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PREPARATION, CHARACTERIZATION AND *IN VIVO* EVALUATION OF NIFEDIPINE-LOADED BIODEGRADABLE PLGA NANOPARTICLES FOR IMPROVED ORAL BIOAVAILABILITY

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ABSTRACT

In recent years, technological advancements have brought us many innovative drug delivery systems. Among those, polymeric nanoparticles systems from biodegradable and biocompatible polymer are interesting option for drug delivery. Poly lactic-co-glycolic acid) PLGA nanoparticles have gained attention for preparation of a wide variety of delivery systems containing several drugs. Nifedipine as a model drug is poorly soluble in water with low bioavailability. Loading nifedipine into PLGA nanoparticles may improve the solubility and bioavailability of the drug. Nifedipine loaded PLGA nanoparticles were prepared by solvent displacement method. For preparation of the PLGA nanoparticles, several parameters were investigated such as PLGA concentration, surfactant concentration, types of surfactants, technique of adding the solvent and ratio of aqueous to organic phases can be characterized by measuring the particle size, size distribution, zeta potential and morphology of PLGA nanoparticles. The results showed that the optimum formulations gave nanoparticles a smaller size and with better distribution and zeta potential. The surface morphology of nanoparticles images showed a spherical shape and smooth surface of blank PLGA nanoparticles and nifedipine loaded PLGA nanoparticles. The drug loaded PLGA nanoparticles were designed in three different formulations with 10, 20 and 30 % w/w of theoretical drug loading. The drug content and the drug entrapment increased with a rise in the theoretical drug loading. It was necessary to examine the interaction between the drug and the polymer during the preparation. The FTIR spectra were used to examine the interaction between the drug and the polymer. Comparing the characteristic absorption bands of nifedipine and PLGA that existed in nifedipine loaded PLGA nanoparticles, no chemical shift was found. In order to assess the *in vivo* release of nifedipine from PLGA nanoparticles, nifedipine level was measured in the rat plasma.

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CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF STUDY

For the past two decades, there have been great research interests in drug delivery system as a carrier for small and large molecules. Particulate systems like nanoparticles have been used as a physical approach to alter and improve the pharnacodynamic and pharmacokinetic properties of a variety of drug molecules. Various polymers have been used in the formulation of nanoparticles for drug delivery because of their quality and ability to sustain drug release over a long period of time and give a steady plasma concentration that may reduce the total required dose and unfavorable reactions (Mohanraj & Chen *et al.,* 2005). A number of polymers have been used for formulating the nanoparticles such as the biodegradable polymeric materials like poly (lactic-co-glycolic) acid (PLGA), polyanhydrides, polycaprolactone and poly-alkyl-cyanoacrylates. These materials have been extensively exploited for controlled drug delivery systems (Park, 1995; Soppimath *et al.,* 2001) because of their desirable properties such as biodegradability, biocompatibility and safety (non toxic) (Jawahar *et al.,* 2009).

Nanoparticles have an important role in the field of drug delivery because of their ability to deliver a wide range of drugs to various body areas in a sustained manner (Hans & Lowman *et al.*, 2002). The nanoparticles can act as a carrier for a variety of agents including proteins, peptides, antigens, drugs, genes and vaccines (Mundargi *et al.,* 2008). They also have applications in non-conventional routes such as ophthalmic delivery, where they can increase the residence time of a drug. In pharmacy, nanoparticles have been used for improving solubility and bioavailability of poorly-soluble drugs, protecting the entrapped drug from gastrointestinal interferences (chemical and enzymatic degradation), controlling the release of drug in the blood and improving intercellular penetration (Anderson & Shieve, 1997). In addition to the abovementioned advantages, nanoparticles also reduce dose and dosing frequency, alleviate side effect and improve patient compliance.