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Formulation and Evaluation of Floating Microsphere of Cephalexin

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Abstract

Recent development focused on the formulation and evaluation of floating microspheres. The sustained release drug delivery system was more popular in this time. This delivery system having a longer residence time in stomach and reduce risk of dose dumping. The aim of present study is to develop and evaluate the floating microspheres of Cephalexin by using natural and synthetic polymers in different ratio, which after oral administration could increase gastric residence and enhance the bioavailability of the by sustained release and decrease the dose dumping and improve patient compliance. Using the natural polymer (Xanthum gum and Guar gum) the side effect of synthetic polymer is reduced and more effective floating capability according to *invitro* buoyancy experiment. The floating microspheres were prepared by Ionotropic gelation method.

Formulation F_2 showed maximum drug release and drug dissolution. From the obtained result, it was concluded that the drug release from the floating microspheres matrix was controlled by polymer.

Keyword: GRDDS, Floating Microsphere, Antibiotics, Cephalexin, Bioavailability, Polymers.

Introduction

The oral route of administration is the most convenient and widely used method of drug administration, and developing stomach-specific oral controlled-release delivery systems is a difficult task due to the variation of pH in different segments of the gastrointestinal tract, the fluctuation in gastric residence time, and the difficulty in localizing an oral delivery system in a specific region of the gastrointestinal tract because the majority of medications are absorbed in the stomach or upper section of the small intestine, rapid gastrointestinal transit can hinder complete drug absorption in the absorption zone and diminish the efficacy of the prescribed dose[(1)].

Polymers have commonly used in the fabrication of floating microspheres. A variety of materials have been studied for the manufacture of floating microspheres, including polymers of natural or synthetic origin, as well as semi synthetic compounds. Both hydrophilic and hydrophobic polymers can be used to make floating microspheres. The concept of floating or porous microspheres can also be used to reduce the irritating effect of weakly acidic medications on the stomach by avoiding direct contact with the mucosa and allowing for low dosing for extended periods.

Cephalexin is an antibiotic of Cephalosporin class drug. This drug belongs to the BCS class–I. In this drug has poor bioavailability (35%) with narrow absorption window. This drug has short biological half – life (1hours) hence it required multiple dosing.

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Therefore, floating microspheres have increasing the residence time in stomach, will increase bioavailability and due to increase residence time, frequency of dosing will be decreased. The floating microsphere that will formed would float in the stomach thus would prevent the unstablity in the intestine. Floating systems are low-density systems that have ability to float on gastric content on stomach due to buoyancy and therefore they remain buoyant for maximum period of time[2].

Material and method

Cephalexin was a gift sample along from Lupin Pharmaceutical Pvt. Ltd., with their analytical reports. Xanthum gum, HPMC, Guar gum, Sodium alginate and calcium chloride was purchased from Loba Chemie. Pvt. Ltd, Mumbai. All the other chemicals used were of analytical grade.

Experimental work:

Preformulation Studies:

The primary goal of the preformulation study is to generate statistical data that is beneficial for formulating and developing secure and bioavailable dosage forms. Preformulation studies were performed for the adequate preparation of formulation.

Identification of Drug:

Organoleptic Properties:

The pure sample of Cephalexin was studied for organoleptic property like Physical appearance, color and odor.

Determination of wavelength using UV Spectrophotometric analysis:

Cephalexin drug was weighed at 20 mg and dissolved up to 20 ml of 0.1 N HCl to prepare 1000µg/ml stock solution. 2ml stock solution was pipetted out and dissolved up to 20 ml of 0.1N HCl to prepare sub stock solution of 100 µg/ml. 1ml of sub stock solution was pipette out and volume makeup up to 10 ml with 0.1 N HCl to prepare 10 µg/ml solution. Baseline correction was performed using 0.1N HCl and the sample were run between 200-400 nm wavelength ranges in spectrum mode[3].

Determination of Cephalexin calibration curve:

The calibration curve of Cephalexin was prepared using distilled water and 0.1 N HCl on UV spectrophotometer. 20 mg of Cephalexin was weighed and dissolved into 20ml of 0.1 N HCl to prepare1000µg/ml stock solution. From stock solution 2ml of solvent was dissolved up to 20ml of 0.1 N HCl to prepare 100µg/ml sub stock solution from which 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, 50µg/ml dilution was prepared. Same procedure was followed for water to prepare calibration curve[3].

