Formulation and Characterization of Isoniazid Nanoparticles for Treatment of Tuberculosis Using Biodegradable Polymer

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Abstract

Nanotechnology is a multi-disciplinary vast scientific field undergoing novel development. A part of this field is the development of Nano-scaled drug delivery devices for targeted drug delivery. Nanoparticles have been developed as an important carrier to deliver conventional drugs, recombinant proteins, vaccines and most recently nucleotides[5]. The aim of the project work was to formulate and characterize isoniazid nanoparticles for pulmonary delivery. Nanoparticles prepared using biodegradable polymers such as chitosan, are degraded in the body into carbon dioxide and water which are biocompatible. Bioavailability of poorly soluble drugs can be increased by reducing their particle size into submicron/Nano size. Various drug / polymer ratio were planned to achieve the objective. The prepared Nanoparticles were evaluated for Particles Size and surface morphology, drug entrapment efficiency, *In Vitro* Release**.** From these studies it can be concluded that IC1 & IC2 formulations were ideal and drug release can be achieved for 24hrs.

Keywords: Isoniazide; Nanoparticles; Gels; Pulmonary Administration; Biodegradable polymer.

Introduction

Nanoparticles (NP) have been used as particulate colloidal carriers in pharmaceutical and medical fields. We can use nanoparticle to provide targeted delivery of drugs on tissue or cell levels. And also may be used for slow effect in targeted tissues and to improve oral bioavailability of drugs which is having a poor bioavailability and also to improve and increase the shelf life of drug against oxidative degradation[1-3].

The pulmonary route has gained increased importance in the recent years due to its unique properties such as a large absorptive area of up to 100m; extremely thin 0.1 µm - 0.2 µm. Devices used to deliver drug by pulmonary route area based on one of three platforms pressurized metered dose inhaler, nebulizer and dry powder. Pulmonary route possesses many advantages over other routes of administration for the treatment of specific disease, particularly lung associated because large protein molecules degrade in the gastrointestinal conditions and are eliminated by the first pass metabolism in the liver and can be delivered via the pulmonary route.

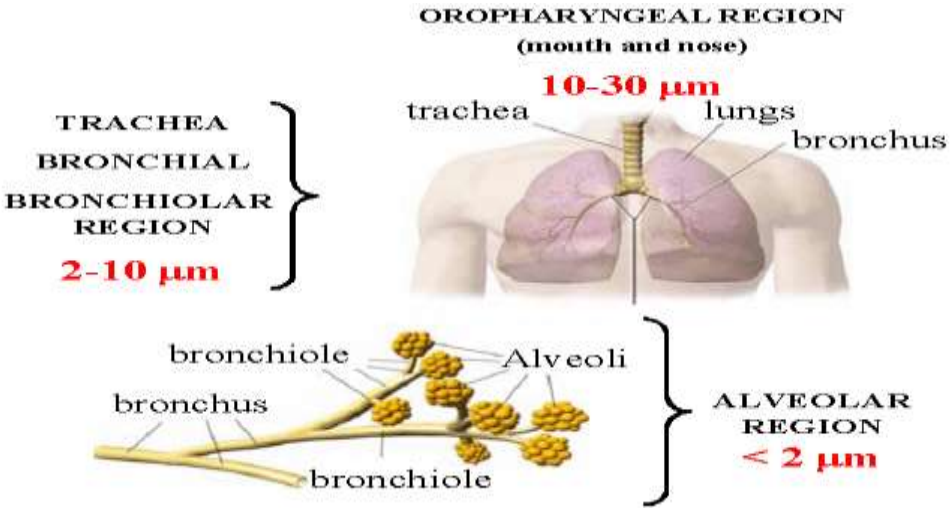

Fig 1: sizes of different region of lungs and their deposition sites

MATERIALS & METHODS

Reformulation studies

Reformulation studies were performed for the obtained sample of drug for identification and compatibility studies.[4]

Standard calibration curve of Isoniazid

Accurately weighed 100 mg Isoniazid was dissolved in 100ml of water to get the stock solution of 100 mg/ml. From this stock solution different concentrations solutions were prepared by dilution technique. The absorbance of the solutions was measured at 262 nm by using UV spectrophotometer.

