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Mucoadhesive Chitosan-Coated Nanostructured Lipid Carriers for Oral Delivery of Amphotericin B

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Abstract : Oral delivery of amphotericin B (AmpB) potentially eliminates constraints and side effects associated with intravenous administration, but remains challenging due to the physicochemical properties of the drug such that it results in meagre bioavailability (0.3%). In an advanced formulation, 1) nanostructured lipid carriers (NLC) were formulated as they can accommodate higher levels of cargoes and restrict drug expulsion and 2) a mucoadhesion feature was incorporated so as to impart sluggish transit of the NLC along the gastrointestinal tract and hence, maximize uptake and improve bioavailability of AmpB. The AmpB-loaded NLC formulation was successfully formulated via high shear homogenisation and ultrasonication. A chitosan coating was adsorbed onto the formed NLC. Physical properties of the formulations; particle size, zeta potential, encapsulation efficiency (%EE), aggregation states and mucoadhesion as well as the effect of the variable pH on the integrity of the formulations were examined. The particle size of the freshly prepared AmpB-loaded NLC was 163.1 ± 0.7 nm, with a negative surface charge and remained essentially stable over 120 days. Adsorption of chitosan caused a significant increase in particle size to 348.0 ± 12 nm with the zeta potential change towards positivity. Interestingly, the chitosan-coated AmpB-loaded NLC (ChiAmpB NLC) showed significant decrease in particle size upon storage, suggesting 'anti-Ostwald' ripening effect. AmpB-loaded NLC formulation showed %EE of 94.3 ± 0.02 % and incorporation of chitosan increased the %EE significantly, to 99.3 ± 0.15 %. This suggests that the addition of chitosan renders stability to the NLC formulation, interacting with the anionic segment of the NLC and preventing the drug leakage. AmpB in both NLC and ChiAmpB NLC showed polyaggregation which is the non-toxic conformation. The mucoadhesiveness of the ChiAmpB NLC formulation was observed in both acidic pH (pH 5.8) and near-neutral pH (pH 6.8) conditions as opposed to AmpB-loaded NLC formulation. Hence, the incorporation of chitosan into the NLC formulation did not only impart mucoadhesive property but also protected against the expulsion of AmpB which makes it well-primed as a potential oral delivery system for AmpB.

Keywords : Amphotericin B, mucoadhesion, nanostructured lipid carriers, oral delivery
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