

CHITOSAN/MALTODEXTRIN AND CHITOSAN/METHYLCELLULOSE NANOGELS: STRUCTURE DEPENDENT DRUG LOADING AND PH-RESPONSIVE RELEASE OF DOXORUBICIN

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Nanogels are three-dimensional polymeric networks at the nanoscale, typically around 200 nm, composed of crosslinked polymers through their functional groups. Among the different types of nanogels, some of them exhibit sensitivity to external stimuli such as pH, temperature, or enzymatic activity, making them promising platforms for drug delivery. Biopolymer-based nanogels are of particular interest due to their biodegradability, biocompatibility, and non-toxicity. In this work, pH-sensitive nanogels were synthesized through a reductive amination reaction between chitosan and partially oxidized maltodextrin or methylcellulose, using safe, biocompatible, and readily available polysaccharides. Some variations in chitosan molecular weight, concentration and pH, as well as the oxidation degree of maltodextrin or methylcellulose (utilized as crosslinker agents), led to differences in the size and surface charge of the resulting nanogels. The pH-responsiveness was confirmed by the increase in size and ζ -potential of nanogels at lower pH values, attributed to particle swelling. Doxorubicin hydrochloride (DOXO-HCl) was successfully encapsulated in both types of nanogels and, depending on the crosslinking polysaccharide structure, ranged from 55% to 75% for maltodextrin/chitosan nanogels and from 90% up to 100% for methylcellulose/chitosan nanogels. Drug release experiments were carried out at 37 °C under physiological (pH 7.4), acidic (pH 5.5, simulating tumor microenvironments), and alkaline (pH 9.0) conditions, and the data were analyzed using five kinetic models. For maltodextrin/chitosan nanogels, the release profile was best described by the Korsmeyer–Peppas model, indicating a pH-dependent Fickian diffusion process. In contrast, methylcellulose/chitosan nanogels exhibited distinct behaviors: at pH 5.5 the release was governed by an erosion-controlled mechanism (Hopfenberg model), whereas at pH 7.4 and 9.0 drug release followed solubility-driven kinetics (Gompertz model). Overall, these findings highlight that chitosan-based nanogels combine high encapsulation efficiency with pH-responsive release, where the nature of the crosslinking polysaccharide plays an important role in both drug loading and release pathways.

Keywords: pH-sensitive nanogels, Biopolymers, Doxorubicin encapsulation and release

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