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Research Article

FORMULATION, CHARACTERIZATION AND INVITRO EVALUATION OF ISONIAZID MICROSPHERES

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ABSTRACT

The aim of present work is to investigate the possibility of obtaining a prolonged, relatively constant effect of isoniazid microspheres by using HPMC and egg albumin as carriers. The present study was aimed to develop and evaluate microspheres of isoniazid (INH) in different drug to polymer ratios using emulsification heat stabilization method. In-vitro drug release studies were performed using the shaking flask method. FTIR studies showed that there was no chemical interaction between the drug and polymers. Scanning electron microscopy showed the microspheres having a spherical structure. Prepared microspheres were characterized for particle size, zeta potential and in-vitro drug release studies. Microspheres showed the particle size of about 70% was in size range of 178.1 nm and zeta potential found to be -49.2 mV. Formulation INH3 showed prolongs drug release. In the present study a satisfactory attempt was made to develop micro particulate drug delivery system of INH with improved bioavailability, efficient targeting and dose reduction.

KEYWORDS: *Microspheres, Isoniazid, Zetapotential, Particle size Analysis, Shaking flask method.*

INTRODUCTION

Oral route drug administration is by far the most preferable route for taking medications. However, their short circulating half-life and restricted absorption via a defined segment of intestine limits the therapeutic potential of many drugs. Such a pharmacokinetic limitation leads in many cases to frequent dosing of medication to achieve therapeutic effect. Rational approach to enhance bioavailability and improve pharmacokinetic and pharmacodynamics profile is to release the drug in a controlled manner and site specific manner. Microspheres are small spherical particles, with diameters 1 µm to 1000 µm [1]. They are spherical free flowing particles consisting of proteins or synthetic polymers which are biodegradable in nature. There are two types of microspheres; microcapsules and micrometrics, which are described as, Microcapsules are those in which entrapped substance is distinctly surrounded by distinct capsule wall. and micrometrics in which entrapped substance is dispersed throughout the matrix. Microspheres are sometimes referred to as microparticles [2]. Microspheres can be manufactured from various natural and synthetic materials. Microsphere plays an important role to improve bioavailability of conventional drugs and minimizing side effects [3].

Isoniazid is Anti tubercular agent, fatty acid synthesis inhibitor. It containing pyridine ring bearing a carboxylic acid group [4]. The plasma half life of INH in patients with normal renal and hepatic function ranges from 1-6 hours [5] depending on the metabolism from 50% to 70% of a dose of isoniazid is excreted in urine within 24 hours, mostly as metabolites [6].

MATERIALS AND METHODS

INH& HPMC was purchased from Labo chem.., Pune, India. Di-sodium hydrogen phosphate, potassium dihydrogen phosphate, acetone, diethyl ether, tween-80 and span-80 were obtained as a gift sample from A.R. Loba Chemical Pvt. Ltd, Mumbai. All other chemicals used were of L.R. grade.

Preparation of micro-spheres of isoniazid by emulsification heat stabilizing method:

300mg of isoniazid (INH) and polymer (HPMC) were dissolved in 20 ml of deionised water and added 5ml of egg albumin solution, 0.1% of Tween 80, stirring it for 30 min. The prepared solute on was used as aqueous phase. The oil phase was prepared by mixing 20 ml of sunflower oil and 5ml of diethyl ether with 1% span80 (as emulsifier) and stirred it for 20 mins at 8001000rpm on magnetic stirrer [7].

The primary emulsion was prepared by adding the oil phase drop wise to the aqueous phase stirred it for 30 mins at 800to1000 rpm.The prepared primary emulsion was added to preheated (65 to 70oC) sunflower oil (80 ml) by using 21 No. needle and stirred it 100to1200 rpm for 2 hrs till the Solidification of microspheres formed. The suspension was then

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allowed to cool to room temperature with continuous stirring using a magnetic stirrer. On cooling, 100 ml of anhydrous ether was added. The suspension containing the microspheres was centrifuged for 15 min and the settled Microspheres were washed three times with ether to remove traces of oil on microspheres. The microspheres were then vacuum dried in a desiccator overnight and stored at 40degrees. Three batches of microspheres were prepared as the above mentioned procedure and labelled as INH-1, INH-2, INH-3 [8].

