WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 19, 1147-1169. Research Article ISSN 2277–7105

FORMULATION AND EVALUATION OF GASTRO-RETENTIVE FLOATING MICROSPHERE

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Article Received on
21 August 2024,

Revised on 11 Sept. 2024,
Accepted on 01 October 2024

DOI: 10.20959/wjpr202419-34047

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ABSTRACT

The aim of present study is to decrease low oral bioavailability limitations of conventional dosage forms and provide a therapeutic amount of drug to the desired site in the body and maintain the desired plasma concentration of the drug for a particular period of time. Rilpivirine hydrochloride an anti-viral drug, choice in the treatment of HIV has been chosen as a model drug in the formulation of controlled drug delivery systems. Various studies reported the absolute oral bioavailability of Rilpivirine hydrochloride (46%) with a half-life of 3-5 hrs. A microparticulate floating drug delivery system was planned for Rilpivirine hydrochloride as such a system maintain desired concentration to the desired site and improve bioavailability of the drug. Microsphere formulations were prepared using solvent evaporation technique using Xanthan gum and Guar gum. The prepared floating microspheres were characterized for their percentage yield, particle size, morphology, drug entrapment, *in-vitro* release, and drug release studies. Almost all the formulations showed fairly acceptable values for all the parameters evaluated. Further, the analysis of the release mechanism was carried out by fitting the drug diffusion data to various kinetic equations. The overall curve fitting into various mathematical models was found to be average and best fitted into the zero-order kinetic model. A stability study was conducted for the prepared microspheres of selected formulations for 60 days. There was no significant change in the drug entrapment and *in-vitro* release study of the microspheres.

KEYWORDS: Microparticulate, drug entrapment, percentage yield, microspheres, drug

diffusion.[1]

1. INTRODUCTION

1.2 Microspheres

Microspheres can be characterized as solid, approximately spherical particles with a diameter between 1–1000μm, including dispersed drugs in a certain solution or microcrystalline shape. Both the terms microcapsules and microspheres are often used as synonyms.[5] Medication That is simply transmitted from the gastrointestinal tract (GIT) and also has a short half-life is immediately destroyed bythe circulatory system in the blood. The oral sustained or controlled release (CR) has also been developed to avoid this problem, as that will Slowly discharge the substance into the GIT and retain a steady medication intensity in the plasma for a prolonged time period. A suitable dosage formulation is one that reaches the required plasma therapeutic Drug concentration and remains constant throughout the treatment period. This can be achieved by delivering a traditional dosage type in a fixed dose and at a specific frequency.[6] A benefit they are not microcarriers over nanoparticles migrate across the range of 100 nm carried by the lymph into the interstitium, and therefore function locally. Probably toxic chemicals can be transported Encapsulated, and in place of liquid the dried microparticles may be known as solids. The intake dose is delivered in several tiny different for multiparticulate particles, which hold and discharge a part of the dosage; therefore the breakdown of a specific subunit does not affect the whole dosage failure.[7] Microparticles used in skin applications required to benefit the release of the medication into the skin ensure that now the drug remains localized at the application site and does not enter the systemic circulation unnecessarily.[8] They act as a reservoir which releases an active ingredient over a longer period of time to maintain effective concentration of drug products in the skin while decreasing undesired side effects.[9] Consequently, cycles of over- and under-medication are reduced. It is especially relevant for the reduction of antimicrobial resistance in the management of infectious diseases. These distribution mechanisms can also boost product safety or integration into appropriate vehicles.[10-11]

1.3 Floating Microsphere

Floating microspheres (Hollow microspheres) (**Figure 1.4**) are gastro-retentive drug delivery systems based on a non-effervescent approach. Hollow microspheres are in a strict sense, spherical empty particles without core, free-flowing powders consisting of proteins or synthetic polymers, ideally having a size in the range of 1-1000 micrometers. When

microspheres come in contact with gastric fluid the gel formers, polysaccharides, and polymers hydrate to form a colloidal gel barrier that controls the rate of fluid penetration into the device and consequent drug release. As the exterior surface of the dosage form dissolves the gel layer is maintained by the hydration of the adjacent hydrocolloid layer. The air trapped by the swollen polymer lowers the density and confers buoyancy to the microsphere. However, minimal gastric content is needed to allow the proper achievement of buoyancy.[18]

2. MATERIALS AND METHODS

2.1 Materials Used in the microsphere formulation

In the formulation of microspheres mainly used polymers, which are classified as follows.

➢ Synthetic Polymers ➢ Natural polymers

A. Synthetic polymers are divided into two types

a) Non-biodegradable polymers

Examples- Poly methyl methacrylate (PMMA), Acrolein Glycidyl methacrylate, Epoxy polymers.

b) Biodegradable polymers

Examples- Lactides, Glycolides and their co-polymers, Poly alkyl cyanoacrylates, Poly anhydrides.

B. Natural polymers

They are obtained from different sourceslike proteins, carbohydrates, and chemically modified carbohydrates. They have also usedproteins like Albumin, Gelatin, and Collagen, Carbohydrates like Agarose, Carrageenan, Chitosan, and Starch, and also Chemically changed carbohydrates used like Poly dextran, Poly starch.[8,9,10]

2.2 Drug Excipient Compatibility Study

FTIR Study

Pure drug and Drug with excipients mixture spectrum analysis performed in the mixture at a range of 400 to 4000 cm-1and the degree is 1.5 cm^{-1} using FTIR spectrophotometer. The drug and drug-excipient mixture in KBR (200-400mg) was compressed into discs by applying a pressure of 5 tons for 5 min in a hydraulic press. The interaction between drug-excipients was observed from IR-spectral studies by observing any shift in peaks of the drug in the spectrum of the physical mixture of drug-excipients.

