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Self-Emulsifying Drug Delivery Systems: Mucolytic Action of N-acetylcysteine (NAC)-Polymer Hydrophobic Complexes for Effective Mucopermeation

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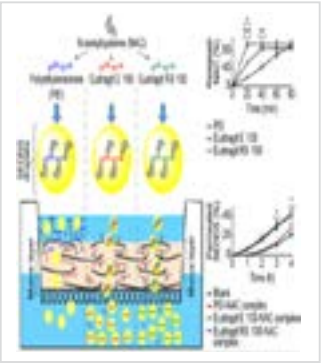
Biography

Ahmad Malkawi is working at Department of Pharmaceutical Technology, Center for Chemistry and Biomedicine, Institute of Pharmacy, University of Innsbruck, Austria.



Abstract

The mucolytic function of N-acetylcysteine (NAC) is necessary for the diffusion of mucoactive self nanoemulsifying drug delivery systems (SEDDS) through the intestinal mucus gel layer. NAC instantly released from SEDDS leads to nonsignificant mucolytic activity and poor mucopermeation. It was the aim of this study to develop a novel mucoactive SEDDS based on the mucolytic function of NAC with improved mucopermeation. Therefore, NAC hydrophobic complexes with the cationic polymers poly ethyleneimine (PEI), Eudragit E and RS were loaded in SEDDS and evaluated for size, polydispersity index (PDI), zeta potential and cytotoxicity. NAC release from the mucoactive SEDDS followed Ellman's method at pH 6.8. Interaction of mucoactive SEDDS with mucus was assayed using in vitro rheology, a Transwell diffusion model and intestinal residence time. SEDDS showed size stability in the range of 76 ± 12 nm over 4 h, as indicated by < 0.3 PDI and caused zeta potential increase from 17.3 mV to 7.7 mV. SEDDS showed no cytotoxicity on Caco-2 cells. The immediate release of NAC in a few seconds from SEDDS of PEI was significantly more sustained in 40e80 min with Eudragit E (p 0.05) and RS (p 0.001). Similarly, the SEDDS complexes showed a concentration- and time-dependent decrease of 52.55 ± 19.88% in mucus dynamic viscosity. Finally, Transwell diffusion showed approximately 2- and 1.8-fold higher amounts of diffused SEDDS anchoring NAC complexes with Eudragit E/RS (p 0.05), respectively. Mucoactive SEDDS slowly releasing low NAC levels while permeating exhibit better mucolytic targeting, which improves overall in vitro mucopermeation.

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