The development of self-assembled hyaluronic acid – transferrin colloidal particles for the formulation of hydrophobic vitamins

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The development of biocompatible drug delivery systems remains an important aspect of modern nanomedicine [1]. Polyelectrolyte complexes (PECs), formed through the spontaneous self-assembly of oppositely charged macromolecules, offer a versatile platform for this purpose. This research explores the development and characterization of a novel polyelectrolyte complex system, investigating the spontaneous self-assembly of oppositely charged macromolecules: the gross positively charged human apo-transferrin (Tr) protein and the negatively charged high-molecular-weight hyaluronic acid (HyA) polysaccharide. While PECs are increasingly recognized as promising candidates for controlled drug delivery, the specific interaction between Tr and HyA has remained unexplored in scientific literature until now. To provide a comprehensive understanding of this unique system, a multi-analytical investigation was carried out, with the physicochemical characterization of the PECs by dynamic light scattering, rheological measurements, ζ- and streaming potential studies. The morphology of the self-assembled particles was investigated with electron microscopy. The structural analysis of the PECs was carried out with CD- and IR-spectroscopy. Our experimental results underscore that the self-assembly mechanism is highly sensitive to the pH of the medium and the mass ratio of the components, proving that electrostatic interactions are crucial from the point of view of particle formation. We identified that a Tr/HyA mass ratio of 2:1 results in the formation of highly stable, negatively charged (ζ-potential -38 mV) colloidal particles with a well-defined diameter range of 240–260 nm at pH = 4.5. CD- and IR-spectroscopy experiments proved that the α-helix content (from 10.6% to 0,4%) of the protein decreases upon the interacting with the polysaccharide, confirming the unfolding of Tr. This unfolding process exposes the hydrophobic regions of the protein, which could enhance the encapsulation of different hydrophobic drugs. To prove this functional utility of these colloidal structures, the encapsulation of several hydrophobic drug molecules was carried out. The potential of the carrier as a drug delivery system was demonstrated with Vitamin D3 and K1, achieving encapsulation efficiency values higher than 60%. Notably, the nanoformulation increased the aqueous solubility of the vitamins almost threefold compared to the unformulated crystalline form. Dissolution studies in simulated physiological conditions showed a burst release mechanism with an almost complete release of the formulated vitamins within 30 minutes, whereas the pure drugs required 120 minutes to reach similar levels [2].

Keywords:
serum protein, polysaccharide, electrostatic interaction, encapsulation, hydrophobic vitamins

References:

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