Determination of λ max

The rilpivirine hydrochloride samplewas dissolved in phosphate buffer pH 6.8, andperformed further dilatation after that scanned for maximum absorbance in a UV double beam spectrophotometer (Shimadzu 1800) in the range from 200 to 400 nm, Calibration curves of Rilpivirine hydrochloride.

Preparation of Standard Stock Solution

The standard solution of Rilpivirine hydrochlorideis prepared by dissolving accurately about 10 mg of theRilpivirine hydrochloride with 6.8 phosphate buffer in a 100 ml volumetric flask and sonicated for 15 mins. This stock solution is further diluted with 6.8 phosphate buffer as per the requirement.

Preparation of Sample Solution

The powder of 10 mg Rilpivirine hydrochlorideis weighed accurately and transferred into a 100 ml standard volumetric flask. The contents were dissolved in 6.8 phosphate buffer and sonicated for 30 minutes. This entire solution is filtered through 0.45micronWhatman filter paper (No. 41) and the final solution is made with 6.8 phosphate buffer to get the solution of 1000 µg/ml. This solution is further diluted 5 -30µg/mlas per the requirement.

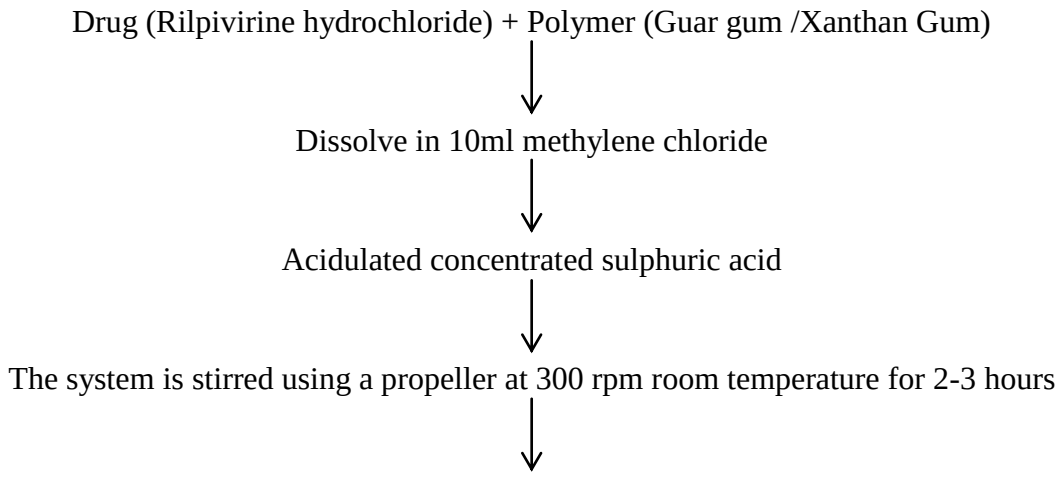
Procedure

The drug solution isscanned (200-400 nm) against a reagent blank i.e., 6.8 phosphate buffer, and the absorption spectrum are recorded. The absorption maximum (λmax) is observed at 305nm and the absorbance of a series of solutions (5-30µg ml) is recorded at that λmax. A graph is plotted by taking the concentration of the drug solutions on the x-axis and the corresponding absorbance values on the y-axis.

2.3 Preparation of microsphere by Solvent Evaporation Method

- Microspheres of Rilpivirine hydrochloride 500mg and polymers were prepared by using various ratios of the drug: natural gum such as 1:1.10, 1:1.20, and 1:1.30,
- Gums were dissolved in the 20ml water 2 hrs.
- In this flowable mass 100mg dug was introduced into 10ml of methylene chloride.
- Drug-gum dispersion was acidulated with 0.5 ml of concentrated sulphuric acid to give a clear viscous solution.
- The system is stirred using a propeller at 300 rpm room temperature for 1hour

- 1.2% w/v dichloromethane was added as an encapsulating agent and 0.15 % w/v of glutaraldehyde as a crosslinking agent, stirring, and heating was maintained for 2.5 hrs.
- Collected microspheres were washed with water to remove surfactant residue and three times with 100 ml aliquots of n-hexane, filtered through Whatman 2 filter paper dried in an oven at 80^0C for 2 hr to collect discrete, solid, free-flowing microspheres and stored in a desiccator at room temperature.
- Process Flow Chart of microspheres



2.4 Formation of microspheres

Table 1: Microsphere formulation Batches of Rilpivirine hydrochloride.

Batches	Rilpivirine hydrochloride(mg)	Guar Gum(mg)	Xanthan Gum (mg)	Liquid Paraffin(ml)	Span 80
B1	100mg	10	-	200	0.5
B2	100mg	20	-	200	0.5
B3	100mg	30	-	200	0.5
B4	100mg	-	10	200	0.5
B5	100mg	-	20	200	0.5
B6	100mg	-	30	200	0.5

Evaluation of Microsphere of Rilpivirine hydrochloride

The prepared Rilpivirine hydrochloride microspheres were characterized for various characters such as particle size, surface morphology, entrapment efficiency, drug content, and *in-vitro* drug release study.

