UNIVERSITI TEKNOLOGI MARA

DESIGN AND FORMULATION OF AN ENTERIC-COATED INSULIN NANOPARTICLES FOR ORAL DELIVERY

MOHD HAFIZ BIN MOHD JAAFAR

Thesis submitted in fulfilment
of the requirements for the degree of
Master of Science

Faculty of Pharmacy

March 2017

AUTHOR'S DECLARATION

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 results of my work, unless otherwise indicated or acknowledged as referenced work. This topic has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

Name of Student	:	Mohd Hafiz Bin Mohd Jaafar
Student I.D. No.	:	2011599469
Programme	:	Master of Science - PH780
Faculty	:	Pharmacy
Thesis Title	:	Design and Formulation of an Enteric-Coated Insulin Nanoparticles for Oral Delivery
Signature of Student	:	
Date	:	March 2017

ABSTRACT

Double-functional nanoparticles with pH-sensitivity and mucoadhesive were developed to prevent insulin from contacting the highly acidic medium in the stomach, prolong the intestinal residence time and increase the permeability of insulin to the systemic circulation. Four different formulations of enteric coated insulin nanoparticles were prepared using polyelectrolyte complexation and ionotropic gelation methods with varying concentrations of alginate and calcium chloride. Optimal gelation was achieved when concentration of alginate and calcium were 3.3 % w/w at pH 3.0. Formulation C containing of 11.630 % (v/v) insulin, 0.100 % (w/v) alginate, 0.045 % (w/v) Pluronic F-68, 0.035 % (w/v) dextran sulphate, 1.160 % (v/v) calcium chloride and 17.440 % (v/v) chitosan showed the best nanoparticle properties with droplet size of 333.27 ± 5.67 nm, polydispersity index of 0.24 ± 0.01 and zeta potential of -17.9 ± 0.98 mV, respectively. A reversed-phase high performance liquid chromatography (HPLC) method has been developed and validated for the qualification and quantification of insulin in rat plasma. The proposed method produced linear response over the concentration range of 0.39 to 50 μg/ml. The mean recovery was 99.6 %, while the coefficient of variation of within-day and between-day measurements was less than 8 %. Their pharmacokinetic profiles were characterised after oral administration. Four groups of rat were administered orally with 100 m/kg of enteric-coated insulin nanoparticles while a control group was given 10mg/kg of pure insulin solution. Blood samples (200 μl) were collected using heparinised syringes at pre-determined time intervals over 240 min. 100 μl of plasma sample were introduced into HPLC and insulin concentration was measured at 210 nm. Pharmacokinetic profiles insulin in each group were calculated using trapezoidal method. Formulation C showed the highest absorption profile with AUC value of 2135.71 ± 68.64 μg/ml·min. The control group exhibited the lowest AUC value of 192.49 ± 10.92 μg/ml·min. In conclusion, delivery systems which exhibit pH-sensitivity and mucoadhesive properties could have an excellent synergistic effect to enhance insulin absorption via oral delivery.

ACKNOWLEDGEMENT

First and foremost, I would like to express my gratefulness to Allah SWT, for his grace, for his opportunity to finish my Master education. My deepest gratitude and thanks for my supervisor, Dr. Khuriah Bt. Abdul Hamid for her guidance and knowledge. I would like to thanks Dr. Tommy Julianto Bustamy Affendi for providing conducive laboratory environment and assisting me during the laboratory work.

My appreciation goes to the laboratory staffs including for sharing their knowledge and provide assistance during analytical work. I would like to thank my colleagues and friend for their help and knowledge throughout my research.

Finally, special thanks to my parents, and
for continuous motivation and support during this challenging period of time. I dedicated this thesis for both of you. Alhamdulillah.

TABLE OF CONTENTS