Preparation And Evaluation Of Ganciclovir Magnetic Microsphere By Solvent Evaporation Method

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Abstract:

The present study involves the preparation and evaluation of floating hollow microballoons of Lopinavir for improving the drug bioavailability by prolongation of gastric residence time.A hollow microballoon of In this present work, preparation of Ganciclovir magnetic microsphere is prepared by solvent evaporation method. Magnetic microspheres are mainly used in the controlled drug delivery system, the ferric oxide is one of the oxides of iron, and in the preparation of magnetic microsphere ferric oxide is used to give the magnetic property to the microsphere. The Ganciclovir is comes under the antiviral drug class, it is mainly used to treat against Cytomegalo virus, hepatitis virus, herpes virus etc. The various evaluation tests are done for the magnetic microsphere containing Ganciclovir as loaded drugs are dissolution test, particle size distribution and FTIR.

Keywords : *Cytomegalo Virus (CMV), Ganciclovir (GCV), Magnetic Microsphere, Solvent Evaporation Method (SEM).*

INTRODUCTION

Microspheres are the solid in which particle size are ranges from 10-1000µm in diameter and the particles are in spherical shape. Magnetic microspheres are the spherical particles composed of metallic iron and activated carbon which serves as a delivery vehicle for the site specific targeting retention and release of pharmaceuticals. Magnetic microspheres are composed of magnetite are well tolerated by the body and it is rapidly cleared by reticular endothelial system. Magnetite is a rock mineral and one of the main iron ores. Magnetic microspheres are free flowing particles having spherical shape they required small particle sizes enough to circulate through blood capillaries without producing any occlusion there several methods produce. There are several methods to prepare magnetic microspheres namely solvent evaporation method (SEM) and phase separation emulsion polymerization (PSEP). Magnetic microspheres Targeting by incorporation of magnetic particles in to drug and Polymers by using an externally applied magnetic field is one way to physically direct these magnetic drug carriers to a desired site. Magnetic microsphere is occasionally referred to as micro particles. Magnetic polymer microspheres are generally contains magnetic cores to make sure for strong magnetic response and polymeric shells to protect from particle aggregation. Magnetic microspheres are considered as one of the important approach in delivering pharmaceutical active substance to the target site in sustained and controlled release fashion. Magnetite offers great potential for advancements in a number of fields including pharmaceutical drug carriers for targeting the specific site and therapy. The advantage of magnetic

microsphere is less dose and less side effects of the drug. The magnetic microspheres many advantages in chemotherapy and better tumor targeting, high therapeutic efficacy and lower toxicity.

MATERIALS AND METHODS

Ganciclovir was obtained as gift sample mylan pharmaceuticals, Bangalore and Ethyl cellulose were purchased from Rolex chemical industries, Mumbai. All other chemicals used were of analytical grade.

PREPARATION OF MAGNETIC MICROSPHERE [6]

The varying mount of ethyl cellulose are weighed accurately and it is dissolved in acetone by stirring, then accurately weighed amount of drug is added to the polymer solution. Finally specified amount of ferric oxide is added to the drug polymer solution this is called organic phase, this organic phase is poured drop wise to another beaker containing light liquid paraffin with vigorous stirring over a mechanical stirrer, stirring is continued until microspheres are formed then it filtered and dried.

EVALUATION OF MAGNETIC MICROSPHERES

1. **Determination of percentage yield of magnetic microsphere :**

The prepared microsphere are dried and weighed accurately by using fallowing formula the percentage yield of magnetic microspheres are calculated.

Percentage yield (%) = (practical yield / theoretical yield) x 100. [7]

2. **Particle size analysis :**

Particle size analysis are carried out by using microsphere along with eye piece micrometer and stage micrometer by containing 150 particles per batch.