Determination of particle size

The selected best micro beads formulation was subjected to the laser particle counting method. Here the sample was injected into the sample delivery and controlling chamber. Then, a suitable solvent was pumped through the chamber. Now a beam of laser light was allowed to fall on the sample cell. After the required number of runs, they were directed toward the detector. From this, the particle size range and the average mean particle size of the formulation can be studied.

Scanning Electron Microscopy

The purpose of the Scanning Electron Microscopy study was to obtain a topographical characterization of microspheres. The microspheres were mounted on brass stubs using double-sided adhesive tape. Scanning electron microscopy photograph were taken with a scanning electron microscope (JSM-5610LV, Joel Ltd, Tokyo, Japan) at the required magnification at room temperature. The working distance of 39mm was maintained, and the acceleration voltage used was 15 kV, with the secondary electron image as adetector.

% Yield of Microsphere

The prepared Microsphere was collected and weighed. The actual weight of the Microsphere obtained divided by the total amount of all non-volatile material that was used for the preparation of the microsphere multiplied by 100 gives the % yield of Microspheres.

$$\% \text{ Yield of Microsphere} = \text{Practical Yield} / \text{Theoretical yield} \times 100$$

Drug Loading and Drug Entrapment

Microspheres are equivalent to 50 mg of the drug were taken for evaluation. The amount of drug entrapped was estimated by crushing the microspheres and extracting with aliquots of 0.1N HCl (pH-1.2) repeatedly. The extract was transferred to a 100 ml volumetric flask and the volume was made up using 0.1N HCl (pH-1.2). The solution was filtered and the absorbance was measured after suitable dilution spectrophotometrically (UV 1700, Shimadzu, Japan) at 305 nm against the appropriate blank. The amount of drug loaded and entrapped in the microspheres was calculated by the following formulas:

$$\% \text{ Drug Loading} = \frac{\text{Weight of the drug loaded in the microsphere}}{\text{Total weight of the microsphere}} \times 100$$

$$\text{Percentage entrapment efficiency} = \frac{\text{Practical drug content}}{\text{Theoretical drug content}} \times 100$$

In vitro drug release study

The prepared microspheres were subjected to *in vitro* drug release sequentially in three different suitable dissolution media. USP type II dissolution apparatus was used. The dissolution medium for the first 2 hr was 900 ml of 0.1 N HCl (pH 1.2) and continued in phosphate buffer pH 6.8 for the next 7 hrs the temperature of the dissolution medium was maintained at 37 ±0.5 °C and the basket was rotated at 50 rpm. An aliquot of 5 ml was withdrawn at predetermined time intervals and replaced with an equal volume of the fresh dissolution medium to maintain sink conditions. The samples were analyzed at 305 nm, for the percentage of drug release using a UV Visible double beam spectrophotometer. The release study was performed in triplicates.

Dissolution Study

Apparatus	:	USP(basket)
Speed	:	50rpm
Time	:	1,2,3,4,5,6,7,8,9,10,11,12thhour
Temperature	:	37°C ±0.5°C
λ_{max}	:	305nm

Release Kinetics

The matrix systems were reported to follow the Peppas release rate and the diffusion mechanism for the release of the drug. To analyze the mechanism for the release and release rate kinetics of the dosage form, the data obtained were fitted into, zero order, First order, Higuchi matrix, Peppas and Hixson Crowell model. In this by comparing the r-values obtained, the best-fit model was selected.

Zero Order Kinetics

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly, assuming that the area does not change and no equilibrium conditions are obtained can be represented by the following equation:

$$Qt = Qo + Kot$$

Where, Qt = Amount of drug dissolved in time t

Qo = Initial amount of drug in the solution

Ko = Zero order release constant

First-Order Kinetics

To study the first-order release kinetics the release rate data were fitted to the following equation.

$$\text{Log } Qt = \log Qo + K1t / 2.303$$

Where, Qt = Amount of drug released in time t

Qo = Initial amount of drug in the solution

K1 = First order release constant.

Higuchi Model

Higuchi developed several theoretical models to study the release of water-soluble and low soluble drugs incorporated in semi-solid and/or solid matrixes. Mathematical expressions were obtained for drug particles dispersed in a uniform matrix behaving as the diffusion media. The Higuchi equation is

$$Qt = KH \times t1/2$$

Where, Qt = amount of drug released in time t and

KH = Higuchi dissolution constant

Korsmeyer-Peppas Model

To study this model, the release rate data is fitted to the following equation.

$Mt / M = K. tn$

Where, Mt / M = Fraction of drug release,

K = Release constant

t = Drug release time and

n = Diffusional exponent for the drug release that is dependent on the shape of the matrix dosage form.

Stability Studies

The stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain with in its physical, chemical, therapeutic, and toxicological specifications. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of

environmental factors such as temperature, humidity, and light, and enables recommended storage conditions.

Procedure

In the present study, a stability study was carried out for a period of up to 60 days for selected formulations. The selected formulations were analyzed for their physical appearance, drug entrapment, and *in-vitro* release study.

RESULT AND DISCUSSION

Preliminary studies

Preliminary physicochemical properties of Rilpivirine hydrochloridepowder were investigated by performing tests forthe organoleptic properties of the drug, Test of purity. The result of characterizations of puredrugsis shown in (**Table8.1-8.3**).

