## 1.4.7. Method of Insulin-Chitosan nanoparticles formulation

Insulin-chitosan nanoparticles (NPs) have been prepared using ionotropic gelation with tripolyphosphate or even simply polyelectrolyte complexation between insulin and chitosan. The work of Sadeghi et al. showed that trimethyl chitosan and diethylmethyl chitosan nanoparticles prepared by the PEC method had higher insulin loading efficiency and zeta potential than ionotropic gelatin method (Sadeghi et al., 2008). The interaction of chitosan and polyanions leads to the spontaneous formation of nanoparticles in an aqueous environment without the need for heating or the use of organic solvents (Gan & Wang, 2007)

The most important factors that have to be controlled during preparation of PEC are the pH of the solution, temperature, ionic strength and order of mixing. In addition, there are secondary factors, related to the components that have to be considered, such as flexibility of polymers, M.W. and DDA % of chitosan (Berger et al., 2004).

However, these PECs dissociate easily in acidic gastric conditions, because both insulin and chitosan are soluble at lower pH such as that of the stomach. In order to protect the PECs from the gastric environment, some researchers have to use of oily vehicle, where the most promising oily-based formulations W/O microemulsions (Figure 1.5) (Elsayed et al., 2009).