3. **Scanning electron microscopy :**

By using scanning electron microscopy the morphology of magnetic microspheres are evaluated. [8]

4. ***In vitro* release study :**

In vitro release studies for magnetic microspheres are perform by using usp dissolution apparatus by using 7.4 phosphate buffer solution by maintaining (37±5) ^{o}c and rpm was set to 100 rpm/min. the sample was withdrawn at various time intervals and add same amount was replaced with buffer solution the drug constant is analyzed by spectrometrically at specific wavelength (nm). [9]

5. % drug entrapment efficiency :

The 100mg of magnetic microsphere are accurately weighed and crushed by using mortar and pestle, the drug is dissolved in 5ml of methanol and volume made up to 100ml by using 7.4 PH phosphate buffer and it is analyses by using uv spectrophotometer against blank. [6]

%Drug Entrapment Efficiency = (% drug content / % Theoretical content) x 100

6. Kinetic modeling :

The kinetic and mechanism of drug release of magnetic microspheres is determined by fitted the results of *in vitro* drug release study to the kinetic equation like zero order (% cumulative release vs. time), first order (log % drug remaining vs. time), Higuchi's model (cumulative % drug release vs. square root of time), Peppas plot (log of cumulative % drug release vs. log time). R2 (coefficient of correlation) and k (release rate constant) values were calculated for the linear curve obtained by regression analysis of the above plots.[10]

7. Stability studies

The magnetic microsphere was taken in a crucible and placed at 45^{o}C and 75%RH for 3 month, the magnetic microsphere were analyzed for their drug content and *in vitro* dissolution studies.[10]

RESULT AND DISCUSSION

Physicochemical characterization of magnetic microspheres

By solvent evaporation method the magnetic microspheres are prepared by using ethyl cellulose as a polymer over a mechanical stirrer. ftir spectrum shows no significant changes in the chemical integrity of the drug and also they indicate drug and polymer are compatible. the prepared magnetic microsphere the prepared magnetic microsphere morphology were analysed by sem (fig.1 a&b), their mean size distribution was found to be 325 µm. magnetic microsphere particle size are less than 1000µm, so this drug delivery system can be used for the parenteral formulations. By parenteral route the drug is directly entered to systemic circulation therefore less dose is required and it avoids the first pass metabolism. The entrapment efficiency of the magnetic microsphere containing drug: polymer in the various ratios of 1:1, 1:2, 1:3, 1:4 and 1:5 were found to be 72.80%, 84.44%, 88.50%, 94.40% and 90.54% respectively (table 2). increasing polymer concentration in the formulation will increase entrapment efficiency. high entrapment efficiency is due to electrostatic interaction between polymer and drug. the zeta potential of the magnetic microsphere FS-4 was found to be -3.2 mV, which indicates they are stable.

