ID 253

Advanced Formulations of Chitosan/Polyethylene Oxide/Ethyl Cellulose Incorporated Desferrioxamine: A Comparison of Cell Permeability, Loading Efficiency and pH-dependant Release Properties

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Desferrioxamine (DFO) is one of the most potent iron chelators, used for the treatment of iron overload conditions. However, its extreme hydrophilicity results in lower cell permeability and low plasma half-life, rendering DFO non-absorbable orally leading to burdensome subcutaneous infusions decreasing patient compliance. The main objective of this study is to synthesize an orally administrable DFO-incorporated nanocomposite. Three advanced formulations incorporating DFO into chitosan (CTS), polyethylene oxide (PEO) and ethyl cellulose (EC) network were produced by varying chitosan%. The synthesized nanocomposites were characterized using a scanning electron microscope, particle size analyzer and Fourier transform infrared spectrometer. The drug loading capacities (LC) and drug entrapment efficiencies (EE%) were determined using the potentiometric titration method. Both LC and EE% increased proportionally to the CTS%. Nanocomposite DFO_PEP_EC_CTS_TPP_1 with 285.56±0.04 mg/g of LC and 85.67±13.35% of EE% was identified as the best formulation. The drug release kinetics were analysed at physiological and intestinal pH values. The kinetic model, Peppas–Sahlin provided the best correlation for the dissolution of DFO at both pH values (7.4 and 6.8) and it indicates the case II relaxation mechanism for the release of DFO. According to in vitro blood compatibility assays, the nanocomposite was found to be hemocompatible. Cell permeability studies were carried out and results show that a three-fold increase of permeability at the highest CTS (56%) compared to the lowest (18%). These results suggest that the DFO_PEO_EC_CTS_TPP nanocomposites with high CTS% are promising candidates for the formation of pH-responsive, orally administered DFO modularity.

Keywords: *desferrioxamine, controlled release, nanocomposite*