P-114 **Colloidosmes a Novel Carrier for Colonic Delivery of Insulin**

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INTRODUCTION AND OBJECTIVE

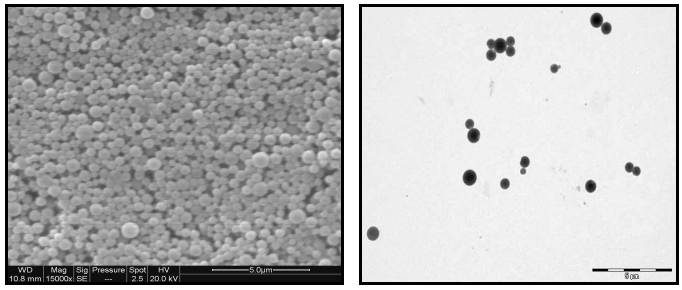
The objective of this study is to securely target insulin to the colon through a novel carrier colloidosomes for effective management of blood glucose level. colloidosomes efficiently encapsulate insulin in their gel aqueous core as well as their surface colloidal spherical particle layer helps in controlling the release of insulin in the colon. Insulin is release from colloidosomes and absorbed in the colon which reduce blood glucose level in albino rabbit.
Efficient encapsulation of active ingredients such as drugs, proteins, vitamins, or even living cells is becoming increasingly important for a wide variety of applications and technologies, ranging from drug delivery to biomedical applications Chaikof et al. (1999). Encapsulation of bioactive macromolecules, especially of peptides and proteins, has received immense attention in recent years. The majority of therapeutic peptides and proteins are administered via the parenteral route presents numerous limitations including patient discomfort and other. To overcome these drawbacks, alternative administrative route, such as oral route have been investigated Shah et al. (2002) but on oral administration of protein and peptide drug, degradation is occur in upper part of GIT to retard degradation one of the techniques adopted for this purpose is development of colloidosomes.
Colloidosomes are microcapsules with shells consisting of coagulated or partially fused colloid particles Velev et al. (1996), Dinsmore et al. (2002). Recently, it was recognized that the colloidosome membranes offer great potential in controlling the permeability of entrapped species. Their major advantage is that the interstices or pore size can be varied by choosing particles of an appropriate size and by controlling their degree of fusion, which can find various applications for development of novel drug and vaccine delivery vehicles and for the slow release of cosmetic and food supplements Velev et al. (1996), Kumaraswamy et al. (1996), Fang et al. (2002), Dinsmore et al. (2002) have recently produced colloidosomes by the assembly of latex particles into shells around water-in-oil emulsion drops, followed by thermal fusion of the particles in the shell and centrifugal transfer into water through a planar oil–water interface.
The present study is aimed at developing colloidosomes for the release of insulin to the colon in such a way that the core encapsulating insulin is coated with polymeric nanoparticles. These colloidosomes were administered to rabbit and seem to be unaffected in the upper part of GIT. Colloidosomes disperse in the colon where insulin gets released from the core from colloidal nanoparticles. Thereafter, this carrier system was also evaluated for its therapeutic efficacy in vivo for the treatment of diabetes mellitus in albino rabbit model.

MATERIALS AND METHOD

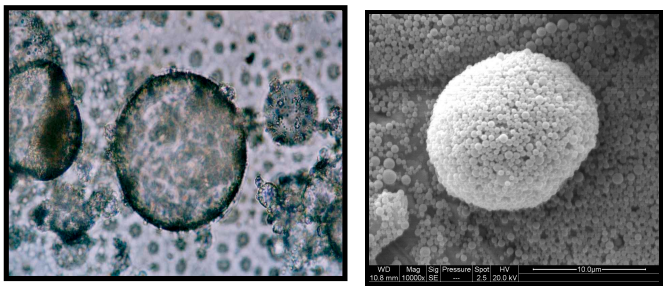
Preparation of this colloidosomes takes place in two steps first the preparation of nanoparticles (NPs) which was based on repercipitation method, reported by Yabu et al. (2005) and second step is the integration of colloidosomal assembly, colloidosomes were prepared according to method which was reported by Weitz et al. (2002) with suitable modifications. The NP's were analyzed for size distribution and zeta potential in 1:100 dilutions with distilled water using a Zetasizer (Malvern Instruments, UK). Shape and surface morphology of nanoparticles and colloidosomes were studied using SEM. Transmission electron microscope (TEM) was used as a visualizing aid for particle morpholgy. The average particle size and polydispersity index of the colloidosomes were determined by optical microscopy using a calibrated occulometer. In vivo antidiabetic study carried by estimating plasma glucose level using glucose-oxidase method (Glucose GOD-PAD kit, Bayers diagnostics). In vitro drug release of insulin loaded colloidosomes was carried in simulated gastric fluid at différent pH with and without rat ceacal content (RCC).