Drug Excipient Compatibility Study Using FT-IR

FT-IR spectra were recorded with a FT-IR Shimadzu FTIR228 IR spectrometer in range 400–4000 cm-1 using a resolution of 4 cm-1 and 10.

Formulation of Nanoparticles

Table 1. Formulation chart of Isoniazid-Chitosan Nanoparticles

S.No	Ingredient	IC1	IC2	IC3	IC4	IC5
1.	Isoniazid	50mg	100mg	150mg	200mg	250mg
2.	Chitosan	0.25%	0.50%	0.75%	1%	1.5%
3.	Acetic Acid	2%	2%	2%	2%	2%
4.	Poly vinyl alcohol	0.25gm/ 10ml	0.25gm/10ml	0.25gm/10ml	0.25gm/10ml	0.25gm/10ml

Preparation of Nanopaticles

Chitosan and Isoniazid were dissolved and mix with Acetic Acid Aq. Solution of different concentrations with magnetic stirrer. Specified amount of poly vinyl alcohol was kept under magnetic stirrer at room temperature, and chitosan drug solution was added in different concentrations. The obtained chitosan Nanoparticle suspension was centrifuged at 25,000 RPM for 30 minutes and liquid part is discarded and nanoparticles were again suspended in

deionized water followed by sonication, centrifugation and the process was repeated and then nanoparticles were dried and collected.

Particles Size and Morphology

The Optical Microscopy was used for the determination of the shape of Isoniazid loaded chitosan Nanoparticles.

***IN VITRO* Release Studies**

In vitro release of Isoniazid Nanoparticles was determined using phosphate buffer (pH 7.4) in order to simulate the condition in the lungs. Nanoparticles were suspended in 500 ml of the dissolution medium. The experiments were carried out at 37 ± 0.1°C at a 100 rpm. quantity of 1 ml samples were withdrawn at appropriate time intervals and centrifuged at 10000 rpm. Supernatants were diluted suitably with acetonitrile and absorbance of the resulting solution was measured at 262nm in a UV spectrophotometer.

RESULTS AND DISCUSSION

Organoleptic properties

Pure Isoniazid compound was examined for colour, odour and appearance.

Table 2: Organoleptic properties of Pure Isoniazid

Parameters	**Result**
Color	White crystalline powder or Colorless crystal
Odor	Odorless
Appearance	Crystalline powder

Fourier transforms infrared spectroscopy

The compatibility between the drug and polymer was compared by FT-IR spectra. It was observed that, there was no interaction between drug and polymer (Figure 2, 3 & 4).