Identification of drug by FTIR:

An FTIR spectrum was taken for the sample using FTIR apparatus to determine the purity of the drug sample. The API alone was mixed with KBr. The sample was compressed to form a pellet using hydraulic press. The prepared pellets were transformed into disk. The disk was applied to the center of the sample holding device and scanned from 4000 to 400cm^{-1} using FTIR spectrophotometer. The IR absorption Spectrum of Cephalexin was obtained using FTIR spectrophotometer (Perkin Elmer) by employing potassium bromide pellet technique and spectra were recorded [4].

Melting Point:

Melting point test was done by using melting point apparatus. Small quantity of pure drug of Cephalexin was taken in a capillary tube and was kept in melting point apparatus and the temperature from which the drug started to melt was noted[4].

Solubility:

The equilibrium solubility technique was used to determine the solubility of Cephalexin in different solvents. In 5ml glass vials containing distilled water, 0.1NHCl an excess quantity of Cephalexin was added. The vials were shaken in magnetic stirrer and the mixture was kept aside for 24 hours. The supernatant solution was filtered and evaluated for solubility using UV visible spectrophotometer (UV- 1800, Shimadzu, Japan) at 257nm. The study was carried out thrice [4].

Compatibility (Drug-excipient interaction) studies:

FTIR spectra were taken for the sample using FTIR apparatus to determine the possible interaction between the drug and polymer. The API with HPMC, Xanthum gum, Guar gum, and Sodium alginate were mixed with KBr. The samples were compressed to form a pellet using hydraulic press. The prepared pellets were transformed into disk. The disk was applied to the

center of the sample holding device and scanned from 4000 to 400cm^{-1} using FTIR Spectrophotometer. The IR absorption spectrum of Cephalexin was obtained using FTIR spectrophotometer (Perkin Elmer) by employing potassium bromide pellet technique and spectra were record [4].

Formulation and Development of Floating Microsphere by Ionotropic Gelation Method:

Floating microsphere containing Cephalexin was prepared by Ionotropic gelation method. The required amount of sodium alginate was weighed accurately and dissolved in distilled water using a mechanical stirrer. After sometime in this solution, the drug and polymer with predefined ratio were added. The above solution was mixed thoroughly using a Mechanical stirrer. Then this solution was sonicated for about 30 min to remove the air bubble. After sonication, the solution was kept aside for 30 minutes. Above prepared solution was injected into100 ml of 1% calcium chloride solution containing water using a 23-gauge needle with constant mixing. After this solution kept aside for some time and microsphere was filtered. This microsphere was dried [5].

Table No.1: Formulation of Cephalexin floating microsphere

S. No.	Ingredients	FM1	FM2	FM3	FM4	FM5	FM6	FM7	FM8	FM9
1	Cephalexin (mg)	250	250	250	250	250	250	250	250	250
2	Xanthum gum (mg)	45	63	81	-	-	-	-	-	-
3	Guar gum (mg)	-	-	-	45	63	81	-	-	-
4	HPMC (mg)	-	-	-	-	-	-	45	63	81
5	PVP (mg)	45	27	9	45	27	9	45	27	9
6	Sodium alginate (mg)	810	810	810	810	810	810	810	810	810
7	Calcium chloride (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%

Evaluation Parameters:

Percentage Yield:

The prepared microspheres have been collected and weighed. The amount of drug and excipients that was utilized to develop the microspheres was divided by the measured weight[4].

$$\%\text{yield} = \frac{\text{Actual weight of product}}{\text{Weight of excipient \& drug}} \times 100$$

Particle Size Analysis:

Optical microscopy was used to determine the particle size and shape of the microspheres. An optical microscope was used to examine the freshly prepared microspheres and a pre calibrated ocular micrometer and stage micrometer were used to measure their sizes. A total of 100 particles of each formulation were observed and measured.

Particle size=(Stage reading) / (Ocular reading) *100

Percentage Drug Entrapment:

The drug content of the different floating microsphere formulations was tested. From each batch, 250 mg of floating microspheres were precisely weighed and crushed. After dissolving the microsphere powder in 25 ml of 0.1 N HCl, the mixture was stirred in magnetic stirrer. The Whatmann filter paper No. 44 is then used to filter this supernatant solution. After filtering, 0.1ml of this solution was removed and diluted with 0.1 N HCl up to 10 ml. The calibration curve approach was used to calculate the percentage of drug entrapment[6].

