

Ph-Triggered Cationic Solid Lipid Nanoparticles Mitigated Colitis in Mice

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Abstract : In this study, we hypothesized that prolonged gastrointestinal transit at the inflamed colon conferred by a pH-triggered mucoadhesive smart nanoparticulate drug delivery system aids in achieving selective and sustained levels of the drug within the inflamed colon for the treatment of ulcerative colitis. We developed budesonide-loaded pH-sensitive charge-reversal solid lipid nanoparticles (SLNs) using a hot homogenization method. Polyetylenimine (PEI) was used to render SLNs cationic (PEI-SLNs). Eudragit S100 (ES) was coated on PEI-SLNs for pH-trigger charge-reversal SLNs (ES-PEI-SLNs). Therapeutic potential of the prepared SNLs formulation was evaluated in ulcerative colitis in mice. The transmission electron microscopy, zeta size and zeta potential data showed the successful formation of SLNs formulations. SLNs and PEI-SLNs showed burst drug release in acidic pH condition mimicking stomach and early small intestine environment which limiting their application as oral delivery systems. However, ES-PEI-SLNs prevented a burst drug release in acidic pH conditions and showed sustained release at a colonic pH. Most importantly, the surface charge of ES-PEI-SLNs switched from negative to positive in colonic conditions by pH-triggered removal of ES coating and accumulated selectively in inflamed colon. Furthermore, a charge reversal ES-PEI-SLNs showed a superior mitigation of dextran sulfate sodium (DSS)-induced acute colitis in mice as compared to SLNs and PEI-SLNs treated groups. Moreover, histopathological analysis of distal colon sections stained with hematoxylin/eosin and E-cadherin immunostaining revealed attenuated inflammation in an ES-PEI-SLNs-treated group. We also found that ES-PEI-SLNs markedly reduced the myeloperoxidase level and expression of TNF-alpha in colon tissue. Our results suggest that the pH-triggered charge reversal SLNs presented in this study would be a promising approach for ulcerative colitis therapy.

Keywords : solid lipid nanoparticles, stimuli-triggered charge-reversal, ulcerative colitis, methacrylate copolymer, budesonide

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