

homeostasis while normal rats have resisted the reduction of glucose levels due to the presence of normal glucose homeostasis.

Formulation into nanoparticles to facilitate insulin cellular uptake represents the most popular configuration for intracellular delivery. Further studies have shown that insulin in nanoparticulate form was more likely to be delivered across the GIT than in its free soluble form (Elsayed et al., 2011; Sadeghi et al., 2008; Bayet et al., 2008). According to the intestinal first pass metabolism, many studies are involved in evaluation the intestinal metabolism. In the current research, absorption and permeation studies were carried out. Our absorption and permeation studies were *ex vivo* everted gut sac and *in situ* intestinal perfusion.

It was found that the absorbed amount of insulin from Rh-insulin solution into the everted sacs was three-folds the absorbed amount from the insulin-loaded nanoparticles formula at 60 min in normal rats. In diabetic gut sacs, however, little amount of insulin from the oral preparation was absorbed compared to the Rh-insulin solution.

Although nanoparticles dispersion system may increase insulin absorption through intestinal mucosa, the currently tested oral formula did not significantly change the permeation behavior of insulin through the small intestinal mucosa on everted gut sac model. Since such effect was seen in both diabetic and normal rats, it might be attributed to the presence of free insulin particles available for absorption. Alternatively, the reasons for such absorption failure perhaps are large particle size, negative surface charge and disturbance in SCOS ratio or emulsifying agent. Also the nanoparticles are bigger size in comparison to the soluble protein molecules and the fact that a lot of particles may get trapped inside the cells within the cellular