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Title :

**Pectinate Micro-And Nano-Matrices
As Small Molecule And Protein Drug
Carrier**

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Pectin has received a widespread application in oral drug delivery system design due to its biodegradability, biocompatibility and non-toxicity. This study aims to formulate sustained-release pectinate beads with diclofenac sodium as small molecule drug model by means of microwave technology and pectinate nanoparticles with insulin as macromolecular drug. The pectinate beads were prepared by an extrusion method with chitosan loading internally in the pectinate beads or externally via coacervation. These beads were treated by microwave at 80 W for 5, 10, 21 and 40 min, and had their drug release examined against physicochemical changes of matrices. Treatment of pectinate beads by microwave did not lead to a decrease, but an increase in the extent of drug released at 4 h of dissolution. The drug release of pectinate beads was reduced only upon core loading of chitosan on treating the externally coacervated pectinate-chitosonium beads with microwave. The treatment of chitosan-pectinate matrix by microwave brought about an increase in the extent of drug released unlike those of pectinate-chitosonium beads. Apparently, the loading of chitosan into the interior of pectinate matrix could effectively

retard the drug release without subjecting the beads to the treatment of microwave. The microwave was merely essential to reduce the release of drug from pectinate beads when the chitosan was introduced to the pectinate matrix by means of coacervation. The calcium pectinate-insulin nanoparticles were prepared by ionotropic gelation method, with alginate, sodium chloride or Tween 80 as additive. Their *in vitro* physicochemical, drug release and *in vivo* blood glucose lowering characteristics were evaluated. Spherical calcium pectinate-insulin nanoparticles were characterized by size, zeta potential, insulin content and insulin association efficiency of 348.4 ± 12.9 nm, -17.9 ± 0.8 mV, $8.4 \pm 1.0\%$ and $63.8 \pm 7.4\%$, respectively. They released less than 25% insulin following 24 h in simulated intestinal medium and exhibited delayed blood glucose lowering effect in rats. Incorporation of solubilizer sodium chloride or Tween 80 into nanoparticles

did not enhance blood glucose lowering capacity owing to sodium chloride reduced matrix insulin content and Tween 80 interacted with water and had its blood glucose dilution effect negated. Combination of nanoparticles with alginate gel to allow prolonged intestinal residence and more insulin release did not enhance their blood glucose lowering capacity because of calcium alginate-cross-linked gel formation that could retard insulin release and migration into systemic circulation. Physicochemical responses of additives *in vivo* affected blood glucose regulation property of pectin-insulin nanoparticles.