% drug entrapment =[(Amount of drug actually present)/ (Theoretically drug loaded expected)] X 100

Buoyancy Percentage:

In vitro, floating studies were conducted using 0.1NHCl containing 0.02% tween-80 as a dispersing medium. Dispersing medium was 100

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ml with microspheres spread over the surface. The mixture was stirrer in magnetic stirrer at 100 rpm for 12 hours to agitate the medium. At Each time interval, the floating microsphere was collected. After drying, the collected samples were weighed [(7)].

%Buoyancy microsphere = [(Weight of buoyancy microspheres)/ (Weight of floating microsphere+ Weight of settled microsphere)] X 100

Floating Time:

It is described as the duration of time in which floating microsphere to remain buoyant. Floating microspheres were placed in a beaker containing 200 ml of 0.1 N HCl and observed for the duration of the time until they floated[(4)].

***In-Vitro* Percent Drug Release Study:**

The drug release from floating microspheres was performed using the USP type II dissolution paddle assembly. A weighed amount of Floating microspheres equivalent to drug were placed on muslin cloth which was tied to the paddle using thread and dispersed in to 900ml of 0.1NHCI (pH1.2) maintained at 37±0.5°C and stirred at 55 rpm. 5ml sample was withdrawn at predetermined intervals and filtered. Equal volume of dissolution medium was replaced in the vessel after each withdrawal. The collected samples were analyzed by UV spectrophotometer at 257nm to determine the concentration of drug present in the dissolution medium[(8)].

Stability Studies:

Stability studies were performed to observe the rate of chemical degradation or physical change of floating microsphere of Cephalexin at temperature 45°C and RH 75%.

Results and Discussion

Preformulation Study:

Organoleptic Properties:

The API of Cephalexin gift sample, obtained from Lupin Pharmaceutical Pvt.Ltd. The organoleptic property of Cephalexin API was such as color, odor, and appearance. The result is compared with COA provided by manufacturer.

Table:2. Colors, Odor and Appearance of Cephalexin

S. No.	Parameter	Cephalexin
1.	Color	White to off White
2.	Odor	Pleasant odor
3.	Appearance	Crystalline powder

Identification of Drug:

- **Identification of drug by FTIR:**

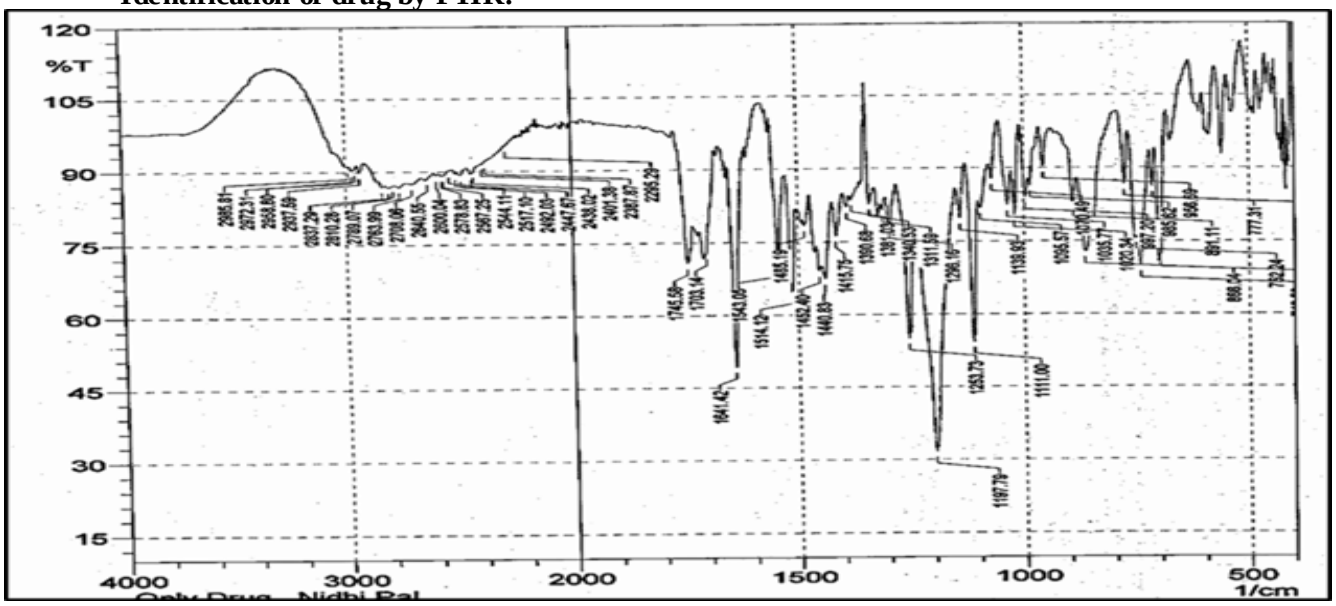

Figure. 1: FTIR study of pure drug Cephalexin

Table.3: Interpretation of FTIR spectra of Cephalexin[9]

Functional Group	Standard Peak (cm^{-1})	Observed Peak (cm^{-1})
Methyne C-H stretch, methylene	3000-2500	2985.81
β lactam C=O stretch	1760	1745.58
Amide C=O stretch	1690	1641.42
C=C stretch	1600	1543.05
Aromatic ring structure	1450	1452.40
Primary amine C-N stretching	1020-1250	1070.49
Thiol group C-S stretching	600-800	698.23-777.31

Determination of Melting point:
The Melting point of Cephalexin was found to be 324°C-325°C which is near to be reported melting point of Cephalexin. The observed value of melting point is given below in table no 4.

Table.4: Melting point of Cephalexin

S.No.	Observed Value	Reported Value
1.	324°C	326.8°C
2.	325°C	
3.	324°C	

Determination of wavelength using UV Spectrophotometer:
The wavelength of Cephalexin was found to be 257nm in 0.1NHCl, distilled water.
Preparation of calibration curve:
The calibration curve of Cephalexin in different solvent like 0.1NHCl, distilled Water was prepared and shown in figure1and 2and the absorbance data are shown in table 3 and 4.

Table.5: Absorbance data of Cephalexin in 0.1 N HCl at 257 nm

S. No.	Concentration (µg/ml)	Absorbance at 257nm (mean ± SD) (n=3)
1.	0	0
2.	10	0.1285±0.0051
3.	20	0.2468±0.0076
4.	30	0.3479±0.0030
5.	40	0.4558±0.1218
6.	50	0.5529±0.0047

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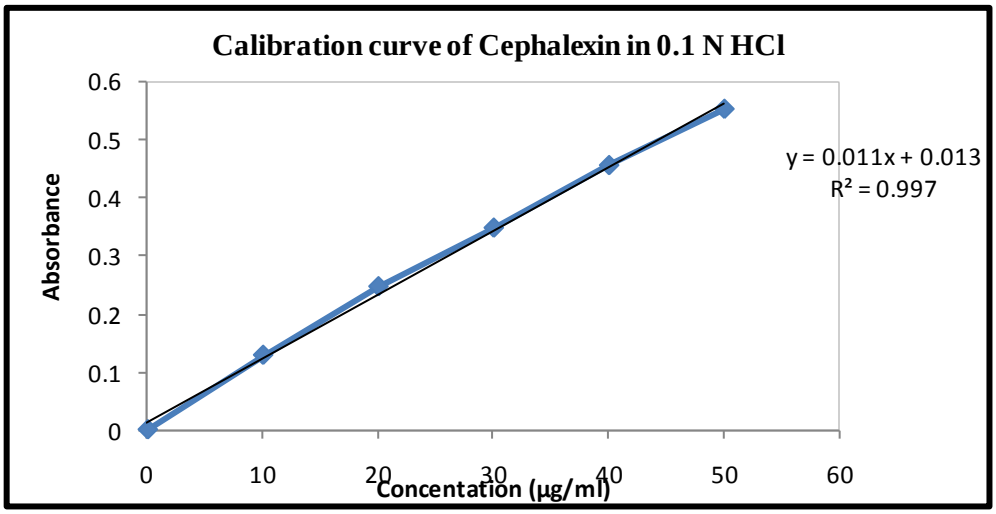

Figure.2: Calibration curve of Cephalexin of 0.1NHCl

Table.6: Absorbance data of Cephalexin in distilled water at 257 nm

S. No.	Concentration (µg/ml)	Absorbance at 257nm (mean ± SD) (n=3)
1.	0	0
2.	10	0.1173±0.00491
3.	20	0.2328±0.005446
4.	30	0.3289±0.007511
5.	40	0.4113±0.006123
6.	50	0.5335±0.005824

