Poly(β amino ester) based tablet formulation for a hydrophobic drug

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Abstract:

Oral drug delivery is the most frequent method used for drug administration; however, its efficiency is often limited by solubility and stability of the drug. This is typically overcome by enteric coatings, which can delay release through pH triggered swelling. However, these systems are less effective when patients take proton pump inhibitors or when the coating is broken. One approach to overcome this limitation is the use of polymeric pro-drug formulations such as poly(β amino ester) PβAE. PβAE gels have shown promising results for the controlled release of drugs by improving the stability and increasing the solubility of these drugs. However, tablet formulations of PβAE gels have not been studied yet. In this work, we have made tablet formulations of PβAE using curcumin as a model drug, which is a potent anti-inflammatory anti-oxidant drug.

Poly(curcumin β amino ester) PCβAE was synthesized by polymerization of a commercial diacrylate (PEG400DA) and a primary diamine, 4,7,10-trioxa-1,13-tridecanediamine (TTD), in combination with acrylate-functionalized curcumin (i.e., curcumin diacrylate – CDA). Based on earlier studies, where the relative composition of CDA and PEG400DA was varied, a 90:10 (CDA:PEG400DA) hydrogel composition was selected. PCβAE gel tablets were made using 20 wt% hydrogel and 80 wt% microcrystalline cellulose (MCC) by compression using a hydraulic press. The hydrogel was first cryo-milled with magnesium stearate and then blended with MCC. During dissolution studies in USP (United States Pharmacopeia) apparatus II, PCβAE tablets showed a sustained release for 16 hours, a release that is useful for colon specific delivery. As controls, free curcumin tablets released within 4 hours. For effective application of this formulation, it is important to study environmental stability. As release is hydrolysis based, tablet stability under accelerated storage conditions was also studied (25°C and 57% RH, and 40°C and 75% RH). In the presence of humidity, tablets stored for more than 2 weeks resulted in release

curves similar to that of free curcumin form, suggesting complete degradation of the polymeric prodrug, demonstrating the importance of dry storage conditions to be maintained for this formulation.