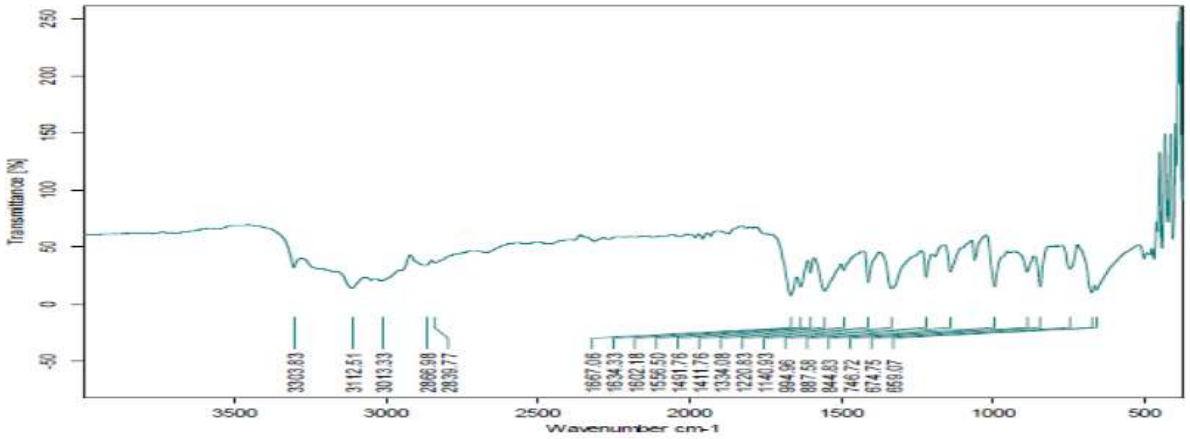

Figure 2: FTIR Spectrum of Isoniazid

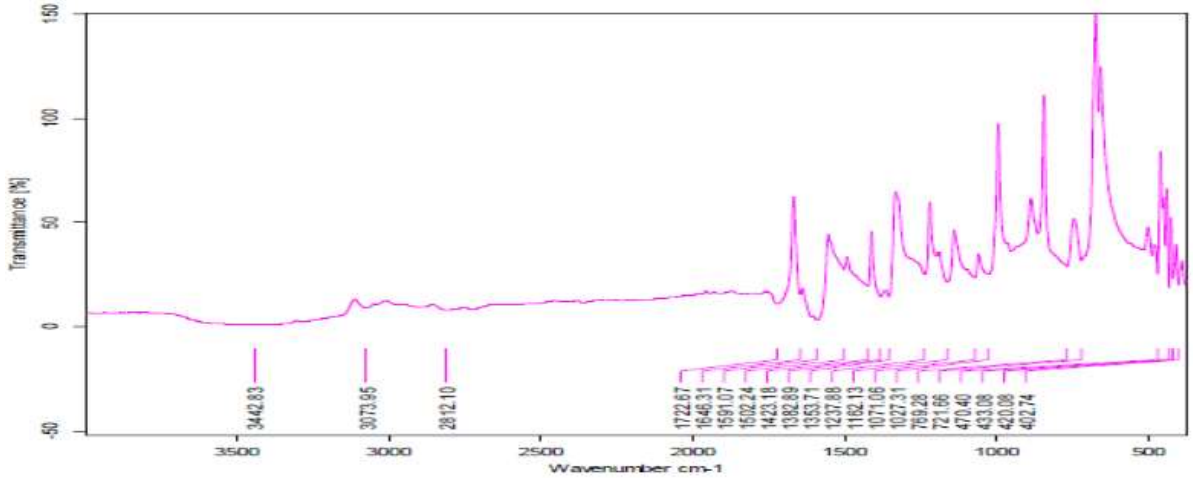

Figure 3: FTIR Spectrum of Chitosan

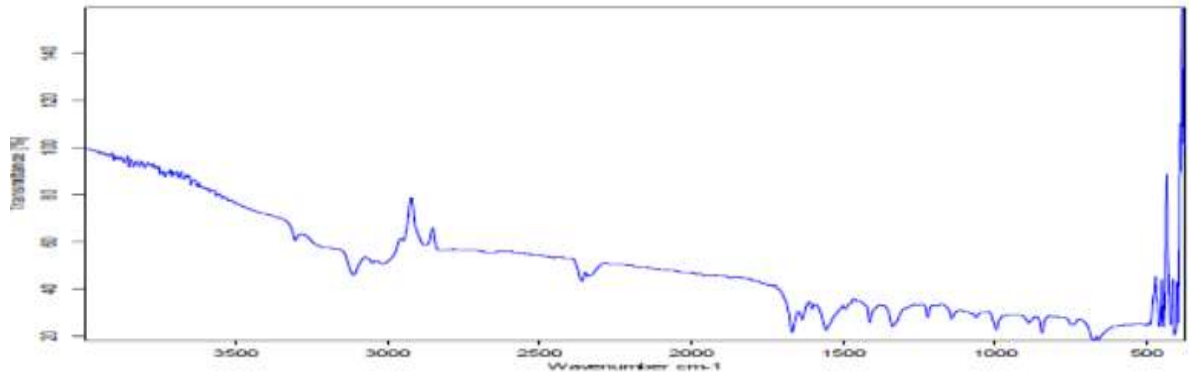

Figure 4: FTIR Spectrum of Isoniazid-Chitosan

Size and Morphological Characteristics of Nanoparticles

INH-loaded chitosan nanoparticles were obtained in the size ranging from 1000 nm to 4000nm.

