

Drug-loaded nanoparticles with polymeric surface modification for controlled pharmacokinetic behavior

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In drug discovery today, a large number of drug candidates have poor oral bioavailability due to their low solubility in water, possibly resulting in insufficient therapeutic effects. To offer efficacious medication with such compounds, enhancement of gastrointestinal (GI) absorption is necessary. On the other hand, even being poorly water-soluble drugs, control of GI absorption is desirable for drugs with narrow therapeutic index or for those whose target sites are GI tissues. Mucosal drug delivery is one of the promising approaches to control GI absorption. In particular, mucopenetrating or mucoadhesive particulate drug delivery is advantageous for enhanced GI absorption or prolonged GI retention of orally-taken drugs, respectively. Drug-loaded mucopenetrating or mucoadhesive particle can be prepared by polymeric surface-coating which weaken or strengthen the following interactions between particle and mucin: electrostatic interaction, hydrogen bond and van der Waals' force, and physical entanglement. Our research group particularly has been focusing on electrostatic interaction as a critical factor determining particle behavior in mucus and has been attempting to control GI absorption of poorly water-soluble compounds with mucosal drug delivery. In this symposium, I would like to present cases on development of cyclosporine A-loaded mucopenetrating nanoparticles and clofazimine-loaded mucoadhesive nanoparticles prepared by flash nanoprecipitation. Also, I would like to discuss application of mucosal drug delivery to inhalants.