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PEGylated Glucose Triggered Liposomes for Insulin Delivery

Mani Bhargava¹, Saurabh Bhargava²

¹Department of Pharmacy, Signa College of Pharmacy, India

²Department of Pharmacy, United Institute of Pharmacy, India

Objectives: The insulin dependent diabetes mellitus (IDDM) results from failure of the beta cells of the pancreas to secrete the hormone insulin. Most current insulin therapies involve subcutaneous injections, or use of infusion devices which are inconvenient and repeated injections, result in localized insulin deposits that lead to local hypertrophy and fat deposits under the skin. Therefore, our study have been focused on self-regulatory insulin release systems that can carry out feedback control of insulin delivery, based on blood glucose levels, or to develop systems like "artificial pancreas".

Hence, it was envisaged to develop glucose responsive serum stable and long circulating liposomes as drug delivery system .The inclusion of PEG derivatized lipids stabilized liposomes in circulation and enhanced encapsulation efficiencies. It also reduced leakage of drug from liposomes, which might contribute to the sustained release of encapsulated insulin.

Methods: Liposomes were prepared by cast film method and and pegylated. Pegylated liposomes were characterized for vesicles shape, entrapment efficiency, vesicles size analysis, pH dependent aggregation, glucose induced aggregation and *in-vitro* drug release.

Results: The Photomicrograph and TEM studies show spherical shape. The in-vitro studies included glucose permeation study and glucose induced aggregation study. In-vivo studies were done on both diabetic and non-diabetic rats and included blood glucose determination. The hypoglycemic effect by PEG-coated liposomes lasted for much longer duration than uncoated liposomes. The slow release of insulin from coated liposomes achieved longer duration of hypoglycemic activity. The difference between glucose responsive and non-glucose responsive systems is more evident in normal rats than diabetic rats.

Conclusions: The PEGylated glucose responsive system confers the longer circulating properties and senses the elevated blood glucose levels and release insulin in higher proportions when compared to Non-PEGylated system.