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Polysaccharide-based nanocomplexes for co-encapsulation and controlled release of 5-Fluorouracil and Temozolomide

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Abstract

Polysaccharide-based nanocomplexes, intended for simultaneous encapsulation and controlled release of 5-Fluorouracil (5-FU) and Temozolomide (TMZ) were developed via the complexation method using chitosan, alginic and polygalacturonic acid. Investigation focused on the influence of polysaccharides on the properties of the system and amelioration of the stability of the drugs, in particular TMZ. The dimensions of particles and their ζ-potential were found to range between 100 - 200 nm and -25 to +40 mV, respectively. Encapsulation efficiency varied from 16% to over 70%, depending on the given system. The influence of pH on the release and co-release of TMZ and 5-FU was evaluated under different pH conditions. The stability of the loaded drug, in particular TMZ, after release was evaluated and confirmed by LC-MS analysis. Results suggested that the amount of loaded drug(s) and the release rate is connected with the weight ratio of polysaccharides and the pH of the media. One-way ANOVA analysis on the obtained data revealed no interference between the drugs during the encapsulation and release process, and in particular no hydrolysis of TMZ occurred suggesting that CS-ALG and CS-PGA would represent interesting carriers for multi-drug controlled release and drugs protection.

Keywords: chitosan, polygalacturonic acid, alginic acid, polyelectrolytes, drug delivery.

Chemical compounds: Chitosan (PubChem CID: 21896651), Alginic acid (PubChem CID: 44630049), Polygalacturonic acid (PubChem CID: 439215), Temozolomide (PubChem CID: 11830328), 5-Fluorouracil (PubChem CID: 3385)

1. Introduction

Polyelectrolytes (PE) are macromolecules carrying a number of functional groups which are charged or can become charged under suitable conditions [1]. PE can be classified according to the nature (natural, synthetic or chemically modified), composition (homopolymer, copolymer) and molecular structure (linear, branched, cross-linked) [2]. By mixing oppositely charged polyelectrolyte solutions, polyelectrolyte complexes (PECs) are formed. Structurally, PECs are polymer-polymer complexes bound together by electrostatic interactions, hydrogen bonds, ion dipole and hydrophobic interactions [3].. Formation and complex stability depend on several factors, i.e. the degree of ionization, charge density, position of ionic groups, charge distribution, ionic strength, molecular weight, chain flexibility, contact time, ratio and order of mixing [4]. The formation of PECs comprises three main steps: i) primary complex formation, where to Coulomb forces are responsible; ii) a formation process within intracomplexes, where formation of new bonds and/or correction of distorted polymer chains occurs; iii) an intercomplex aggregation process, in which the aggregation of secondary complexes mainly take place through hydrophobic interactions. In the literature, two structural models for polyelectrolyte complexes are discussed [2]. These models have been