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Noninvasive Trends in Peptide Delivery using thiolated microspheres

Mani Bhargava
Department of Pharmacy, Signa College of Pharmacy, India

Objectives: The aim of this study is to determine the potential of thiolated microparticles as a nasal peptide delivery system. As insulin is a polar, hydrophilic peptide of a high molecular mass, its nasal delivery is a challenging task, so to gain this goal, insulin-loaded microparticles based on thiolation were generated.

Methods: The thiomer (carbopol–cysteine) was prepared immobilizing cysteine on carbopol using EDAC. Microspheres were prepared using the water-in-oil (w/o) emulsification solvent evaporation technique. The microspheres were studied for particle shape, size, drug content, swellability, mucoadhesion and *in-vitro* insulin release. Drug mucosal permeation study was performed along with *in-vivo* studies included assessment of anti-diabetic activity in streptozotocin induced diabetic rabbits.

Results: The particle shape and size of the prepared microspheres were analyzed by SEM and laser particle size analyzer (CILAS). The shape of the microspheres from that of nonthiolated carbo was found to be spherical but in the case of carbo–cys microspheres the surface was found to be rough as compared to smooth surface of nonthiolated carbo microspheres. The thiolated microspheres exhibited higher mucoadhesion due to formation of covalent bonds via disulfide bridges with the mucus gel layer. *In-vitro* permeation study through mucosal membrane goat nasal mucosa was observed that thiolated polymer-based microspheres showed better permeation than the non-thiolated polymer. Thiolated microspheres bearing insulin showed better reduction in blood glucose level (BGL) in comparison to nonthiolated microspheres as 31.23_2.12% and 75.25_0.93% blood glucose of initial BGL were observed at 6 h after nasal delivery of thiolated and nonthiolated microspheres in streptozotocin-induced diabetic rabbits.

Conclusions: Thus, administration of insulin through nasal route using thiolated polymer resulted in a significantly higher effect than microparticles comprising nonthiolated polymer. This drug delivery system might represent a useful drug vehicle for the nasal administration of therapeutic peptide drugs.