properties made chitosan a polymer of choice for insulin delivery. While chitosan has important functional properties, nevertheless, the high molecular weight, high viscosity and insolubility at physiological pH of chitosan restrict its use *in vivo* (Qinna et al., 2015). However, LMWC can be more beneficial than HMWC due to their higher water solubility, and their ability to form nanoparticles (Lavertu et al., 2006). A recent study by Qinna et al. has shown that W/O nanosized system containing LMWC–insulin PEC achieved the highest glucose reduction with 1.3 KDa LMWC (Qinna et al., 2015). For all the above, expected that using LMWC (13KDa) would be able to entrap insulin and could stabilize insulin within their nanostructure.

Therefore, this research was performed to evaluate the first pass metabolism of insulin when delivered orally in normal and STZ-intoxicated rats since oral insulin may denature or degrade before it reaches its target.

Based on formulation of oral delivery system for insulin was carried on previous study (Elsayed et al., 2009). The adopted nanoparticle system was (W/O) microemulsion that consist from mixing LMWC (13 KDa, 99 DDA%) with insulin (with HPβCD) to form a PEC (aqueous phase) which was then solubilized in the oily phase made from Labrasol® and Plurol Oleique® as Surfactant/Cosurfactant (SCOS), and DAGs dissolved in oleic acid.

In the current study, two new materials were added to the previously reported oral delivery system. Zhang et al. reported that hydroxypropyl-β-cyclodextrin (HPβCD) protect insulin encapsulated in CS–alginate nanoparticles from enzymatic degradation (Zhang et al., 2006). Moreover, HPβCD used to enhance the stability of insulin formulation and improve their shelf-time (Sajeesh & Sharma, 2006). In the preparation, HPβCD was added in the aqueous phase during insulin-chitosan PEC