UNIVERSITI TEKNOLOGI MARA

PECTINATE MICRO- AND NANO- MATRICES AS SMALL MOLECULE AND PROTEIN DRUG CARRIER

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ABSTRACT

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 ± 1.0% and 63.8 ± 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.

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INTRODUCTION

1.1 OVERVIEW

1.1.1 Pectin

Biodegradable polymers are able to encapsulate and protect drugs for long periods of time while offering some control over drug release kinetics ranging from periods of hours to more than a year resulting in a less frequent administration and improving patient comfort and compliance [1–4]. Biodegradable polymers can be used to create drug depots, which offer high local drug concentrations and low systemic concentrations thereby minimizing adverse side effects. Many biodegradable polymers break down into molecules that can be removed naturally by the human body namely pectin [5–8]. Pectin consists mainly of the partial methyl esters of polygalacturonic acid and is obtained by aqueous extraction of appropriate edible plant material, usually citrus fruits or apple pomace [9–12]. Pectin may be used to fabricate particulate structures on the nanometer or micrometer scales [13–19]. The particles formed may be used to protect or deliver pharmaceutical or nutrient components, such as drugs, vitamins or minerals.

1.1.2 Drug Delivery System

Over the past few decades, the rise of modern pharmaceutical technology and growth of the biotechnology industry have revolutionized the approach to drug discovery and development. The close association of people from various fields such as chemistry, biology, medicine and engineering in drug development research has led to the uncovering of the cellular and molecular basis for the action of many drugs [1, 20, 21]. There is a vast database of scientific knowledge available, for example the regulation of enzymes and hormones in the human body, and the effects of various chemicals on different types of cells. The utilization of this knowledge has led to the development of