UNIVERSITI TEKNOLOGI MARA

DESIGN AND DEVELOPMENT OF POLYMERIC LEVODOPA NANOPARTICLES FOR INTRANASAL DRUG DELIVERY

MOHD ZULHELMY BIN AHMAD

Thesis submitted in fullfillment
of the requirements for the degree of
Master of Science
(Pharmacy)

Faculty of Pharmacy

July 2018

ABSTRACT

Nasal delivery is an alternative route of delivery to deliver levodopa (L-dopa) to the brain. It provides high permeability towards drugs in the nasal epithelium, rapid absorption across the central nervous system (CNS) and avoidance of first-pass metabolism. Importantly, transport of exogenous materials directly from nose-to-brain is a potential route for bypassing the blood brain barrier (BBB). In this study, we developed a carrier system for L-dopa using polymers such as poly lactic co-glycolic acid (PLGA) and chitosan. Screening of suitable polymers as a drug carrier is important to ensure optimum percentage of L-dopa encapsulated in the carrier system. Total of three formulations (P1, P2 and P3) using PLGA nanoparticles were prepared using modified water in oil in water (W/O/W) solvent evaporation technique while four formulations of chitosan nanoparticles (C1, C2, C3 and C4) were prepared by ionic gelation method with sodium tripolyphosphate as a crosslinking agent. Based on particle size analysis, zeta potential and encapsulation efficiency (EE) study, Formulation C2 demonstrated the best results with droplet size of 553 ± 52 nm, polydispersity index (PDI) value of 0.522, zeta potential of 46.2 ± 2.3 mV and EE value of 82.38% ± 1.63, respectively. Morphology study includes Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) showed that Formulation C2 have almost same particle size with good uniformity which corroborated with our particle size analysis study. Additionally, X-ray diffraction analysis (XRD) revealed that Formulation C2 was in amorphous state and from Fourier Transform Infra-Red (FTIR) analysis, there were no chemical interactions observed that might change the structure of L-dopa in the nanoparticles. Furthermore, the validated High Performance Liquid Chromatography (HPLC) method exhibited mean recovery of above 95% at all conditions and concentrations with the limit of detection (LOD) and quantification (LOQ) were 0.19µg/ml and 0.39µg/ml, respectively. Based on *in vivo* intranasal study, absorption of L-dopa loaded chitosan nanoparticles was significantly increased ($P<0.05$) by almost two-fold with the concentration of 70.008 ± 5.77 µg/ml compared to concentration of unprocessed L-dopa; 50.018 ± 3.25 µg/ml. This study showed the potential use of chitosan nanoparticles as a drug carrier to improve the delivery of L-dopa to the brain hence increase its therapeutic effects.

ACKNOWLEDGEMENT

First and foremost I would like to thank Allah for his blessing and grant me with patience to complete this study. I wish to acknowledge my deepest gratitude to my academic supervisor, Dr. Khuriah Abdul Hamid for her continuous support and encouragement throughout my project. I also wish to acknowledge Dr. Tommy Julianto Bustami Effendi for sharing his ideas and knowledge in assisting my work and for guiding me in the laboratory work. This research would not be completed without the help of Assistant Science Officer, Normeliza Jamil for her technical support and guidance. Special thanks to my friends at the Faculty of Pharmacy, especially Mohd Hafiz Mohd Jaafar and Nurfazreen Anuar for their support and help during tough moments in my research study.

My thankful and love go to all family. I am indebted to my mother and father for their continuous encouragement, support and active interest in my education. To my wife, who is always there for me, I would like to thank her for her patience, encouragement and support and most of all for believing in me. Lastly I would like to thank Faculty of Pharmacy UiTM Puncak Alam for providing great facilities that enabled me to complete my research work.

TABLE OF CONTENTS