PHBV Nanoparticles of FTY720 (Fingolimod) : Drug Loading and Release Studies of a Water In-Soluble Drug

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ABSTRACT SUMMARY

Nanospheres based on a poly(hydroxybutyrate-hydroxyvalerate) copolymer (PHBV) were loaded with fingolimod using emulsion-solvent evaporation process. The influence of the concentration of PVA and the polymers was tested on particle size of prepared particles. The processing parameters involved in the method were optimized, including drug amount, concentration of surfactant and polymer to obtain small nanoparticles with maximum drug entrapment.

INTRODUCTION

Fingolimod is a synthetic compound based on modification of the natural immunosuppressant, myriocin (ISP-1). [1,2] It was approved by the U.S. Food and Drug Administration in 2010 as the first orally bioavailable drug for patients with multiple sclerosis (MS). [3,4,5] In addition to MS, FTY720 has also been tested in phase III clinical trials as an immunosuppressant for kidney transplantation[4,5]. The current available capsule formulation enables daily administration with dose proportional pharmacokinetics to achieve active steady-state levels in MS patients at 0.5 mg daily.

Controlled-release formulations of different medicines have been used to reduce the adverse effects of drugs and maintain clinical remission of diseases. [6,7] Furthermore, alternative formulations for reducing daily dose is preparation of subcutaneous controlled release form of fingolimod.

Nanoparticle drug delivery systems from biodegradable and biocompatible polymer are interesting option for controlled drug delivery and drug targeting. Among a number of biodegradable, natural and synthetic polymers, poly(3-hydroxybutyrate-co-hydroxyvalerate) (PHBV) have attracted attention as alternative biodegradable polymers because of reported excellent biocompatibility and non-toxicity. [7] The purpose of this study was to prepare fingolimod nanoparticles with emulsion-solvent evaporation method and optimization of nanoparticles to result in controlled delivery of fingolimod.

EXPERIMENTAL METHODS

Fingolimod loaded poly(3-hydroxybutyrate-co-hydroxyvalerate) (PHBV) nanoparticles (NPs) were prepared using the emulsion-solvent evaporation method which can be applied for Water In-Soluble drugs.

In this study B ox-Behnken design, one of the major RSM techniques, was used for designing of experiments. Box-Behnken is an independent quadratic design with the advantage of investigating three independent factors with fewer numbers of experiments [8]. In this study, one series of experiments is designed for preparation of nanoparticle. For the experiments the independent variables are the concentration of PHBV (A), PVA (B) and amount of fingolimod (C).

RESULTS AND DISCUSSION

All suggested models for optimization of nanoparticles were acceptable because of R square above 0.8. The obtained model for loading efficacy is shown for instance.

Loading Efficacy (LE): Calculated LE% of nanoparticles in the range of 5-73 % depended on all three variables (A, B, C). The effects of concentration of PHBV and PVA on loading efficacy are shown in Fig 1.
Model validation: The optimum results of trials was obtained with entrapment efficacy of 73.79, loading capacity of 22.11, poly dispersity index of 0.207 and mean diameter of 230nm, that confirm predicted data by Box-Benkehn design.

Scanning Electron Microscopy (SEM): The SEM micrograph of the optimum NPs is shown in Fig. 2 that is in agreement with the dynamic light scattering measurements. It seems the shape of nanoparticles is discrete spherical which assign them suitable features to be used as injectable delivery system.

In-vitro release study: Preliminary studies on the release of the fingolimod from nanoparticles have been made and are shown in Fig. 3.

CONCLUSION
All these results indicate that Fingolimod loaded biodegradable PHBV are promising sustained drug delivery system and these types of nanoparticles can be widely used as effective carriers for controlled release injectable drug delivery system.

REFERENCES