FTIR:

Fourier-transform infrared spectroscopy (FTIR) is a technique used to obtain an infrared spectrum of absorption or emission of a solid, liquid or gas. An FTIR spectrometer simultaneously collects high-spectral-resolution data over a wide spectral range. This confers a significant advantage over a dispersive spectrometer, which measures intensity over a narrow range of wavelengths at a time.

Determination of % yield of microspheres:

The dried microspheres were collected and weighed accurately. The percentage yield was then calculated using formula given below [9].

$$\% \text{ Yield} = \frac{\text{Mass of microspheres obtained}}{\text{Total weight of Drug \& Polymer}} \times 100$$

Determination of drug content:

INH content in the micro-spheres was estimated by an UV spectrophotometer method based on the measurement of absorbance at 243 nm in phosphate buffer of pH 7.4. The method was validated for linearity, accuracy and precision [10].

$$\% \text{ drug loading} = \frac{\text{Weight of drug in microspheres}}{\text{Weight of microspheres}} \times 100$$

Scanning Electron Microscope:

Scanning Electron Microscopy (JEOL 5400, Tokyo, Japan) was used to determine shape, surface topography and quality and used to inspect the morphology of fractured or sectioned surface. SEM is a commonly used method for characterizing drug delivery systems, owing in large part to simplicity of sample preparation and ease of operation [11]. The sample is spread on a small square plate. The sample was then coated with gold ion for 5-6 min. The prepared sample was kept inside the chamber, images are captured with different magnification.

Zetapotential:

Zeta potential was considered by using the (Beckman Coulter Delsa Nano C, Brea, USA Instrument). The sample was diluted with double distilled water and taken in the cuvettes and temperature maintained at 25^0c.

Invitro release studies (shaking flask method):

Drug loaded microspheres equivalent to 100 mg of drug were weighed and transferred into a 100 ml conical flask. To this 100ml of pH 7.4 phosphate buffer saline was added, then the flasks were kept in a metabolic shaker and the shaker was adjusted to 50 horizontal shakes per minutes at 37 ± 0.5oC12One ml of the drug releasing media was withdrawn at various time interval of 30 min, 1, 2, 3, 4, 5, 6, 7, 8,9, 10 and11hours and replaced by the same volume of phosphate buffer saline. These samples were filtered through 0.45 µm membrane filter. The filtrate was diluted suitably. The drug was estimate in each batch by UV spectrometer at 267nm.

RESULTS AND DISCUSSION

In the present study an attempt was made to formulate INH as microparticulate drug delivery system in order to localize drug at the absorption site, enhance its bioavailability, reduce dose, thereby improving patient compliance. Microparticulate system of INH was formulated using HPMC as carrier by emulsification heat stabilizing method. Prior to formulation, Preformulation studies were carried out in order to establish compatibility between drug and polymer by IR spectroscopy. Three formulations (INH1, INH2, and INH3) were prepared by varying the ratio of drug and polymer. Preformulation studies revealed that the drug zidovudine and HPMC were satisfactorily compatible, without any significant changes in the chemical nature of the drug. These formulations were subjected to various evaluation parameters like % practical yield, drug entrapment efficiency, particle size distribution, and Zetapotential, SEM and *invitro* release studies. The results of all parameters are tabulated (Table 1 and Table 2*)* and depicted graphically (Figure.4).

Table No. 1: Particle yield, % practical yield, encapsulation efficiency % and actual drug content of INH microspheres

Code	Drug: Polymer	Particle size (µm)	% Practical yield	% Encapsulation efficiency
INH1	1:1	185.6 ± 6.0	70.80	86.0
INH2	1:2	240.8 ± 2.5	82.45	62.2
INH3	1:3	425.5 ± 8.3	86.82	57.33

The size analysis of different batches of microspheres showed that about 70% were in the size range of 350 µm. The size distribution of the microspheres was found to be normal in all the batches. The mean size of the microspheres was increased as the proportion of polymer in the microspheres was increased. The mean size of the microspheres was found to be 185.6 ± 6.0, 340.6 ± 9.5, 438.1 ± 10.3, respectively in the batches of microspheres prepared employing core: coat ratio of 1:1, 1:2, 1:3.

FTIR:

Prior to formulation, Preformulation studies were carried out in order to establish compatibility between drug and polymer by IR spectroscopy. Preformulation studies revealed that the drug z and HPMC were satisfactorily compatible, without any significant changes in the chemical nature of the drug.