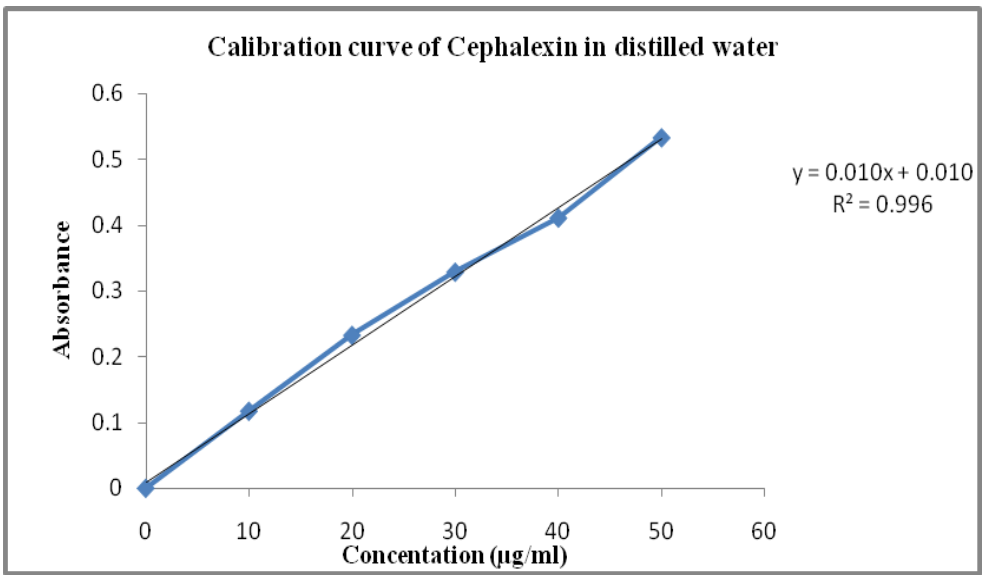

Figure.3: Calibration curve of Cephalexin of Water

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Solubility:

The solubility of API was determined by dissolving in distilled water, 0.1N HCl is given in table no.7

Table.7: Solubility data of Cephalexin in different medium mean± SD (n=3)

S. No.	Solvents	Solubility (mg/ml) mean ± SD (n=3)
1.	0.1 N HCl	44.1±0.438
2.	Distilled water	18.83±0.166

Compatibility (Drug-excipient interaction) studies:

Fourier Transform Infrared Spectroscopy(FTIR):

FTIR spectrophotometry was used to determine the compatibility of the pure drug i.e., Cephalexin with Guar gum, Xanthum gum, HPMC. Figure and table show the FTIR spectrum of Cephalexin, Cephalexin with Guar gum, Xanthum gum and HPMC respectively.

Interpretation of FTIR spectra of physical mixture (Drug with Excipient)