Table 8.1: Organoleptic properties ofRilpivirine hydrochloride powder.

Sr. No	Parameters	Observation/Result
1	Colour	off-white
2	Odour	Characteristic odour

Table 8.2: Solubility of Rilpivirine hydrochloride powder.

Sr. No	Solubility	Observation/Result
1	Water	Insoluble
2	DMSO	Soluble
3	Phosphate buffer pH-6.8	Soluble

Table 8.3: Melting point of Rilpivirine hydrochloride powder.

Sr. No	Melting point	Observation/Result
1	Rilpivirine hydrochloride powder	238°C
2	Rilpivirine hydrochloride powder	242° C
3	Rilpivirine hydrochloride powder	241°C
Average		240°C

Based on the above physical characterization of Rilpivirine hydrochloride, The Organoleptic, the solubility of the drug and melting point match with the reference data which confirms the purity of the drug.

Drug Excipient Compatibility Study

FTIR study

FTIR Study of selected drug Rilpivirine hydrochloride and their Physical mixture of selected all excipients with the drug was performed, theresult is shown in (**Figure8.1** and **Figure 8.2).**

The drug excipient compatibility study gives an idea about the physical interaction of active pharmaceutical ingredients and excipients for better stability of the formulation.

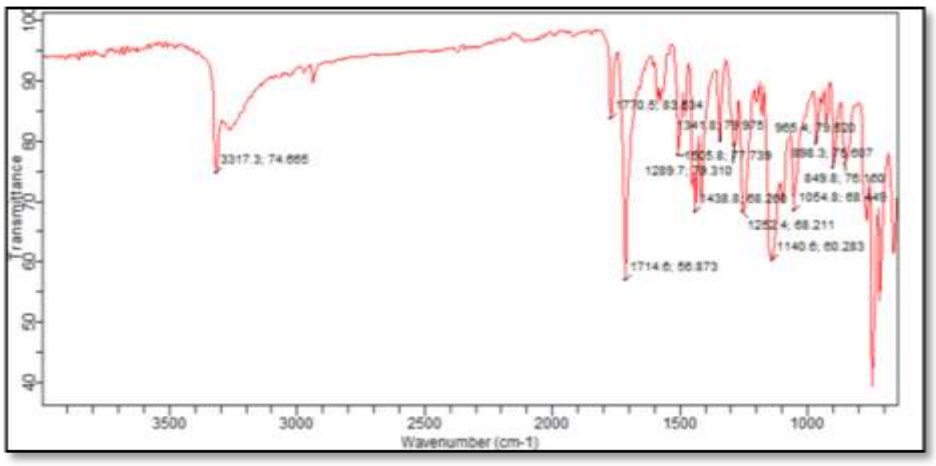


Figure 8.1: FTIR Spectra of Pure Drug.

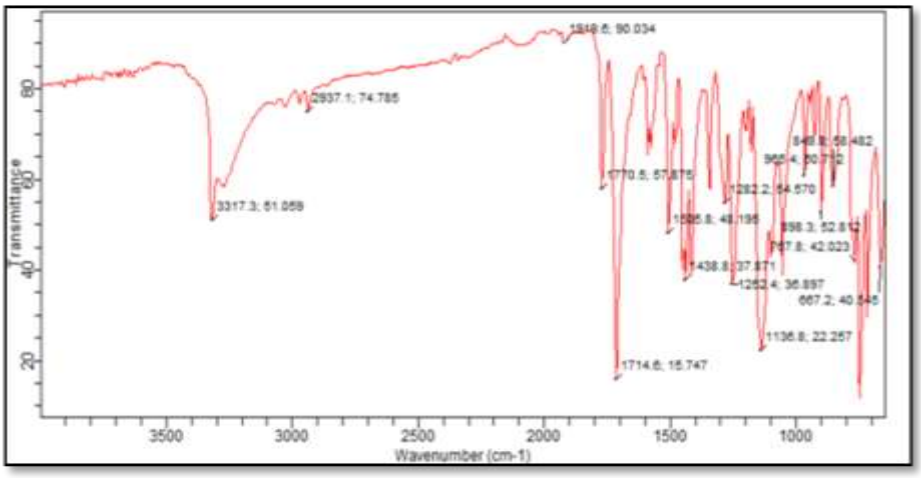


Figure 8.2: FTIR Spectra of Pure Drug and Polymers.

DISCUSSION

The principle FTIR absorption peaks of Rilpivirine hydrochloride at. 3317.3 cm-1 (-C=Ostretch) 1770.5, 1714.6 cm^{-1} (C-Hstretch, C-H wagging), 1140.6 cm-1 (systematic NH), were observed in Rilpivirine as well as near about the same in the formulation. Thus, the FTIR studies indicated that there were no interactions.

Calibration curves of Rilpivirine hydrochloride

λ max determination of Rilpivirine hydrochloride

In phosphate buffer 6.8 Rilpivirine hydrochloridegives maximum absorbance (λmax) at 305 nm, the absorbance of a series of solutions (5-30µg ml) was recorded at that λmax. The

standard curve and calibration date of Rilpivirine hydrochlorideis shown in (**Figure 8.3** and **Table8.4**).

Table 8.4: Calibration data of drug at 305 nm.