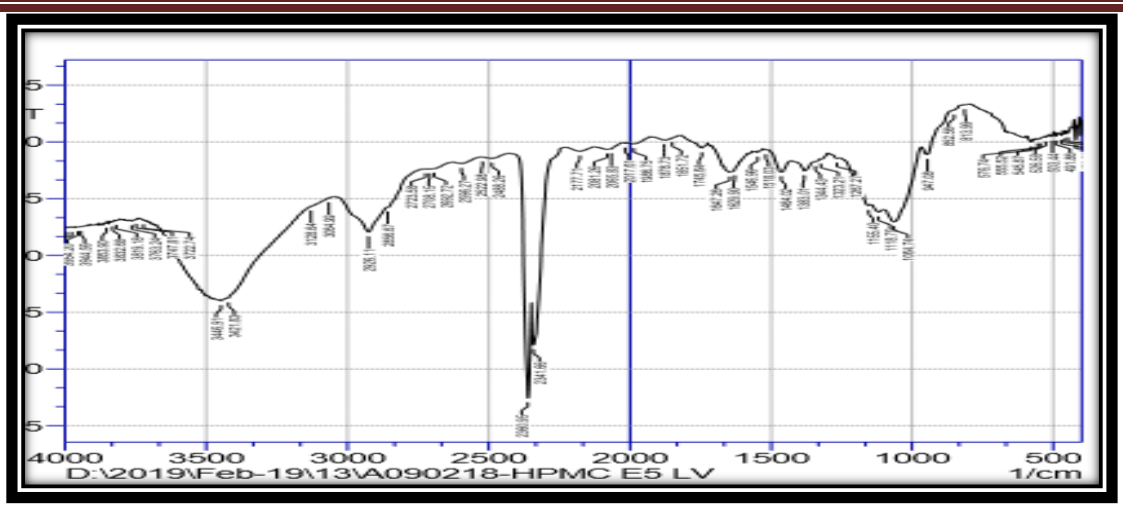

Fig. 1: FTIR Graph of HPMC

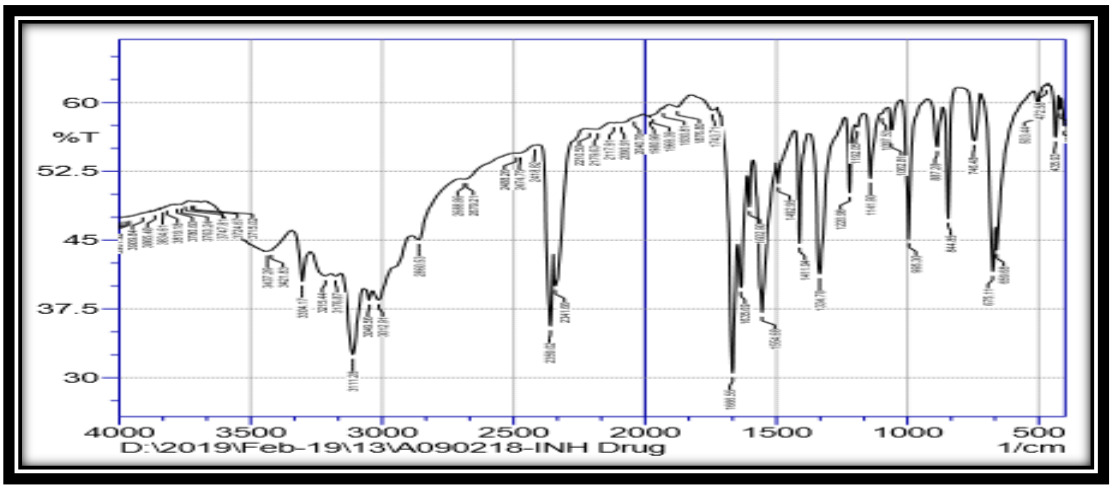

Fig. 2: FTIR Graph of INH

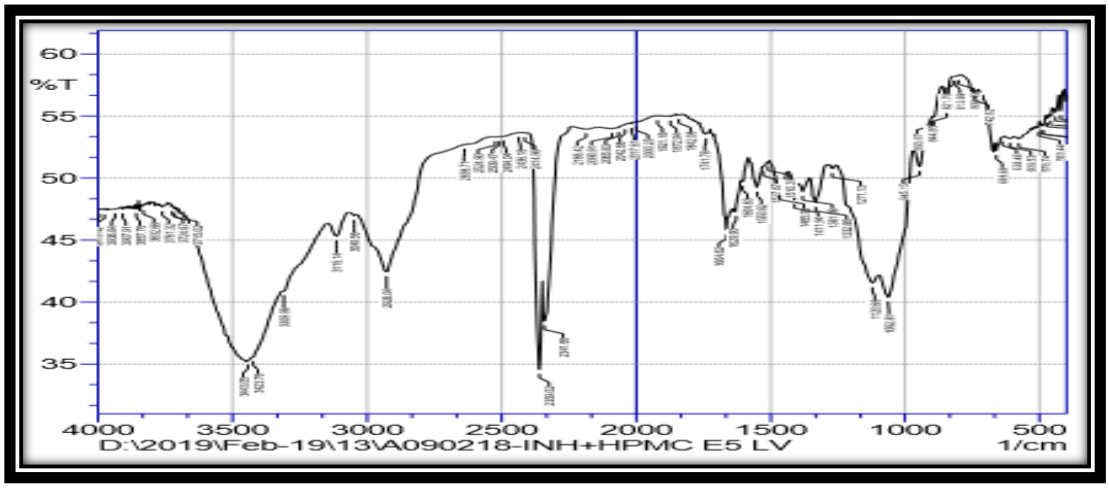

Fig. 3: FTIR Graph of INH+ HPMC

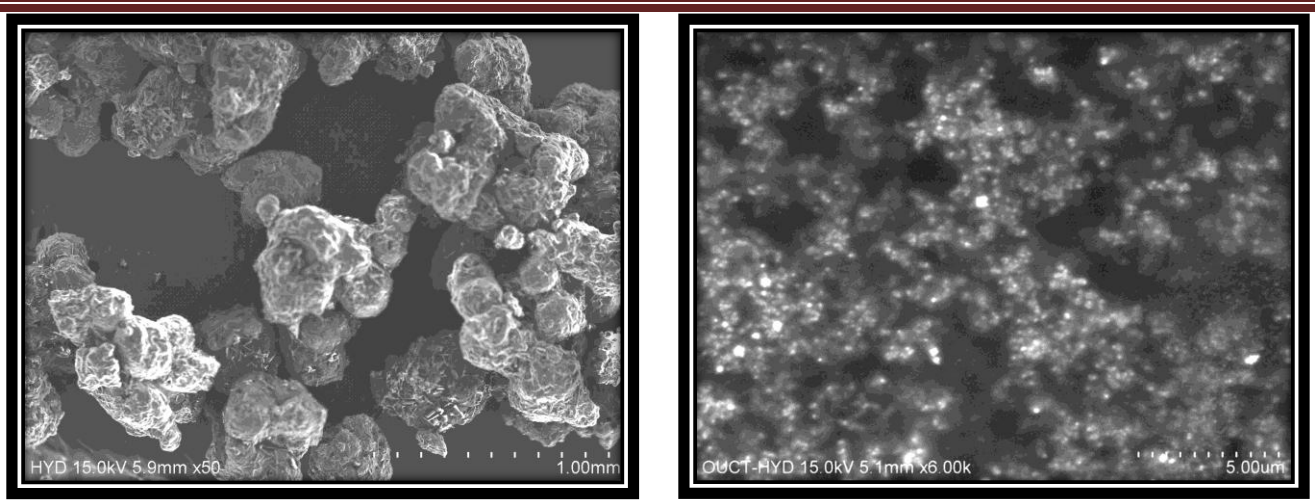

Fig. 4: SEM Photographs of INH3 Microspheres

The scanning electron microscopy of the microspheres was shown in Figure 4. The most of the microspheres were spherical in shape and size ranges from 180-225 µm. But some spheres were in large size.

The size analysis of different batches of microspheres showed that about 70% were in the size range of 178.1nm. The size distribution of the microspheres was found to be normal in all the batches. The mean size of the microspheres was increased as the proportion of polymer in the microspheres was increased. The mean size of the microspheres was found to be 183.8 nm in the batches of microspheres prepared employing core: coat ratio of 1:3.

Zeta Potential:

Zeta potential is used to conclude the electrophoretic mobility of particles. The scale of the zeta potential gives a signal of the possible stability of the colloidal system. It was determined for the optimized formulation INH and was found -49.2 mV.

