Enhanced stability of novel chitosan-based nanoparticles and its application as an anticancer drug delivery system

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Chitosan-based nanoparticles prepared by ionotropic gelation are prone to stability issues. The aim of this work is to chemically modify chitosan by grafting to succinate, phthalate, glutarate and phenylsuccinate moieties and to investigate the suitability of the resulting polymers as covalently-crosslinked nanocarriers. Corresponding nanoparticles (NPs) were formulated by ionotropic gelation using tripolyphosphate (TPP) anion then they were covalently crosslinked using 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC). Infrared and thermal analysis confirmed the formation of phosphoramide bonds within the NPs indicating the involvement of TPP in covalent crosslinking. This is the first time to report phosphormide covalent crosslinking within nanoparticles matrices. The resulting NPs were found to resist drastic pH and calcium ion conditions. Size analysis indicated the NPs to be spherical and less than 500 nm in diameter. Loading studies using Safranine O showed enhanced NPs drug loading upon covalent crosslinking compared to ionotropic gelling. Doxorubicin-loaded NPs were of superior cytotoxic properties compared to free doxorubicin.