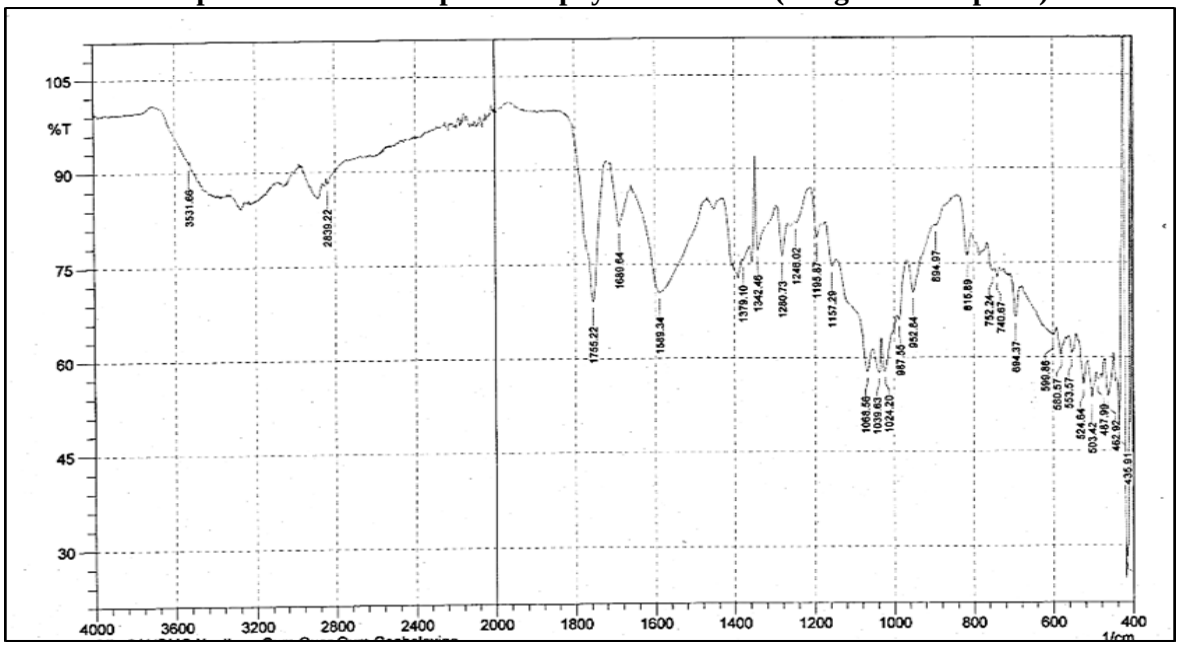

Figure.4: FTIR study of Drug+Excipients

Table.8: Interpretation of FTIR spectra of (Cephalexin with Excipients) [9]

Functional Group	Observed Peak in drug (cm^{-1})	Observed peak in physical mixture frequency (cm^{-1})
Methyne C-H stretch, methylene	2937.59	2839.22
β lactam C=O stretch	1745.58	1755.22
Amide C=O stretch	1641.42	1689.64
C=C stretch	1543.05	1589.34
Aromatic ring structure	1452.40	1450
Primary amine C-N stretching	1070.49	1068.63
Thiol group C-S stretching	698.23-777.31	694.37-752.24

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Formulation and Development of Floating Microsphere by Ionotropic Gelation Method:

Floating microsphere containing Cephalexin was prepared by Ionotropic gelation method.

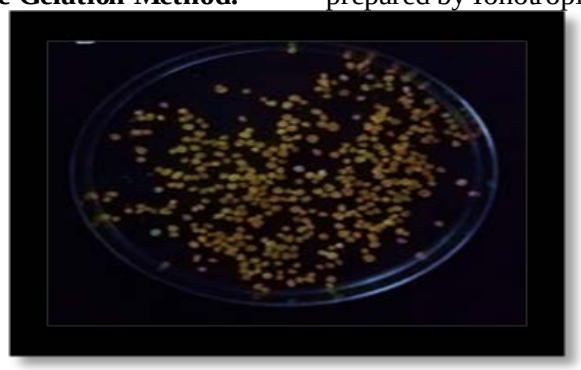

Figure 5: Formulation of floating Microsphere

Evaluation of Cephalexin Floating Microsphere:

Percentage Yield:

The highest percentage yield was found to FM2 formulation which was noted to be 73.06% among all formulations. The result was showed in the table 9.

Particle Size:

The average particle size range for formulation FM1 to FM9 was found to be 43µm to 85µm.The result was showed in the table 9.

Percentage Drug Entrapment Efficacy:

In floating microsphere formulation, the % drug content was evaluated, and the formulation showed the drug content was found to be range 87.67% to 99.13%. The highest drug content was found in batch FM2 and the lowest drug content was found in batch FM7. % drug content of all formulations is given in table 9.

Percentage Buoyancy:

Buoyancy of prepared floating microspheres was found by in-vitro buoyancy test and the buoyancy of the all formulation were found to be in the range 70.02% - 81.81%. The result was showed in the table 9. Formulation FM7 showed least percentage buoyancy of 70.02 %, while FM2 showed highest buoyancy of 81.81%.

Floating Time:

The formulations prepared with various drug and polymer ratios were evaluated for floating time. In the test of floating time more than microspheres remained floating for more than 12hours.The result was showed in the table 9.

