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Transport of Self-Nano Emulsifying Drug Delivery System (SNEDDS) across mucus and cellular internalization

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Purpose: The aim of this study was to investigate SNEDDS as a carrier system for targeted delivery of drugs and/or genes to mucosal epithelial cells.

Methods: SNEDDS formulation contained 30% (m/m) Cremophor EL, 30% (m/m) Capmul MCM, 30% (m/m) Crodamol and 10% (m/m) propylene glycol. Initially droplet size and surface charge was determined to characterize the SNEDDS formulations. Mucus permeation ability of SNEDDS was investigated by the silicon tube method. Florescent microscopy was performed to establish viability of SNEDDS over Caco-2 cells using concentration gradient (0.1, 0.5 and 1.0 %). Furthermore, the interaction of SNEDDS formulation in terms of level of internalization and pathway was evaluated withCaco-2 cell monolayer (model of intestinal epithelium) cultured in 24-well plates.

Results: Droplet size was observed to be 35.50±8.37 nm withzeta potential approaching neutral value (-0.52 mV). Mucus permeability of 1% SNEDDS formulation evaluated with silicon tube filled with mucus demonstrated diffusion of 15.6%, 4.08% and 0.71% of the marker in initial three segments (2 mm each) after 4 h of incubation at 37oC. Cytotoxicity analysis established 0.5% SNEDDS formulation to be feasible for the cellular internalization studies. Confocal microscopy revealed that droplets of the formulation were successfully internalized in the cytoplasm of Caco-2 cells. Moreover, quantitative analysis demonstrated that 1.34% and 1.87% of fluorescein diacetate having been incorporated in SNEDDS as markerwas effectively internalized after 2 h and 4 h of incubation, respectively. By using pharmacological inhibitor block method, cell internalization pathways were explored. A substantial decrease of 50.82% occurred in the presence of indomethacin (caveolae mediated pathway inhibitor) and 29.80% in the presence of chlorpromazine (clathrin pathway inhibitor).

Conclusion: SNEDDS permeating the mucus gel layer and reaching the cytoplasm after being transported by multiple endocytosis pathways appear to be promising carrier system for mucosal epithelial delivery.

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