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DESIGN OF CONTROLLED-RELEASE CHITOSAN SPHEROIDS PREPARED BY EXTRUSION-SPHERONIZATION TECHNIQUE USING MICROWAVE

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DECLARATIONS

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

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ABSTRACT

The interplay effects of matrix formulations with microwave on drug release were investigated using an agglomerate system. Chitosan spheroids were formulated with stearic acid and/or sodium chloride by extrusion-spheronization technique, and chlorpheniramine maleate as water-soluble model drug. The spheroids were treated by microwave at 80 W for 5 to 40 min. The profiles of drug dissolution, drug content, drug-polymer interaction, polymer-polymer interaction, sodium leaching, matrix morphology and integrity were determined. Unlike chitosan matrix prepared by ionotropic gelation method, the retardation of drug release from chitosan spheroids by microwave required a more complex formulation containing both stearic acid and sodium chloride unless a high stearic acid fraction was used. These spheroids demonstrated a high resistance to disintegration during dissolution owing to salt-induced bridging by sodium chloride. In response to microwave, sodium chloride aided stearic acid spread and effected domain interaction via C=O moiety over a matrix with reduced specific surface area thereby reducing drug dissolution. The drug release of spheroids can be retarded by microwave through promoting the layering of hydrophobic stearic acid in a matrix structure sustained by sodium chloride.

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CHAPTER 1

INTRODUCTION

1.1 Background of the Research

The main interest of this research is to formulate chitosan spheroids prepared via extrusion-spheronization technique with controlled characteristics with respect to drug release. The controlled-release characteristics of chitosan spheroids can be achieved via modulating the physicochemical properties of spheroids using new formulation strategy and microwave technology.

Controlled-release technology has been rapidly developed over the past three decades as a new interdisciplinary science that offers novel approaches to the delivery of bioactive agents into systemic circulation at a predetermined rate (Kim, 2000; Aulton, 2002). The development of controlled-release technology is aimed to eliminate the limitations of conventional dosage forms whereby repetitive administration of conventional dosage forms leads to fluctuations of drug concentration in plasma and site of action over successive dosing intervals and hence not possible to maintain a constant therapeutic concentration of drug at site of treatment. The unavoidable fluctuations of drug concentration in plasma and at site of action can result in patient being overmedicated or undermedicated. In addition, the need of patient for frequent administration of conventional dosage forms is accompanied by reduced patience compliance which forms the main reason for therapeutic inefficiency or failure.

The development of controlled-release dosage form is translated to reduce frequency in drug administration and fluctuation in therapeutic plasma drug concentration (Aulton, 2002; Ražem, 2008). Constant therapeutic plasma drug