Sr.no	Concentration ((µg/mL)	Absorbance
1	0	0
2	5	0.156
3	10	0.32
4	15	0.49
5	20	0.65
6	25	0.801
7	30	0.969
Slope		0.0323
R^2		0.999
Equation		y = 0.0323x + 0.0009

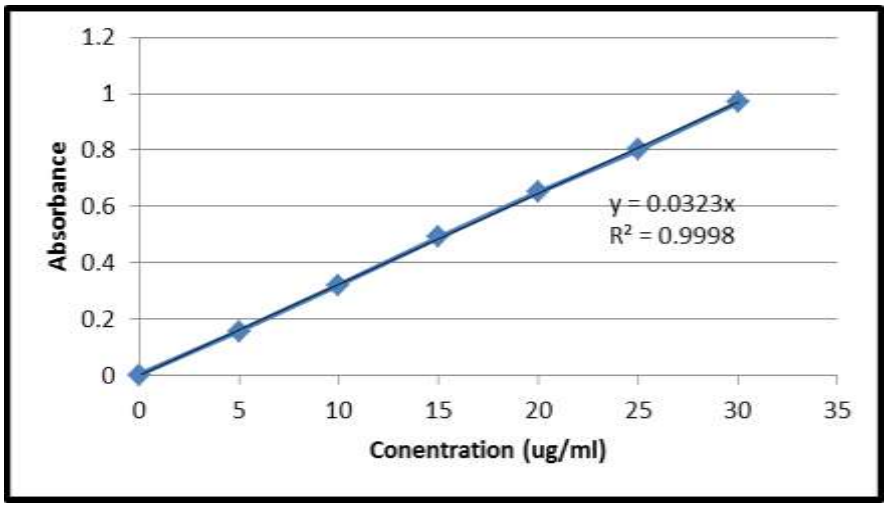


Figure 8.3: Calibration curve of Rilpivirine hydrochloridein phosphate buffer 6.8 at 305 nm.

In calibration curves the r^2 & the regression equation (y) for Rilpivirine hydrochloride were calculated it indicating the capability. The mean regression equations were found as y = 0.0323x + 0.0009. The regression coefficient (R2) was found to be 0.999.

Evaluation of Microsphere of Rilpivirine hydrochloride

The prepared Rilpivirine hydrochloride microspheres were characterized for various characteristics such as particle size, surface morphology, entrapment efficiency, drug content, and in-vitro drug release study, Results given as follows:

Determination of particle Size

The average particle size of microspheres as determined by optical microscopy by using stage micrometer and ocular micrometer are shown in (**Table 8.5**).

Table 8.5: Particle size data of prepared Microsphere.

Formulation Batch code	Average particle size (µm)±SD
B1	991±10.73
B2	940±11.28
B3	572±12.51
B4	913±6.35
B5	456±12.42
B6	278±7.14

From the above observation. The mean particle size for the formulation B1 to B3 containing Guar gum was found to be in the range from µm 572±12.51to 991±10.73 µfor formulation B4 to B6 containing Xanthan gum the mean particle size was found to be in the range from 278±7.14to 913±6.35µm respectively. With the increase in polymer concentration in the microspheres from B1 to B6, the particle size of microspheres increases respectively. This is because the viscosity of the polymer solution increases with increasing polymer concentration, which in turn decreases the stirring efficiency.

Scanning Electron Microscopy

The determination of shape and surface morphology was done by scanning an electron microscope. (Figure8.4). Microsphere of Rilpivirine hydrochloride with Guar gum and Xanthan.

Gum

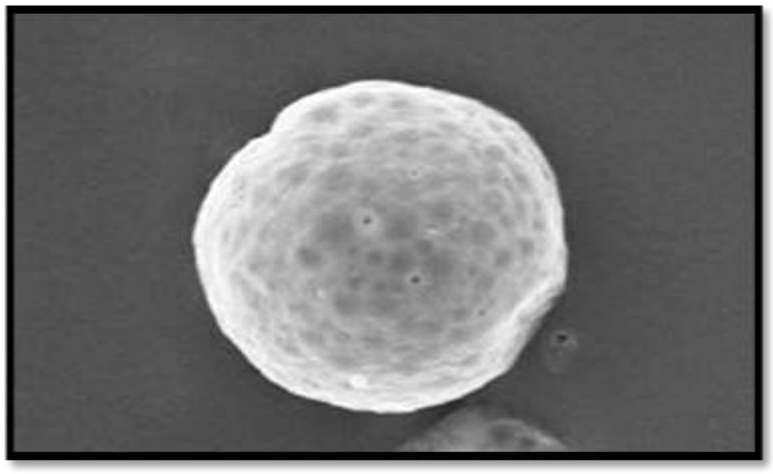


Figure 8.5: Microsphere of Rilpivirine Hydrochloride with Xanthan.

