

Abstract

Several attempts for delivering proteins through the oral route have been reported. However, most of these attempts revealed low bioavailability of the administered proteins. As first pass metabolism might be attributed to such loss in the bioavailability, the current investigation aims to study the first pass metabolism of insulin, as a model protein, delivered orally in normal and STZ-diabetic rats.

The oral insulin formulation adapted in this work combines the advantages of using LMWC in the fabrication of W/O microemulsion. The utilized LMWC was initially prepared and characterized. Later, the oral insulin preparation was evaluated for its biological stability. The nanosized preparation was found to possess a unimodal particle size distribution with a mean diameter of 85 ± 3 nm. *In vivo* studies performed on normal and STZ-diabetic rats confirm that insulin retained its biological activity and stability as evidenced by the remarkable reduction of blood glucose levels post oral administration. Such hypoglycemic effect was sustained for a longer period of time post oral insulin administration compared to subcutaneous administration.

In order to study the first pass metabolism of the current insulin formula, different studies were established. The absorption and permeation of the orally administered insulin was conducted utilizing everted gut sac model and *in situ* intestinal perfusion technique. While the absorption of insulin nanoparticles compared to the free insulin solution was reduced in the everted gut sacs, the *in situ* intestinal perfusion study confirmed the ability of the nanoparticles to be absorbed by the intestine as evident by the significant hypoglycemic effects seen in both normal and diabetic rats.