 4000), hydroxypropyl methylcellulose E5 LV premium (HPMC) and polyvinyl pyrrolidone (PVP K30), were mixed at different concentrations (5,10 and 20%) with Avicel PH 101 to prepare the sustained release formulae. Moreover, a mixer torque rheometer was used to quantitatively determine the suitable moisture content in the pastes before the extrusion process. The resulting pellets were characterized for content, particle size, shape and dissolution profile. The studies on the effect of the polymers used on Avicel rheological properties revealed that the magnitude of torque for the system was decreasing as the polymer concentration increased. The in vitro release of IM from the prepared Avicel pellets was found to be dependent upon the type and concentration of the added polymer. The rank order of IM release in the presence of the investigated polymers was as follows: PEG > HPMC > PVP. Furthermore, the magnitude of IM release rate from the pellet formulations was found to be dependent on the magnitude of the peak torque of the pellet forming paste, which in turn depends on the type and concentration of the added polymer. Increasing IM loading from 5 to 10% has led to an increase in dissolution rates. At least two of the prepared pellet formulations showed dissolution profiles similar to the commercial product Bonidon 75 SR capsules. In conclusion, the formulation of IM sustained release pellets successfully controlled the drug release which might be beneficial in lowering the risk of side effects and improving patient convenience as an advantage of the pellets as a drug delivery system.

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