Gum

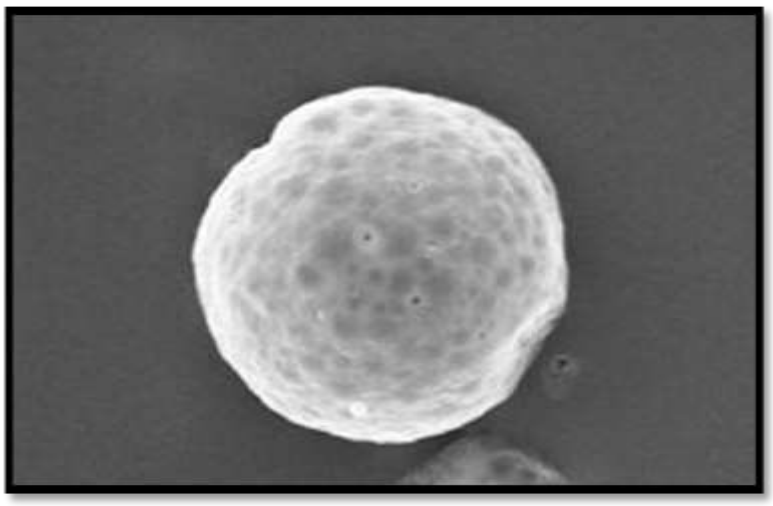


Figure 8.4: Microsphere of Rilpivirine hydrochloride with Guar gum.

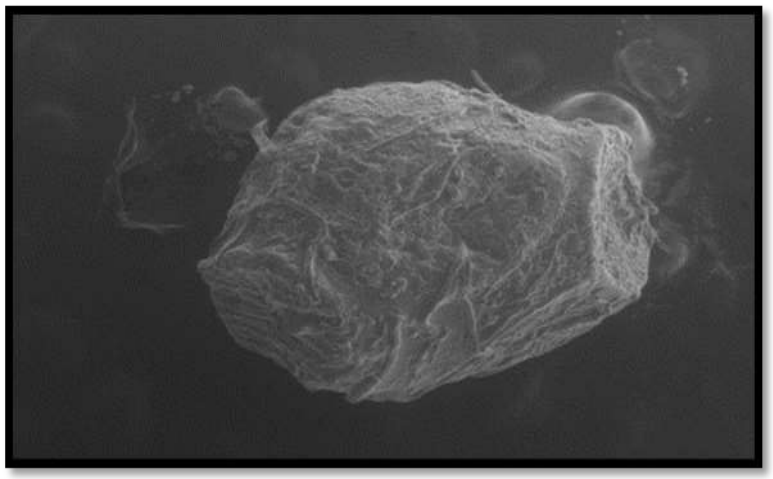


Figure 8.5: Microsphere of Rilpivirine hydrochloride with Xanthan Gum.

SEM analysis of the samples revealed that all microspheres prepared were spherical in shape. The microspheres of Rilpivirine hydrochloride with Guar gum were smooth; spherical when compared with the microspheres of xanthan gum.

The percentage yield of microsphere

The Percentage yield of the microsphere for formulation B1–B6 was calculated, and Observation was given in (Table 8.6) and the comparison of the % Yield of the Prepared Microspheres was given in (Figure8.6).

Table 8.6: Percentage yield of microsphere.

Sr.No	Formulation Batch Code	% Yield
1	B1	76.4
2	B2	74.4
3	B3	80.5
4	B4	78.3
5	B5	79.5
6	B6	79.0

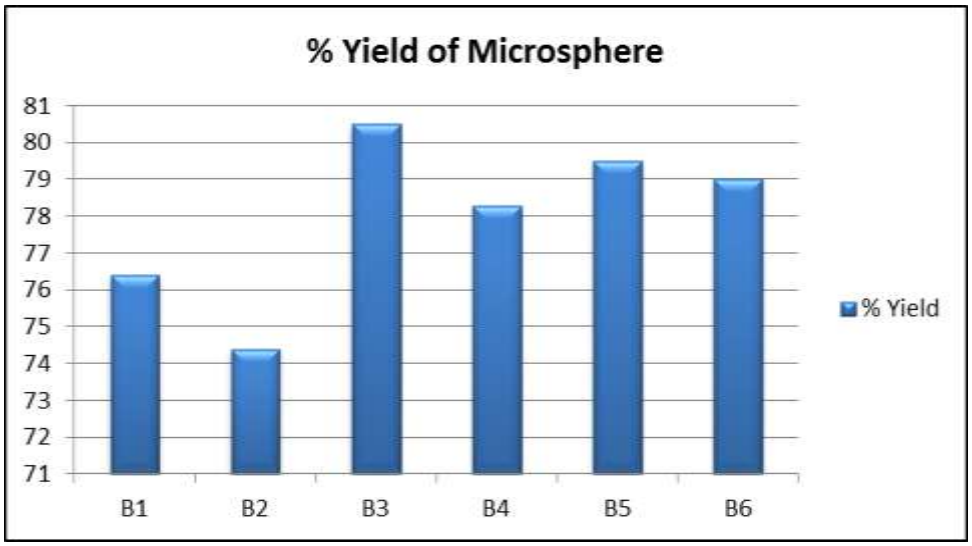


Figure 8.6: Comparison of % Yield of the Prepared Microspheres.

The Percentageyield of the microsphere for formulation B1–B6 was calculated from the above observation it was found that batch B3 gives more % yield of the microsphere.

Drug Loading and Drug Entrapment

The amount of drug loaded and entrapped in the microspheres was calculated andthe result is given in (Table8.7) and Comparison of % drug loaded and % drug Entrapment is shown in (Figure8.7 and Figure 8.8).

Table 8.7: Data of %drug loaded and % Drug Entrapment.

