Harnessing Hydrogel Interaction with Functional Polymeric Nanoparticles for Sustained Co-Delivery of Therapeutics

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INTRODUCTION

Hydrogel-nanoparticle composites have recently represented a promising strategy to develop hybrid platforms with enhanced properties in the biomedical scenario. This combination has led to superior properties, overcoming the limitations associated with the single systems, such as lack in hydrophilicity and fast clearance, to mention a few. In this work, a nanocomposite hydrogel integrated with functional NPs is proposed to achieve sustained the co-delivery of therapeutics with distinct physicochemical properties.

METHODS

Amphiphilic copolymers composed either by poly(glycerol methacrylate) (PGMA), poly(ethylene glycol methacrylate) (PEGMA), or poly(dimethylaminoethyl methacrylate) (PDMAEMA) and poly(ε-caprolactone) (PCL) were synthesized via a combination of Atom Transfer Radical Polymerization and Ring-Opening Polymerization, and then used to form nanoparticles (NPs) loaded with dexamethasone (DEX) via nanoprecipitation. Hydrogels were chemically crosslinked via polycondensation within agarose, carbomer, and hyaluronic acid. Drug-loaded NPs were incorporated into the hydrogel through different formulation strategies, depending on their superficial functional groups to investigate the DEX release, upon different conditions. Hydrogel were simultaneously loaded with BSA to study the co-delivery ability of the system.

RESULTS

The three NPs were either chemically, physically or ionically entrapped within the hydrogel, according to the NPs shell functionalities (Figure 1). Physical encapsulation favoured rapid NPs release within 24h and complete DEX release in 6 days, while electrostatic or chemical linkages displayed limited NPs release, offering sustained DEX release profiles over 21 days, for optimized therapeutic efficacy. Simultaneously, in presence of non-ionic NPs, BSA was completely release in 3 days, while its retention time was increased with presence of cationic micelles.

CONCLUSIONS

The proposed strategy enabled the design of composite drug delivery systems tailored to specific applications. The different encapsulation methods showed influence on both properties and release kinetics of the composite system. The dual-compartment system facilitated the co-delivery of therapeutics, enabling tunable release profiles for combination therapies.

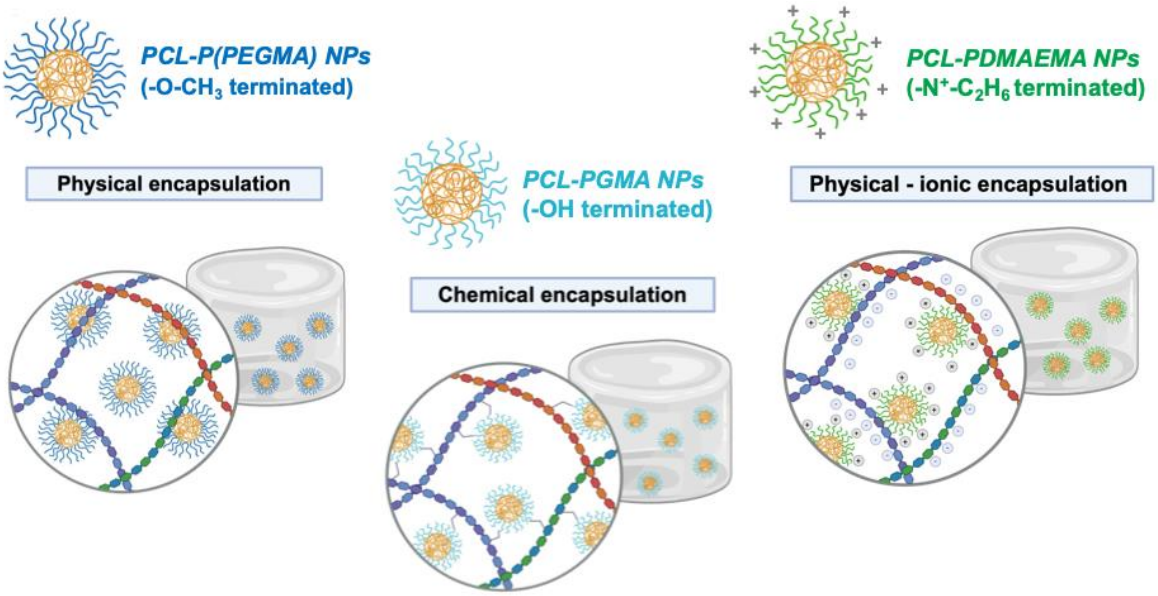

Figure 1. *Representation of NPs-hydrogel composite depending on NPs corona functional groups.*