

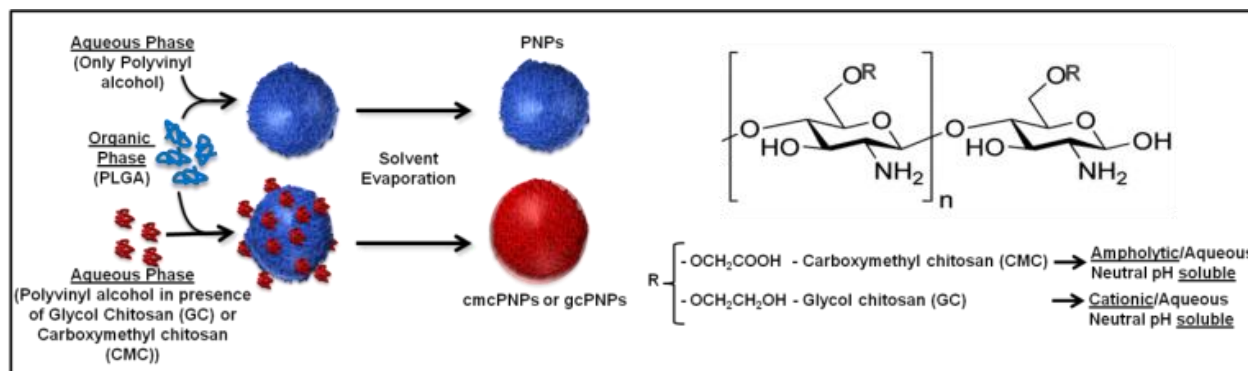
Physico-chemical effect of cationic and ampholytic water soluble chitosan coating on lipophilic drug nanoformulations

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Abstract: Chitosan coating on PLGA nanoparticles have been reported to control release of encapsulated lipophilic payloads. The disadvantage of chitosan being soluble only at lower pH makes it difficult to be an ideal surface coating on acid degradable nanocarriers. Glycolation or carboxymethylation of chitosan provides superior aqueous solubility at neutral pH, thereby enabling *in situ* surface coating. The present work explores effect of cationic glycol chitosan (GC) and ampholyticcarboxymethyl chitosan (CMC) coating over PLGA nanoparticles on loading of paclitaxel (Ptxl), a model lipophilic drug. When high molecular weight PLGA (44 KDa) was used, with ~ 12 %, ~ 10 % and ~ 28 % loading content (LC) in uncoated (PNPs), GC coated nanoparticles (gcPNPs) and CMC coated nanoparticles (cmcPNPs) respectively, SEM analysis revealed spherical nanoparticles predominantly sized at ~ 250 nm, ~ 300 nm and ~140 nm respectively with very few extraneous pristine Ptxl (EPP) nanorodsobserved only for cmcPNPs. At the same drug-feed ratio, low molecular weight PLGA (17KDa) yielded ~ 7 %, ~ 2.5 % and ~ 4 % LC for PNPs, gcPNPs and cmcPNPs respectively with SEM analysis revealing a mixture of spherical and EPP nanoparticles, where PNPs and cmcPNPs showing predominantly anisotropic EPP microcrystals and gcPNPs showing countable EPP nanorods amidst significantly spherical nanoparticles. In general, we observed that GC and CMC coating on nanocrystals reduced the length of Ptxl nanorods in comparison to uncoated control. The data indicates possible formation of extraneous spherical pristine drug nanocrystals during conventional emulsion or nanoprecipitation process of PLGA nanoformulations of lipophilic drugs. Overall, this work attempts to provide insight into parameters to be noted for taking advantage of polyelectrolyte coating towards controlled release applications.



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