Table.9: Evaluation of floating microsphere

Formulation code	Percentage Yield	Average Particle size (µm)	% Drug Entrapment	Percentage buoyancy	Floating time (Hours)
FM1	70.81±0.004	46.66±0.33	93.57±0.12	79.3±0.057	8
FM2	73.06±0.002	43.13±0.46	94.75±0.08	81.81±0.109	9
FM3	71.33±0.003	57.43±0.29	94.28±0.06	80.76±0.014	9
FM4	69.57±0.002	74.23±0.39	90.73±0.12	77.58±0.081	7
FM5	72.38±0.004	65±0.57	92.44±0.07	79.01±0.046	8
FM6	71.15±0.002	70.33±0.33	91.28±0.05	78.57±0.277	7
FM7	68.73±0.004	87.8±0.15	87.67±0.05	70.20±0.574	6

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FM8	70.62±0.002	80.2±0.41	89.74±0.01	72.54±0.233	6
FM9	69.15±0.003	84.9±0.32	88.29±0.04	71.47±0.101	7

In-Vitro % Drug Release:
To assess the In-vitro drug release from prepared floating microsphere of Cephalexin, in-vitro drug release studies was carried out. Table summarizes the result of all formulation in- vitro drug release studies.

Table.10: In-vitro percent drug release of Cephalexin floating microsphere

S. No.	Time (hrs.)	Percent In-vitro drug release								
		FM1	FM2	FM3	FM4	FM5	FM6	FM7	FM8	FM9
1.	0	0	0	0	0	0	0	0	0	0
2.	0.5 hr	11.16±0.18	13.11±0.03	12.19±0.04	14.32±0.07	15.06±0.01	14.15±0.01	8.68±0.01	12.01±0.01	10.83±0.03
3.	1 hr	23.85±0.42	26.24±0.06	24.53±0.01	20.22±0.07	23.24±0.04	22.48±0.02	16.96±0.01	19.71±0.02	18.28±0.025
4.	2 hr	35.24±0.31	38.14±0.05	36.43±0.04	33.05±0.06	35.06±0.04	34.38±0.02	25.81±0.00	29.96±0.02	27.94±0.027
5.	4 hr	41.57±0.37	48.53±0.07	44.42±0.07	42.07±0.07	46.07±0.01	45.35±0.02	39.63±0.00	42.49±0.01	40.51±0.021
6.	6 hr	50.17±0.30	56.90±0.03	55.14±0.06	53.20±0.03	56.65±0.04	55.59±0.03	47.21±0.00	51.09±0.02	49.94±0.036
7.	8 hr	63.36±0.23	68.79±0.46	66.31±0.09	63.05±0.35	68.44±0.73	64.37±0.44	56.69±0.00	61.23±0.0	58.34±0.030
8.	12 hr	80.22±1.22	89.19±0.20	86.39±0.33	76.84±1.73	79.17±0.45	77.36±0.73	78.26±0.25	82.14±0.18	79.57±0.15