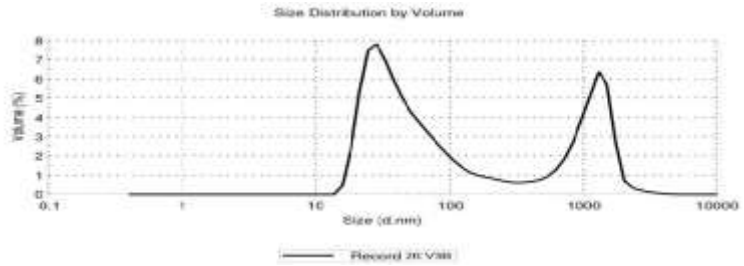

Figure 5: Measurement of particle size

Entrapment Efficiency (E %)

Figure -6 shows the entrapment efficiency (E %) of the nanoparticles.

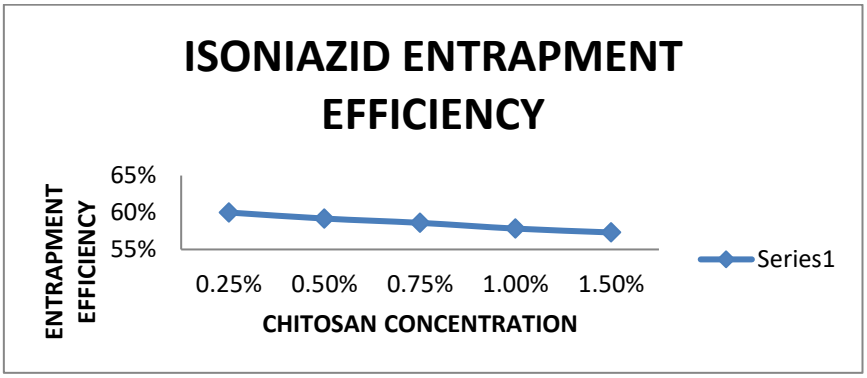

Fig 6: Isoniazid entrapment efficiency

***IN VITRO* STUDIES**

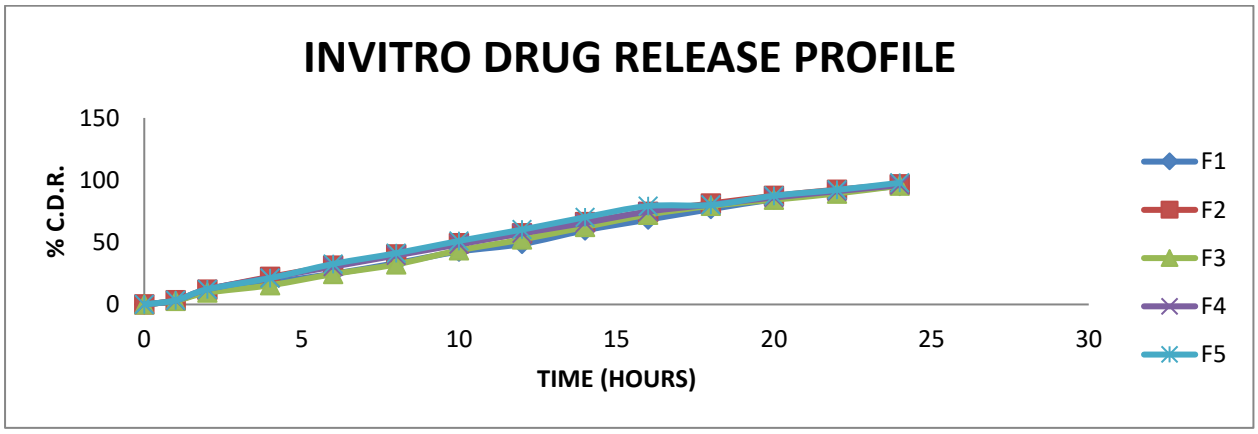

Fig 7: in vitro drug release profile graph of isoniazid loaded chitosan nanoparticles

CONCLUSION

The objective of the present study was to develop isoniazid-Chitosan nanoparticles for treatment of tuberculosis with range of 1-5µm. The nanoparticle formulations were prepared using different concentration of chitosan and drug. The prepared nanoparticles were evaluated for performulation studies, drug interaction, particle size, drug entrapment

efficiency and in vitro drug release. From the results of the present experimental work, it can be concluded that Nano particulate delivery of isoniazid using chitosan polymer can be very promising controlled and targeted drug delivery formulation for treatment of tuberculosis.

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