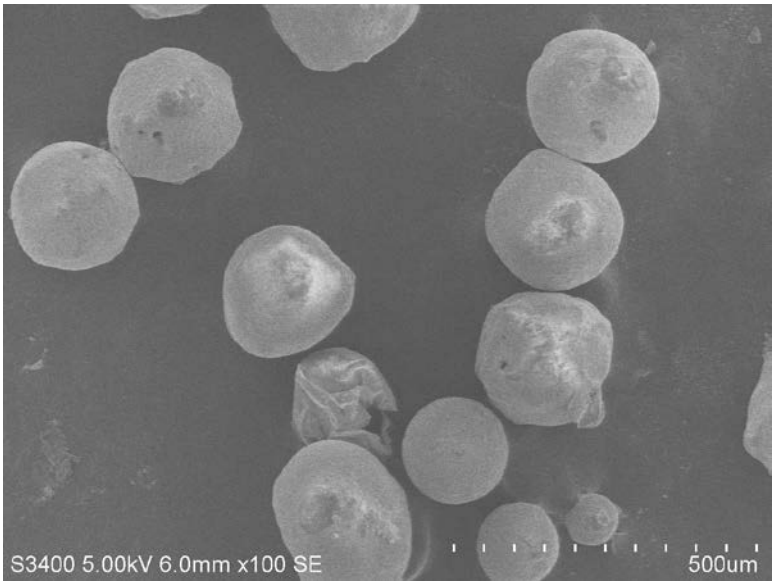

Fig.1 A: SEM of FS-4

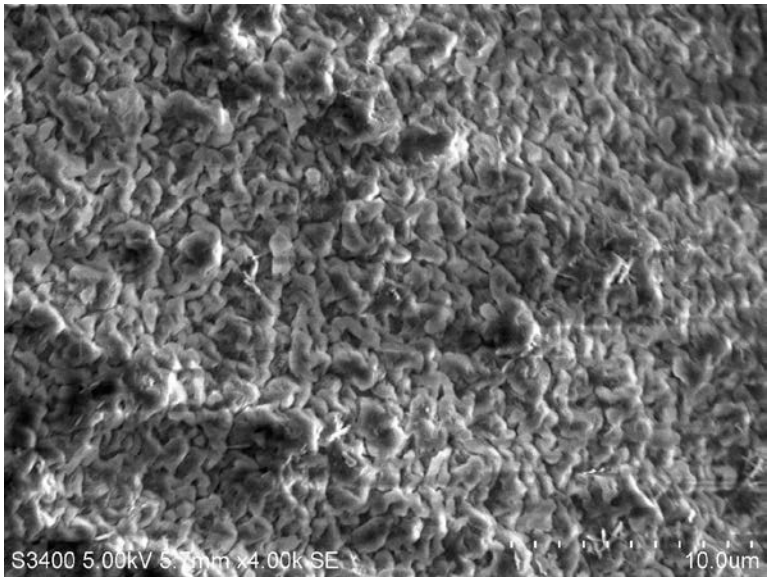

Fig.1 B: SEM of FS-4

In vitro release of magnetic microspheres

The cumulative drug release of the formulations FS1-FS5 is shown in (fig.2). The formulation FS1, FS2, FS3, FS4 & FS5 showed the percentage drug release 66.94%, 63.47%, 61.26%, 58.1% and 66.15% at the end of 12hrs respectively. Among all the formulations FS4 formulation was found to be best formulation, as it release ganciclovir in controlled manner.

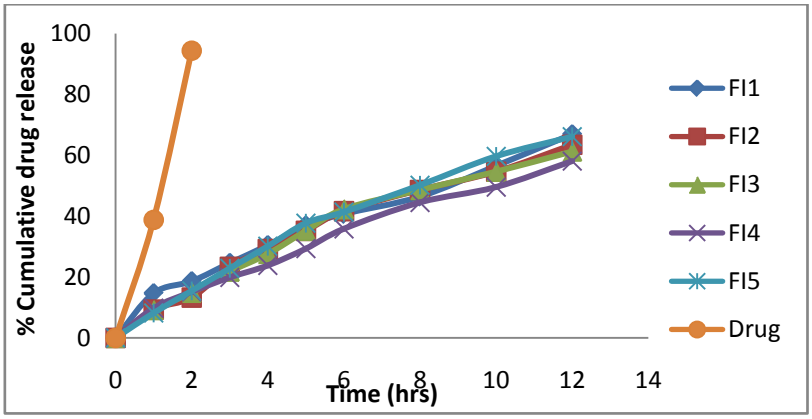

Fig.2: Cumulative release of magnetic microsphere

Stability studies

The drug content result of the optimized formulation FS-4 after 3 month of stability testing period at different storage conditions were shown in fig. 3. The *in vitro* release profile for the FS-4 formulation stored at the different storage conditions was shown infig.4.

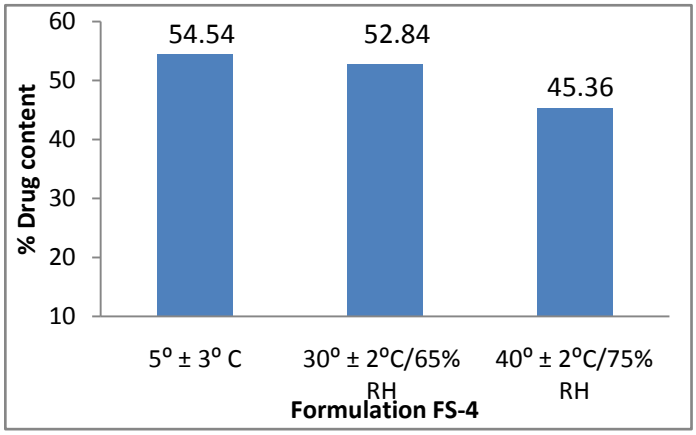

Fig.3: Stability study: comparison of drug content of formulation FS-4 at 5°C, room temperature 30 °C and 40° ± 2°C/75%RH

