UNIVERSITI TEKNOLOGI MARA

IN VITRO AND *IN VIVO* CHARACTERIZATION OF PLGA NANOPARTICLES LOADED WITH IBUPROFEN A POORLY WATER SOLUBLE DRUG

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AUTHOR'S DECLARATION

I declare that the work in this thesis/dissertation 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.

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.

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ABSTRACT

Nanoparticles both pharmaceutical and biomedical have many advantages such as enhancing drug bioavailability and the ability to cross barriers after oral and parentral administration by improving the solubility of poorly water soluble drugs. However, physical properties of nanoparticles, such as size and morphological characteristics are critical for the drug release in the body, hence the importance of understanding these parameters. Poly (lactic-co-glycolic acid) (PLGA) has been studied extensively as a polymeric starting material for the fabrication of biodegradable and biocompatible nanoparticles. The pharmaceutical parameters of nanoparticles preparation have been studied using a model Class II drug, ibuprofen. The solvent evaporation technique using oil-in water (O/W) is commonly adopted for the preparation of polymeric nanoparticles. This method involves mixing an aqueous phase containing distilled water and stabilizing agent, polyvinyl alcohol (PVA) and an organic phase including the polymer and an organic solvent. The effect of preparation parameters on the particle size, size distribution, zeta potential and morphology of PLGA nanoparticles was studied. Amongst the many parameters only four critical parameters namely, homogenizing speed, homogenizing time, stabilizer concentration and temperature were investigated. The optimum parameters identified were then adopted for the preparation of ibuprofen loaded-PLGA nanoparticles. The mean particle size, polydispersity index (PDI) and zeta potential of blank PLGA nanoparticles were determined and found to be 679 nm, 0.101 and -34.5 mV, respectively. Loading the drug into the PLGA nanoparticles resulted in an increase in the, mean size, PDI and zeta potential of the nanoparticles. The surface morphology of nanoparticles was investigated by scanning electron microscopy (SEM), transmission electron microscopy (TEM) and atomic force microscopy (AFM). The thermal behavior, crystalinity and chemical interaction of ibuprofen loaded-PLGA nanoparticles were investigated by differential scanning calorimetry (DSC), X-ray diffraction (XRD) and Fourier transform infrared spectroscopy (FTIR), respectively. Three different formulations of ibuprofen loaded-PLGA nanoparticles were prepared to study the drug release behavior. The drug content and encapsulation efficiency (EE) of the three formulations were determined using HPLC and UV. The results showed an initial rapid release (burst effect) followed by a slower drug release for all formulations at different conditions. Bioavailability studies were conducted following the 2 week crossover design to evaluate the drug concentration in blood serum of rats. The following pharmacokinetic parameters (AUC, T_{max} and C_{max}) were calculated using PK add-ins of Microsoft Excel. Statistical analysis was conducted using a two-way ANOVA followed by a one-way ANOVA. Results revealed that the loaded nanoparticles showed significantly ($p<0.05$) higher AUC_{0-t} and C_{max} compared with the control. In conclusion, the PLGA nanoparticles have the potential to improve the bioavailability Class II drugs and as such are likely to reduce the dose needed and minimize possible side effects.

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After working on this project and understanding the materials and thoughts related to the discipline, I have finally come to the completion of this study. All the experiences I have accrued while producing this nano-biodegradable polymers have enabled me to propose a more effective method to increase the solubility of poorly water soluble drugs besides sustaining the rate of drug release.

But I believe that there is no end to the pursuit of knowledge. I realize that this project report is far from perfect. However, I have done my utmost to produce a useful work based on my abilities, experience and support from various people around me.

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