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Formulation and Evaluation of Ciprofloxacin Microspheres for Targeted Drug Delivery"

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ABSTRACT:
Microspheres are drug delivery systems which are prepared to get extended or controlled drug delivery to strengthen bioavailability, stability and target the drug to particular site at a predetermined rate. Microparticles are generally have the particle size range from 1– 1000 µm size, serve as multiunit drug delivery systems with clear physiological and pharmacokinetic benefits in order to improve the effectiveness, tolerability, and patient compliance. It has been shown that it not only enhances the dissolution of poorly soluble drugs but also employ a remarkable effect on fat metabolism in the body. Microspheres can successfully increase the biological half-life and reduce the therapeutic dose of their drug, thereby reduce the adverse drug reaction. The present review provides detailed discussion of therapeutic feature of microsphere drug delivery including the advantages and disadvantages of microspheres, preparation of microspheres, carriers used, characterization, and applications of microspheres. Microspheres are one of the most promising targeted and effective drug deliveries. A microsphere has a drug located centrally within the particle, where it is closet within a single polymeric membrane. A Microspheres has its drug distribute throughout the particle i.e., the internal structure is a matrix of drug and polymeric excipients. It is the dependable means to deliver the drug to the target site with specificity, if modified and to maintain the desired concentration at the site of interest without unpredictable effects.

KEYWORDS: ciprofloxacin, solvent evaporation method, Eudragit- s 100, chitosan, agarose, ethylcellulosfloatingmicrospheres.

I. INTRODUCTION

The term microspheres, which explains as a spherical particle with size varying from 1µm to (1000 µm) 1 mm, containing a core substance. Microspheres comprises of strict sense, spherical empty particles. However, the terms microcapsules and microspheres are often used synonymously.

The concept of targeted drug delivery is designed for attempting to concentrate the drug in the tissues of interest while reducing the relative concentration of the medication in the remaining tissues. As a result, drug is localized on the targeted site. Hence, surrounding tissues are not affected by the drug. So, carrier technology offers an intelligent approach for drug delivery by coupling the drug to a carrier particle such as microspheres, nanoparticles, liposomes, niosomes etc. which modulates the release and absorption characteristics of the drug. Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers which are biodegradable in nature and ideally having a particle size less than 200 µm. It is the reliable means to deliver the drug to the target site with specificity, if modified, and to maintain the desired concentration at the site of interest without untoward effects. Microspheres received much attention not only for prolonged release, but also for targeting of anticancer drugs to the tumour. In future by combining various other strategies, microspheres will find the central place in novel drug delivery, particularly in diseased cell sorting, diagnostics, gene & genetic materials, safe, targeted and effective in vivo delivery and supplements as miniature versions of diseased organ and tissues in the body[1,2]

II. MATERIALS

Ciprofloxacin drug got gift Sample from KAPL, Polymers Such as Ethyl cellulose and Eudragit S-100 were obtained from Yarrow chem products, Ethyl cellulose were obtained from Indian Fine Chemicals, Mumbai, Agarose were obtained from Yarrow Chem Products, Chitosan

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and Acetonewere obtained from Himedia Laboratories Pvt Ltd, Mumbai

Table 1 Formulation of ciprofloxacin microspheres

Sl.no.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
01.	Ciprofloxacin (mg)	250	250	250	250	250	250	250	250	250
02.	Eudragit S 100 (mg)	50	100	150	-------	-------	-------	-------	-------	-------
03.	chitosan (mg)	-------	-------	-------	50	100	150	-------	-------	-------
04.	Acetone(ml)	25	25	25	25	25	25	25	25	25
05.	Ethylcellulose(mg)	------	------	-------	-------	-------	------	50	100	150
06.	Agarose (mg)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5

PREPARATION OF MICROSPHERES Floating microspheres containing the antibiotic drug ciprofloxacin were prepared by a solvent evaporation method. In this technique the drug and polymer like Eudragit S-100, chitosan and ethyl cellulose, agarose various proportions were dissolved in a 25 ml of acetone which was placed in a small beaker with a magnetic bead on the magnetic stirrer. And subsequently stirred by the stirrer.at ranging agitation speed for 4h. And allow to volatile solvent to evaporate. The microspheres formed were filtered. Washed with water and air dried for 24h.and stored in a desiccator. [3]

