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Crosslinked and PEGylated Pectin Chitosan nanoparticles for delivery of Phytic acid to colon

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ABSTRACT

Polysaccharide-based nanoparticles (NPs) such as pectin/ chitosan (PN/CN) had always been of greatest interest because of their excellent solubility, biocompatibility, and higher suitability for oral drug delivery. This study employed blending-crosslinking of polymers (PN&CN) followed by emulsification-solvent evaporation to prepare and compare two sets of PEGylated NPs to deliver phytic acid (IP6) to colon orally as it has potential to manage colon cancer but fails to reach colon when ingested in pure form. The first set was crosslinked with Glutaraldehyde (GE) (GE*PN-CN-NPs) while the second set was crosslinked with sodium tripolyphosphate (TPP) (TPP*PN-CN-NPs). IP6-loaded-GE/TPP*PN-CN-NPs were optimized using a central composite design. Developed TPP*PN-CN-NPs had a smaller size (210.6 ± 7.93 nm) than GE*PN-CN-NPs (557.2 ± 5.027 nm). Prepared NPs showed <12% IP6 release at pH 1.2 whereas >80% release was observed at pH 7.4. Further, NPs were explored for cytocompatibility in J774.2 cell lines, cytotoxicity, and cellular uptake in HT-29 and DLD-1 cell lines. While exhibiting substantial cytotoxicity and cellular uptake in HT-29 and DLD-1, the NPs were deemed safe in J774.2. The PEGylated-TPP*PN-CN-NPs showed time-dependent uptake in J774.2 cell lines. Conclusively, the employed NP development method successfully delivered IP6 to colon and may also open avenues for the oral delivery of other drugs to colon.

1. Introduction

Polysaccharides are very attractive candidates for the fabrication of various carriers for drug delivery owing to their low cost, biocompatibility, biodegradability, as well as convenience of chemical modifications (Bostanudin, Arafat, Sarfraz, Górecki, & Barbu, 2019; Gazzaniga et al., 2022; Quiñones, Peniche, & Peniche, 2018; Tao et al., 2018). Pectin (PN), a plant cell wall component, present in the middle lamella is usually extracted from citrus zest or apple pomace. It is an anionic polysaccharide predominantly comprised of linear chains of d-galactopyranosyluronic acid units connected by 1,4 α glycosidic linkages (BeMiller, 1986; R. Mishra, Banthia, & Majeed, 2012). PN has exceptional aqueous solubility and has been exploited to target multiple proteins and drugs in several formulations like films, hydrogels, and micro/nanoparticles (NPs) due to its superior biocompatibility and biodegradability (Sinha & Kumria, 2001; Vandamme, Lenourry, Charrueau, & Chaumeil, 2002). PN-based systems were primarily employed for targeted colonic delivery, but they were also used to deliver drugs to the brain in certain instances (Charlton, Davis, & Illum, 2007a; Charlton et al., 2007b). Chitosan (CN) is another linear biopolymer obtained from the deacetylation of chitin found in crustacean shells. It is a biodegradable, safe, inexpensive, and easily accessible cationic polysaccharide comprising β-D-glucosamine and N-acetyl-D-glucosamine units arranged randomly (Attallah, Shetta, Elshishiny, & Mamdouh, 2020; Dudhani & Kosaraju, 2010; Younes & Rinaudo, 2015). Countless drugs, particularly anticancer agents (Hwang & Shin, 2018; M. Sharma et al.,

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