Sr. No.	Formulation Batch	%Drug loaded	%Drug Entrapment
1	B1	37.88	73.62
2	B2	32.86	78.44
3	B3	29.44	84.88
4	B4	38.56	78.12
5	B5	27.5	82.48
6	B6	22.60	90.40

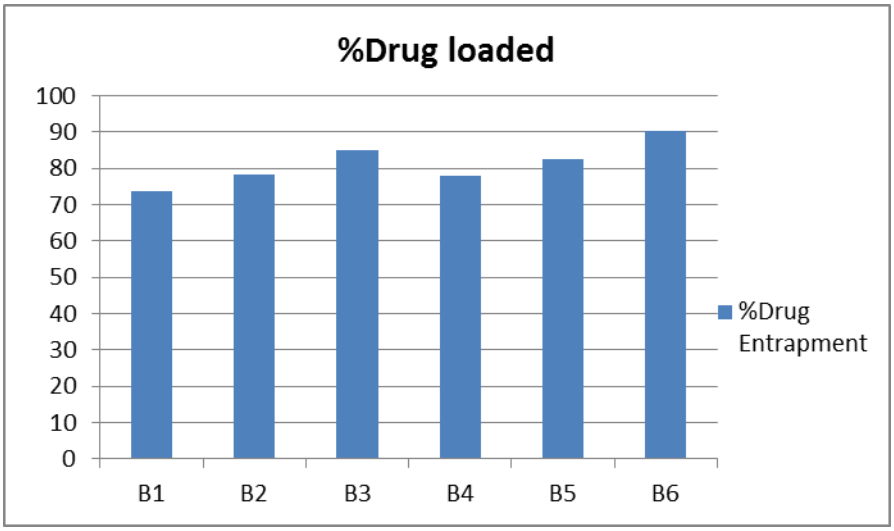


Figure 8.7: Comparison of % Drug loaded of the Prepared Microspheres.

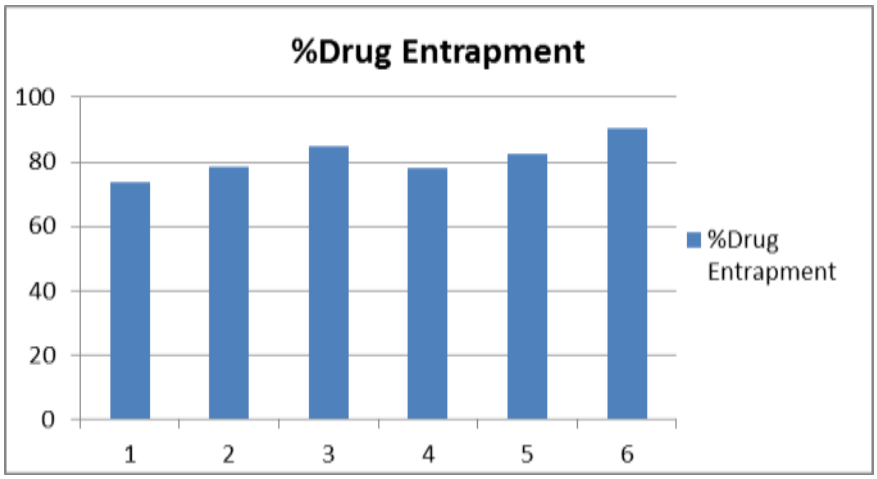


Figure 8.8: Comparison of % Drug Entrapment of the Prepared Microspheres.

From the above observation, as the polymer concentration was increased the %drug loading decreased and the %entrapment efficiency was increased due to an increase in the viscosity of the solution. This can be attributed to the permeation characteristics of each polymer used, which could facilitate the diffusion of part of the entrapped drug to the surrounding medium during the preparation of microspheres.

In-vitro drug release studies

Dissolution studies on all nine formulations of Rilpivirine hydrochloride microspheres were carried out using a USP dissolution apparatus Type II. 0.1N HCl (pH 1.2) and pH 6.8 was used as the dissolution medium. The *in-vitro* drug release data of different formulations are shown in (Table8.8 and Figure8.9).

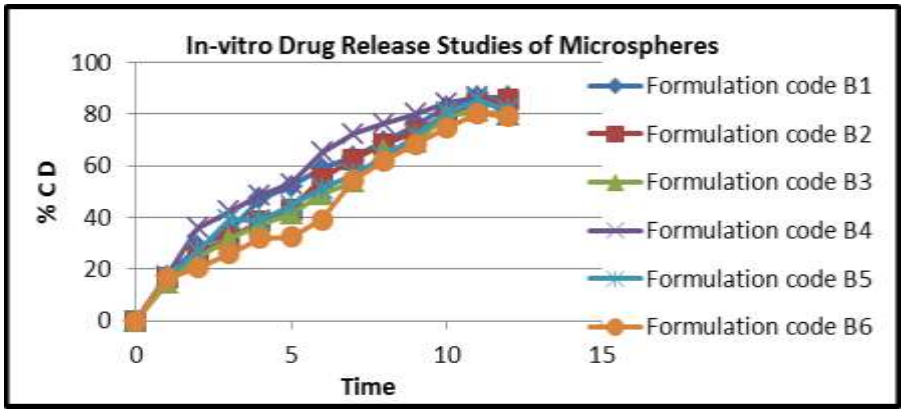


Figure 8.9: The *in-vitro* drug release data of different formulations.

Table 8.8: In-vitrodrug release data of different formulation.