EVALUATION PARAMETERS
COMPATIBILITY STUDIES

A proper design and formulation of a dosage form requires consideration of the physical, chemical and biological characteristics of both drug and excipients used in fabrication of the product. Compatibility must be established between the active ingredient and other excipients to produce a stable, efficacious, attractive and safe product. If the excipients(s) are new and if no previous literature regarding the use of the particular excipients with an active ingredient is available, then compatibility studies are of paramount importance. Hence, before producing the actual formulation, compatibility of Acyclovir with different polymers and other excipients were test reducing the Fourier Infrared Spectroscopy (FT-IR) technique.[4]

FOURIER TRANSFORMS INFRARED SPECTROSCOPY (FT-IR):

In order to check the integrity (compatibility) of drug in the formulation, FT-IR spectra of the formulations along with the drug and other excipients were obtained and compared using Shimadzu FT-IR 8400 spectrophotometer. In the present study, Potassium bromide (KBr) pellet method was employed. The samples were thoroughly blended with dry powdered potassium bromide crystals. The mixture was compressed to form a disc. The disc was placed in the spectrophotometer and the spectrum was recorded. [5]

Differential Scanning Calorimetry (DSC):

The Physical nature of drugpolymer and optimizedformulations were studied by DSC.DSC analysis was performed by using Q-1000 TA Instruments, USA.The instrument was calibration with indium standard. [6]

MICROMERITICSTUDIES[7, 8, 9]

Bulk density

The bulk density is calculated by dividing the powder mass by the bulk volume. Weighed to a precision of 10 gm. A 25 ml measuring cylinder was used to hold the granule sample. The volume occupied by the granules was measured without disturbing the cylinder, and the bulk density was calculated using the equation (values expressed in gm/cm^3).

EQ Number 1.Bulk density= $\frac{Weight\ of\ sample}{volume\ of\ sample}$

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Tapped density

Tapped densities can be calculated using the tapping process. The volume of weighted amounts of microspheres was measured after 100 and 1000 taps using tapped density apparatus.

EQ Number 2. $Tapped\ density = \frac{weig\ htofsample}{tappedvolume}$

Compressibility Index and Hausner's Ratio

From the values of bulk density and tapped density, the compressibility index and Hausner's ratio were calculated using the following formulas:

EQ Number 3. Compressibility index= $\frac{tappeddensity\ -bulkdensity}{tappeddensity} \times 100$

EQ Number 4. Hausner's Ratio= $\frac{Tappeddensity}{Bulkdensity}$

Angle of Repose

The funnel method was used to measure the powder blend's resting angle. The right weighted powder blend was placed in the funnel. The funnel's height was adjusted so that the funnel's tip just touched the powder mixture's apex. The powdered mixture was permitted to flow freely through the funnel to the surface. The diameter of the powder cone was determined and, using the following equation, the angle of repose was estimated.

EQ Number 5 $\tan\theta = h/r$

$$\theta = tan^{-1}\ h/r$$

Therefore.,

Where, θ = angle of repose,

h = height of the pile

r = radius of the pile.

EVALUATION AND CHARACTERIZATION OF THE PREPARED MICROBALLOONS

PERCENTAGE YIELD

The prepared floating microspheres were collected and weighed from different formulations. The actual weight of the floating microspheres was divided by the total weight of the drug and polymer which were used for the preparation of the floating microspheres. [10]

The percentage yield was calculated using the following formula:

EQ Number 6∴ % Yield = $\frac{Actualweig\ htofmicrosp\ heres}{Totalweig\ htofdrugandpolymer} \times 100$

DRUG ENTRAPMENT EFFICIENCY

The floating microspheres equivalent to 50mg of Acyclovir from all batches were accurately weighed and crushed. The powdered of microspheres placed in 50ml volumetric flask and add 0.1N HCl make up to the mark and filtered through Whatman filter paper No.44 After filtration, from this solution accurate quantity (1ml) was taken and diluted up to 10ml with 0.1N HCl. From this solution accurate volume (1ml) was pipette out and diluted up to 10ml with 0.1N HCl. The absorbance was measured at 254 nm against 0.1N HCl as a blank. [11]

The drug entrapment efficiency was calculated using the following formula:

EQ Number 7∴%Drug Entrapment Efficiency = $\frac{PracticalDrugCont\ ent}{TheoriticalDrugContent} \times 100$

DEGREE OF SWELLING

The swelling ability of the uncoated microspheres in physiological media was determined by immersing an accurately weighed amount (500 mg) of microspheres in a little excess of 100 ml of 0.1N HCl and kept for 24 h. [12]

The formula to compute the degree of swelling.