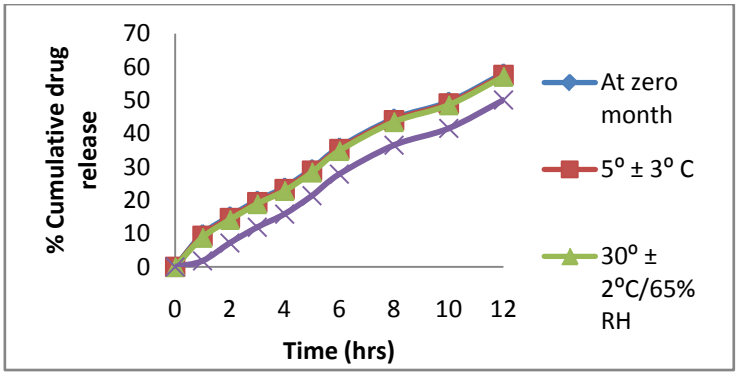

Fig.4: Stability study: comparison of *in vitro* drug release profile for formulation FS-4 at zero month, 5°C, room temperature 30 °C and $40^0 \pm 2^0$C/75%RH after 3 month storage

By comparing this data with the earlier data of the FS-4 it observed there is minor decrease in the drug content when the formulation FS-4 was stored at the 5°C and at room temperature. But the formulation stored at $40^0 \pm 2^0$C/75% RH shows significant decrease in the drug content. It was because at the higher temperature there may be a chances of the drug degradation so that will decreases the drug release.

Table 1: Formulation details of Ganciclovir Magnetic microsphere

SI.NO	INGREDIENTS	F1	F2	F3	F4	F5
1	Ganciclovir(mg)	300	300	300	300	300
2	Ethyl cellulose (mg)	300	600	900	1200	1500
3	acetone(ml)	10	10	10	10	10
4	Ferric oxide (mg)	30	30	30	30	30
5	Liquid paraffin(ml)	30	30	30	30	30

Table 2: Physicochemical characterization of Ganciclovir Magnetic microsphere

SI.NO	Batch code	Drug: carrier ratio	Entrapment efficiency (%)	Particle size (µm)
1	FS-1	1:1	72.80	210
2	FS-2	1:2	84.44	280
3	FS-3	1:3	88.50	330
4	FS-4	1:4	94.40	396
5	FS-5	1:5	90.54	410

Table 3: Correlation coefficients according to different kinetic equations

Formulation code	% CDR	Zero order	First order	Higuchi plot	Peppas plot	'n' values
FS-1	66.94	0.971	0.981	0.973	0.984	1.120
FS-2	63.47	0.968	0.993	0.963	0.985	0.956
FS-3	61.26	0.964	0.993	0.965	0.991	0.961
FS-4	58.1	0.982	0.995	0.961	0.994	0.996
FS-5	66.15	0.975	0.998	0.963	0.992	0.943

CONCLUSION

The Magnetic microsphere of the ganciclovir with ethyl cellulose polymer was successfully prepared by the solvent evaporation method. Based on the drug entrapment efficiency, drug content, zeta potential, particle size morphology and *in vitro* release formulation FS-4 was selected as an optimized formulation. The stability studies were carried for this optimized formulation FS-4 shows that maximum drug content and closest *in vitro* release as the earlier data was found for the FS-4 stored at the 5^{o}C and room temperature. Hence the Magnetic microsphere of ganciclovir (FS-4) were found to be suitable for control release.

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