Time Hrs	Formulation code					
	B1	**B2**	**B3**	**B4**	**B5**	B6
0	0	0	0	0	0	0
1	17.215	16.557	14.472	17.215	16.959	16.553
2	28.410	25.765	24.433	35.765	26.557	20.535
3	34.714	32.406	31.723	42.406	39.146	25.844
4	47.375	38.389	37.073	48.389	38.811	31.817
5	52.038	43.050	41.369	53.050	44.477	32.497
6	59.000	54.998	49.069	64.998	51.063	39.136
7	63.306	62.318	53.716	72.318	56.712	54.469
8	69.320	68.331	65.697	76.331	63.350	61.803
9	75.633	72.994	69.020	79.994	71.669	68.447
10	82.723	80.038	79.389	84.146	80.574	74.474
11	86.521	84.526	80.890	86.560	85.569	80.26
12	86.523	85.450	79.869	79.860	81.560	78.99

The cumulative percent drug release after 12 hours was found to be in the range of 86.53, 85.45, and 79.869% for the formulations B1, B2, and B3 respectively whereas cumulative percent drug release after 12 hours was 79.86, 81.56 and 78.99 % for formulations B4 to B6 respectively. The cumulative drug release significantly decreased with an increase in polymer concentration. The increased density of the polymer matrix at higher concentrations results in an increased diffusional path length. This may decrease the overall drug release from the polymer matrix. Furthermore, smaller microspheres are formed at a lower polymer concentration and have a larger surface area exposed to the dissolution medium, giving rise to faster drug release.

Release Kinetics

The results obtained from in-vitro drug release were plotted adopting five different

mathematical models of data given (**Table8.9**). To understand the mechanism and kinetics of drug release, the drug release data of the in-vitro dissolution study are analyzed with various kinetic model like zero order, first order, Higuchi's, Peppa's and coefficient of correlation (r) values are calculated for the linear curves by regression analysis of the above plots.

Table 8.9: Model fitting data for in-vitro release kinetic parameters.

Formulation Code	Zero order [r]	First order [r]	Higuchi [r]	Hixson Crowell [r]	Korsmeyer-Peppas [r]	'n'-Values
B1	0.92	0.95	0.991	0.804	0.651	0.520
B2	0.97	0.88	0.991	0.815	0.704	0.649
B3	0.98	0.91	0.981	0.830	0.746	0.744
B4	0.99	0.86	0.926	0.933	0.942	0.902
B5	0.99	0.82	0.935	0.921	0.951	1.079
B6	0.99	0.85	0.93	0.92	0.95	1.076

Based on the highest regression values(r^2), fitting of the release rated at various models revealed that all the formulations (B1 to B6) follow zero-order release kinetics with regression values ranging from 0.92- 0.99.

Stability Studies

A stability study was conducted for the prepared Rilpivirine hydrochloride microspheres of formulation Batch B1 and Batch B4 at 40°C/75% RH respectively for a period of 60 days.

Then, the sample was analyzed for physicalappearance, entrapmentefficiency, and drug release studies of the microsphere at the end of 15, 30, 45, and 60 days. The results of stability studies are given in the (**Table 8.10**).

Table 8.10: Stability study of Rilpivirine hydrochloride microspheres of formulation Batch B1 and Batch B4.

Tested after days	% Drug Entrapment		% CDR	
	B1	B4	B1	B4
15	78.12	73.26	81.723	82.175
30	77.37	73.29	80.234	82.147
45	77.41	72.23	81.173	81.765
60	78.26	72.32	81.69	82.251

There was no significant change in the drug entrapment and *in-vitro* release study of the microspheres.

CONCLUSION

The drug delivery system aims to provide a therapeutic amount of drug to the desired site in the body and maintain the desired plasma concentration of the drug for a particular period of time. However, the incomplete release of the dug and shorter residence times of dosage forms in the upper GIT lead to lower oral bioavailability. Such limitations of conventional dosage forms have paved the way to an era of controlled and novel drug delivery systems.

Rilpivirine hydrochloride an anti-viral drug, choice in the treatment of HIV has been chosen as a model drug in the formulation of controlled drug delivery systems for the present work. Various studies reported the absolute bioavailability of Rilpivirine hydrochloride (46%) when administrate orally with a half-life of 3-5 hrs. A microparticulate floating drug delivery system was planned for Rilpivirine hydrochloride as such a system release for a prolonged period of time and the drug would be available in the dissolved form. This would lead to improvement in the bioavailability of the drug. In this way, it stands an advantage over conventional dosage forms.

Microsphere formulations were prepared using solvent evaporation technique using Xanthan gum and Guar gum. The prepared floating microspheres were characterized for their percentage yield, particle size, morphology, drug entrapment, *in-vitro* release, and drug release studies. Almost all the formulations showed fairly acceptable values for all the parameters evaluated. Further, the analysis of the release mechanism was carried out by fitting the drug diffusion data to various kinetic equations. The overall curve fitting into various mathematical models was found to be average and best fitted into the zero-order kinetic model. A stability study was conducted for the prepared microspheres of selected formulations for 60 days. There was no significant change in the drug entrapment and *in-vitro* release study of the microspheres.

The Rilpivirine hydrochloride Floating Gastro Retentive Microsphere was successfully formulated and evaluated for various parameters. In the present study of Rilpivirine hydrochloride floating microspheres, a satisfactory attempt was made to develop a formulation with improved bioavailability, efficient targeting capacity, and dose reduction capacity. From the experimental results, it can be concluded that the Xanthan gum and guar gum were suitable polymers for the preparation of floating hollow Microspheres of Rilpivirine hydrochloride with improved patient compliance.

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