EQ Number 8 $\boldsymbol{\alpha = W_s - W_O / W_O}$

Where, α- Degree of swelling

Wo- Weight of microspheres before swelling

Ws- Weight of microspheres after swelling

PARTICLESIZEANALYSIS

Size of ciprofloxacinmicrospheres was measured by optical microscopy method. A standard stage micrometer was used to calibrate the eyepiece micrometer. Size of 200 microspheres from each batch was measured and average particle size was calculated. Any dispersion of particles is usually poly-disperse in nature containing different particle sizes. It is necessary to know not only the size of a certain particle, but also how many particles of the same size exist in the sample. Thus, we need an estimation of the size range and the number of particles present in each size range. This is called the particle size distribution and from this, we will be able to calculate an average particle size for the sample. When the number of particles lying within a certain size range is plotted against the size range or mean particle size, the frequency distribution curve is obtained. Such a plot gives a visible representation of the distribution that an average diameter will not be able to define. From the frequency distribution data, it apparent that which particle size occurs most frequently within the sample. Many methods are available for determining particle size, such as optical microscopy, sieving, sedimentation and particle volume measurement. Optical microscopy is most

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commonly used for the particle size determination. (13)

SHAPE AND SURFACE MORPHOLOGY

The shape and surface characteristics of the prepared microspheres were evaluated by means of scanning electron microscopy. The samples for scanning electron microscopy were prepared by gently sprinkling the microspheres on a double adhesive tape, which is stickled to an aluminum stub. The stubs were then coated with gold using a sputter coater under high vacuum and high voltage to achieve a film thickness of 30nm. The samples were than imaged using a 20KV electron beam. (14)

IN-VITRO DRUG DISSOLUTION STUDIES

Dissolution studies were carried out for all the formulation. A weighed amount of floating microspheres equivalent to 100mg of drug were filled into a capsule and placed in the basket. Dissolution media used was 900ml of 0.1N HCl maintained at 37±0.5˚C and stirred at 100rpm. At predetermined time intervals, 10ml of sample was withdrawn and replaced with equal amount of 0.1N HCl. The collected samples were filtered and suitably diluted with 0.1N HCl and analyzed spectrophotometrically at 254nm to determine the amount of drug released in the dissolution medium.(15)

STABILITYSTUDIES

The optimized formulation was subjected for stability studies over a period of 3 months. The microspheres were packed in amber colored screw capped and kept for the stability at room temperature. Samples were taken after 3 months analyzed for the drug content, %Drug Entrapment Efficiency, Buoyancy percentage, In-vitro dissolution profile. In-vitro drug release at 0 month and after 3monthsofstabilitystudy was compared. (16)

III. RESULT AND DISCUSSION

Standard Calibration Of Ciprofloxacin

10 ml of stock solution was made to 100 ml with 0.1N HCl thus giving a concentration of 100 µg/ml. Aliquot of standard drug solution ranging from 0.2 ml to 1 ml were transferred in to 10 ml volumetric flask and were diluted up to the mark with 0.1N HCl. Thus the final concentration ranges from 2-10 µg/ml. Absorbance of each solution was measured at 275 nm against 0.1N HCl as a blank. A plot of concentrations of drug vs. absorbance was plotted.

COMPATIBILTY STUDIES

FOURIER TRANSFORMS INFRARED SPECTROSCOPY (FT-IR): In order to check the integrity (compatibility) of drug in the formulation, FT-IR spectra of the formulations along with the drug and other excipients were obtained and compared using Shimadzu FT-IR 8400 spectrophotometer. In the present study, Potassium bromide (KBr) pellet method was employed. The samples were thoroughly blended with dry powdered potassium bromide crystals. The mixture was compressed to form a disc. The disc was placed in the spectrophotometer and the spectrum was record.