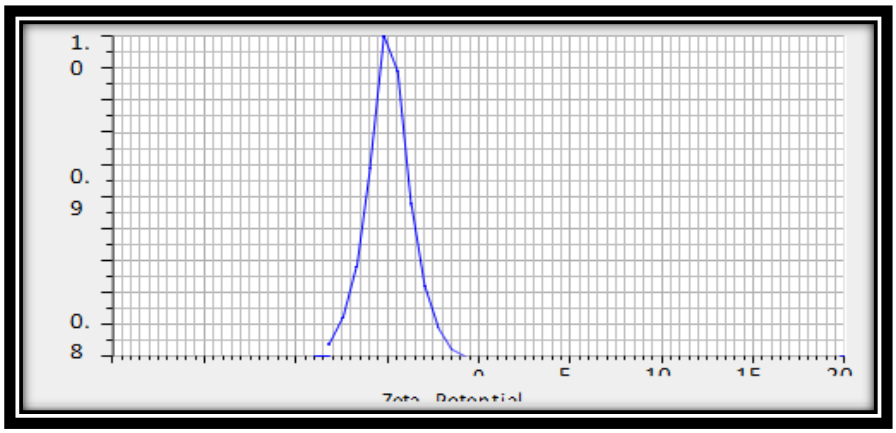

Fig. 5: Invitro release of INH1, INH2, INH3

Table No. 2: % drug release

Time (hrs.)	Abs	Concentration	Amount present	% released
0.5	1.06	10.75	10.75	10.75
1	2.311	23.34	23.34	23.34
2	2.98	30.15	30.15	30.15
3	3.68	37.25	37.25	37.25
4	4.75	47.97	47.97	47.97
5	5.25	53.03	53.03	53.03
6	6.80	68.8	68.8	68.8
7	7.15	72.22	72.22	72.22
8	7.93	80.13	80.13	80.13
9	8.56	86.46	86.46	86.46
10	9.22	93.13	93.13	93.13
11	9.62	97.17	97.17	97.17

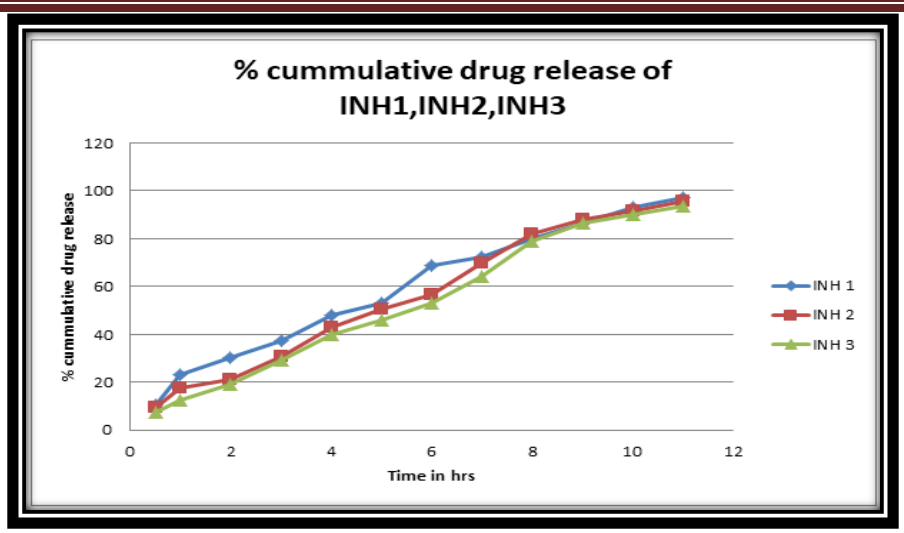

Fig. 6: % Cumulative drug release of INH1, INH2, INH3

CONCLUSION

In the present study a satisfactory attempt was made to developmicroparticulate drug deliverysystem of INH with improved bioavailability, efficient targeting and dose reduction. From the experiment results it can be concluded that:

- HPMC polymer is a suitable macromolecule for the preparation of microspheres of isoniazid.
- FTIR shows that drug and polymer are compatible.
- SEM studies showed that particles are spherical shape.
- Particle size analysis revealed that the microspheres were in the range 175±180nm and all the formulations showed ideal surface methodology.
- Zeta potential value was found to be -49.2 mv
- Formulation INH3 showed prolongs drug release

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