RESULT AND DISCUSSION

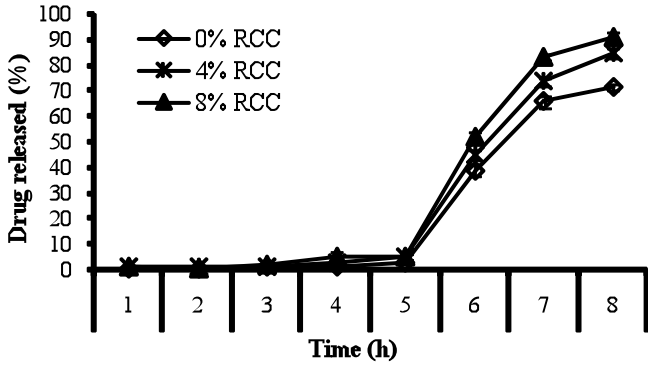
Prepared nanoparticles were found in spherical shape with average size 257.20±0.9 nm having small polydispersity index (0.074)**.** In SEM and TEM photographs we observed that prepared nanoparticles were spherical in shape.The average size of colloidosomes was found to be 50.4±1.2 µm. The encapsulation efficiency was found to be 69.16±1.6. colloidosomes showed a matrix diffusion controlled first order release with 70–80% release in 24 h. A significantly prolonged decline of the plasma glucose level was obtained over 10 h after administration of the insulin-loaded colloidosomes at a dose of 100 IU/kg of body weight.



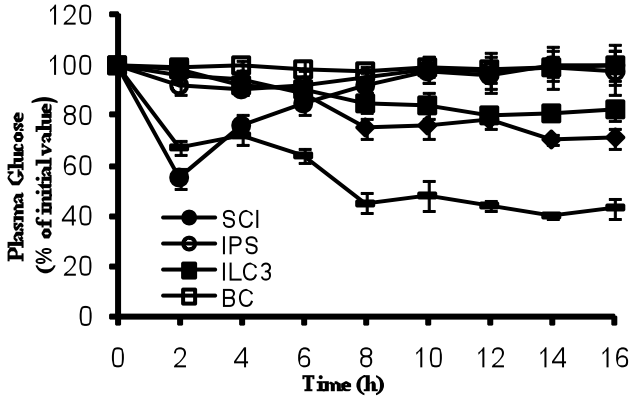
SEM and TEM photomicrograph of prepared nanoparticls



Lieca and SEM photomicrograph of prepared colloidosomes



In vitro drug release profile of insulin from colloidosomes [ILC2] in simulated fluids containing different concentrations of Rat Caecal Content (RCC), (Mean ± S.D., n=6).



Plasma concentration profile of glucose after oral administration in different dosage forms. [SCI: Subcutaneous insulin, IPS: Insulin PBS solution, ILC: Insulin loaded colloidosomes (ILC1-ILC3), BC: Blank colloidosomes]. [Results are expressed as mean ± S.D. (n=6); compared to control; Blank colloidosomes]

CONCLUSION

The study describes the production of drug delivery system bearing protein. These particles were found to protect entrapped insulin against gut proteases. Colloidosomes showed a release profile that was suitable for oral delivery systems of proteins. In vivo results indicate that oral delivery of insulin loaded colloidosomes shows considerable promise in complimenting the therapy of diabetes. This is apparent from the exciting results in diabetic rats with significant blood glucose reduction for prolonged period. This is the first report of insulin loaded colloidosome system, and a successful carrier of the oral insulin strategies tried. However, the limitation of this system, such as optimization of drug release in a more controlled fashion is a compromise to develop protein friendly carriers. These results warrant further optimization and elaborate investigations in various in vivo models to develop a successful oral delivery platform.
Therefore, it is conclude that colloidosomes as drug delivery vehicle containing insulin can be successfully exploited for the treatment of diabetes mellitus.

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