

UNIVERSITI TEKNOLOGI MARA

**DESIGN AND DEVELOPMENT OF
POLYMERIC LEVODOPA
NANOPARTICLES FOR
INTRANASAL DRUG DELIVERY**

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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 $82.38\% \pm 1.63$, 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 $0.19\mu\text{g/ml}$ and $0.39\mu\text{g/ml}$, 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 $\mu\text{g/ml}$ compared to concentration of unprocessed L-dopa; 50.018 ± 3.25 $\mu\text{g/ml}$. 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.

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