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Mucoadhesive Nanospheres based ocular delivery of Insulin

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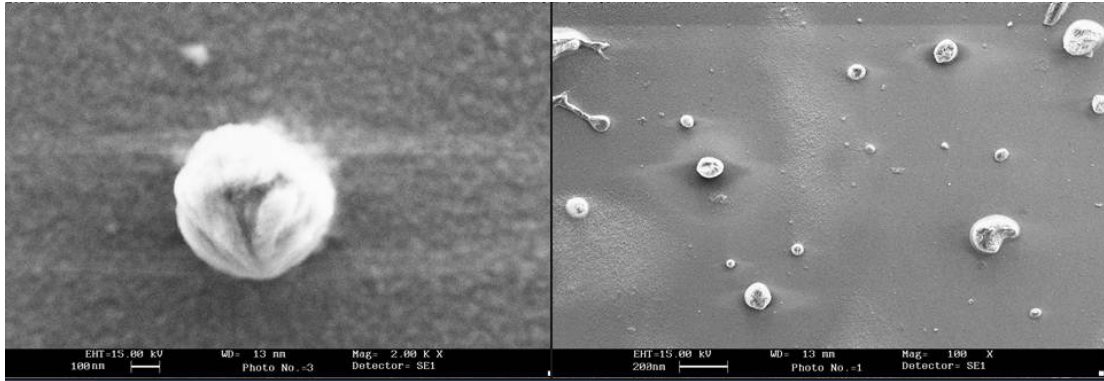
Objectives: Diabetes mellitus was known in antiquity and remains today a worldwide, increasing health problem. It occurs because of lack of insulin, with or without factors that oppose action of insulin. We aimed to develop biocompatible, biodegradable mucoadhesive nanospheres for effective delivery of insulin through ocular route. It is envisaged that chitosan is biocompatible mucoadhesive polymers and enhances permeability of biological membrane. It facilitates the mucoadhesion with the corneal surface and nasolacrimal duct and enhances delivery of entrapped drug molecule.

Methods: Chitosan Nanospheres were prepared by ionotropic gelation method under mild conditions and characterized for their shape, size by Scanning electron microscopy(SEM), percent drug entrapment and stability. The mean particle size was determined by using a Malvern Zetasizer. Structural integrity was confirmed by FTIR and Mucoadhesion studies were performed. Drug release study was done in stimulated artificial tear solution(ATS). In-vitro Drug permeation study was performed through mucosal membrane using modified franz-diffusion cell. Ocular Irritation Test(HET-CAM Test) was also carried out. The in-vivo studies were done with periodic monitoring of blood glucose level and included in-vivo permeation study along with fluorescence microscopy.

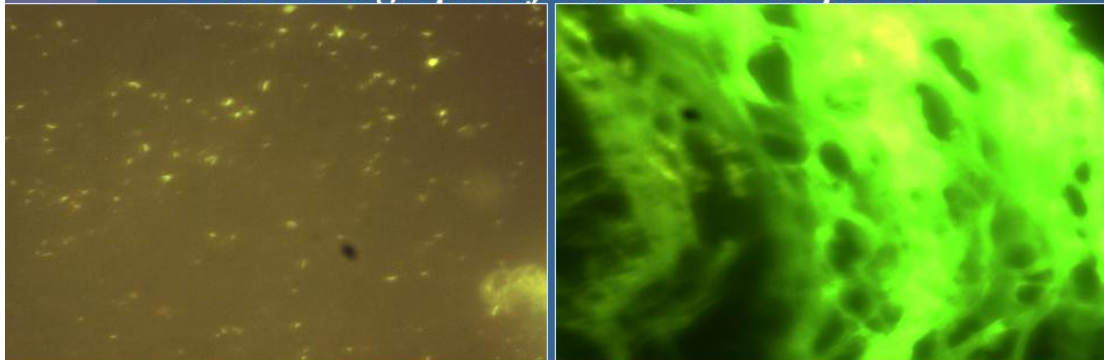
Results: SEM micrographs show clustered spherical particles with smooth surfaces. FTIR confirmed ionic interactions between chitosan-TPP and between insulin-chitosan. Mucoadhesion studies reveal good adhesive property of chitosan. Release studies shows that insulin was released in sustained manner upto 24 hr with lower burst effect. Drug permeation studies reveal a well known transmucosal enhancer property of chitosan. Ocular irritation test results that formulation is non-irritant to mild irritant and is well tolerated. In-vivo studies shows, a much delayed but more prominent response in blood glucose reduction as compared with plain insulin.

Conclusions: Fluorescence microscopy confirms penetration of the drug carrier in corneal membrane. Our finding should be helpful for possible exploitation of mucoadhesive nanospheres as future delivery system for treatment of Diabetes.

SEM & Fluorescence Images of Nanospheres



SEM Photographs of chitosan nanospheres



Fluorescence images of chitosan nanospheres