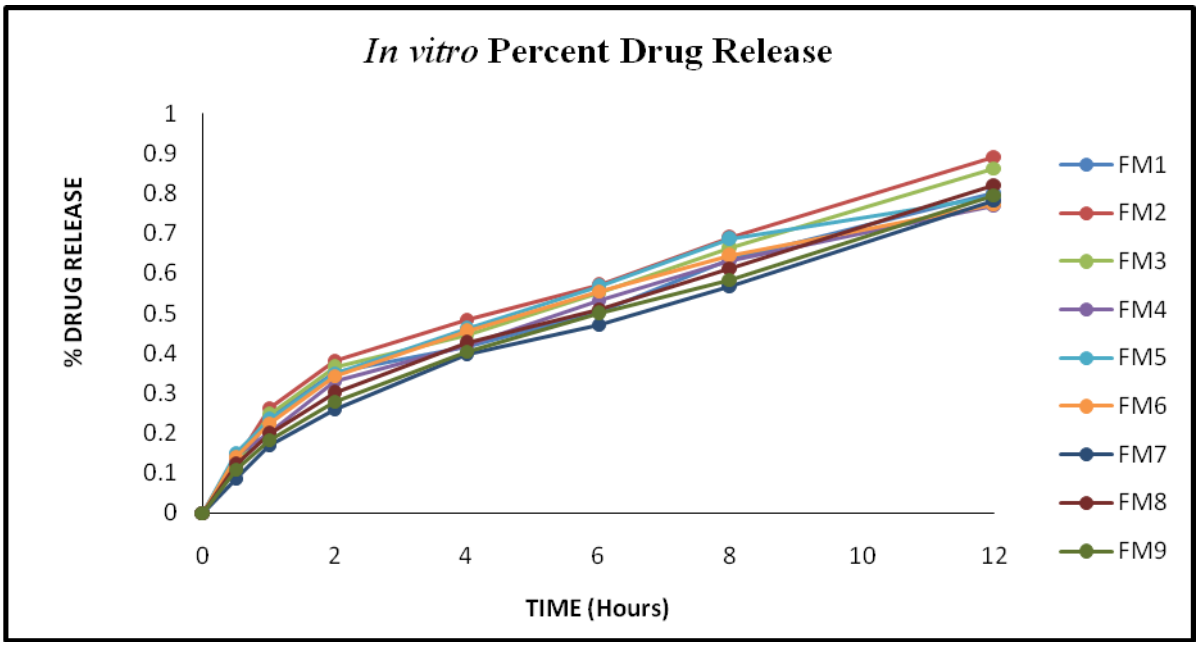

Figure 6: In-vitro Percent drug release

Stability Studies: Data of stability study performed at temperature at 45°C for 30 days is given below in table no. 11

Table.11: Stability study of Cephalexin floating microsphere

Evaluation parameter	Days	Changes observed at temperature 45°C
Physical Appearance	Initial day	No Changes
	After 15 day	No Changes
	After 30 day	No Changes
% Drug Entrapment	Initial day	94.75%
	After 15 day	94.18%
	After 30 day	93.97%
% Buoyancy	Initial day	81.81%
	After 15 day	81.80%
	After 30 day	81.76%
% Drug release	Initial day	89.36%
	After 15 day	89.34%
	After 30 day	89.30%

Conclusion

On the basis of extensive review of literature done floating microsphere was selected as a dosage form. Because it will help to enhance the biological half-life and bioavailability of the drug by providing sustained release as remain the upper part of stomach for extended period of time. Hence due several advantages of above mentioned dosage form floating microsphere were finalized. Cephalexin was selected as suitable candidate for floating microsphere as it has narrow absorption window, low bioavailability and short biological half-life. Therefore to overcome above mentioned draw back floating microsphere of Cephalexin were formed.

Preformulation studies were performed like UV spectroscopy in distilled water, 0.1 N HCl, Solubility, Melting point and drug and excipient studies using FTIR was performed. All the batches were evaluated for evaluation parameter like Percentage yield, particle size, drug content, percentage buoyancy, floating time, In vitro drug release and stability drug studies. Hence the aim to formulate and evaluate floating microsphere of Cephalexin was carried out successfully and among all the batches FM2 showed better results.

References

1. Mishra R. Development and Optimization of Floating Microspheres in Amethopterin. Bioscience Biotechnology Research Communication 2021;14(4).Page no. 1538-1541.
2. Dhanapal, R. and Ratna, J. (2012) Floating Drug Delivery System: A Novel Approach. International Journal of Pharmaceutical Development and Technology, 2(1),29-36.
3. Mali, A. Bathe, R. (2017) Development and Evaluation of Gastroretentive Floating Tablet of A Quinapril HCl By Direct Compression. International Journal of Pharmaceutical Science,9(8), 35-4.
4. Pandey, N., Sah, N., A., Mahara, K.,(2016) Formulation and Evaluation of Floating Microspheres of Nateglinide, International Journal of Pharma Science and Research,7(11),453-464.
5. N.S., M.N.R, Muneer., S.,(2020) Formulation and Evaluation of Pentoprazole Sodium Microspheres, International Journal of Pharmaceutical Research and Applications,5(2):650-656.
6. Shardendu., P., Bhandari., A., Mishra., R., Sharma., K., P., (2015) Development and Optimization of Floating Microspheres of Gliclazide, International Journal of Pharma Science and Research, 6(5):807-817.

7. Goyal., P., Gill., S., Gupta., D.,U., Rath., G.,(2011) Development and Characterization of Rifampicin Loaded Floating Microsphere, Artificial Cell, Blood Substitute, and Biotechnology, 39(5),330-334.
8. Patel., B., Kushwaha., S., R., Jain., S.,(2019), Formulation, Development and Evaluation of Floating Microsphere of Losartan Potassium Using Natural Polymer, Journal of Drug Delivery and Therapeutics, 9(3-S),223-228.
9. Sharma, R., Y., Elementary Organic Spectroscopy, Published By S. Chand & Company PVT. LTD., 5th Edition, 75-13.

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