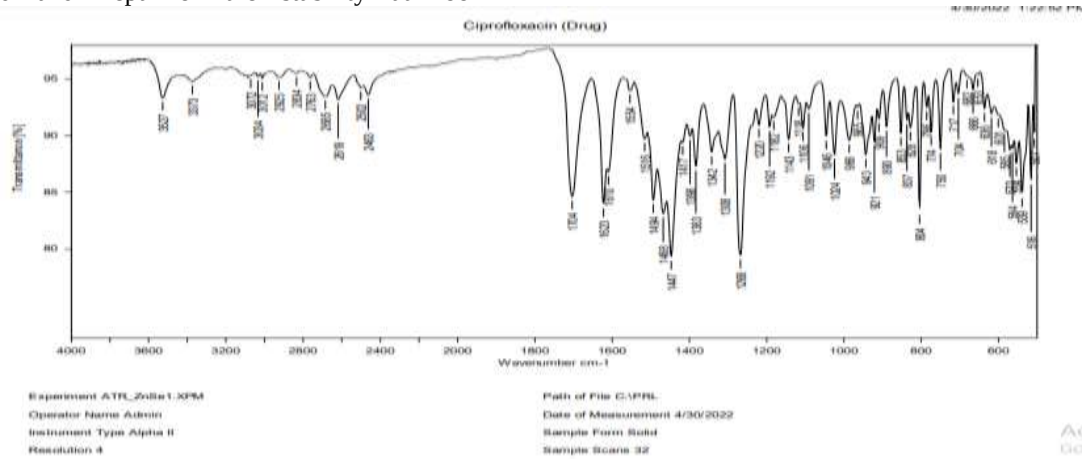

Fig01 FT- IR spectra of ciprofloxacin

International Journal of Pharmaceutical Research and Applications
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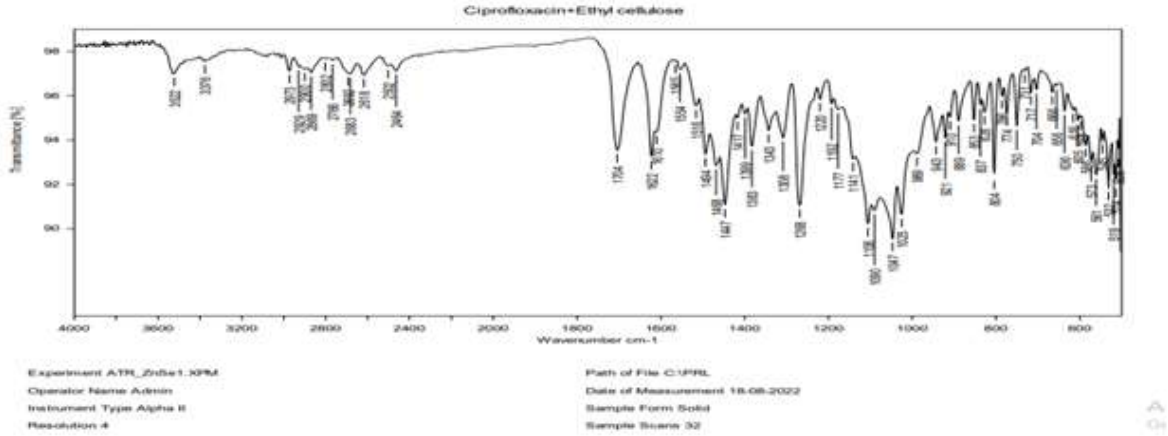


Fig02 FT- IR spectra of ciprofloxacin+ ethyl cellulose

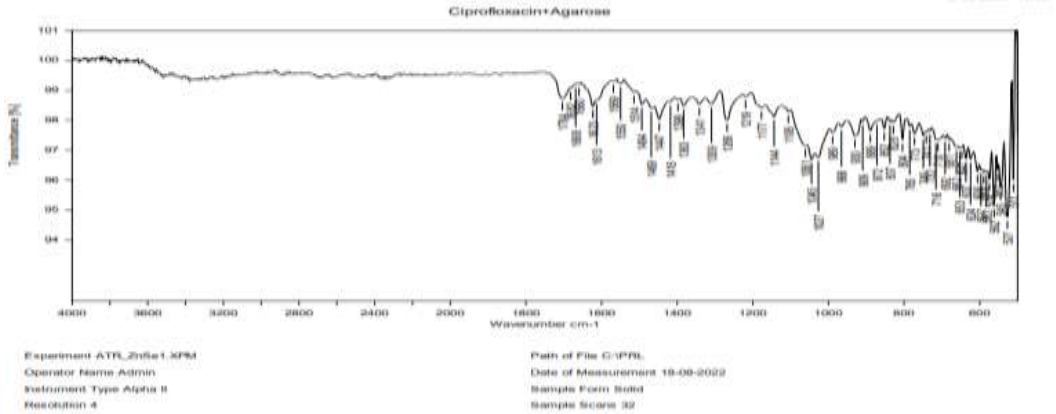


Fig03 FT- IR spectra of ciprofloxacin +Agarose

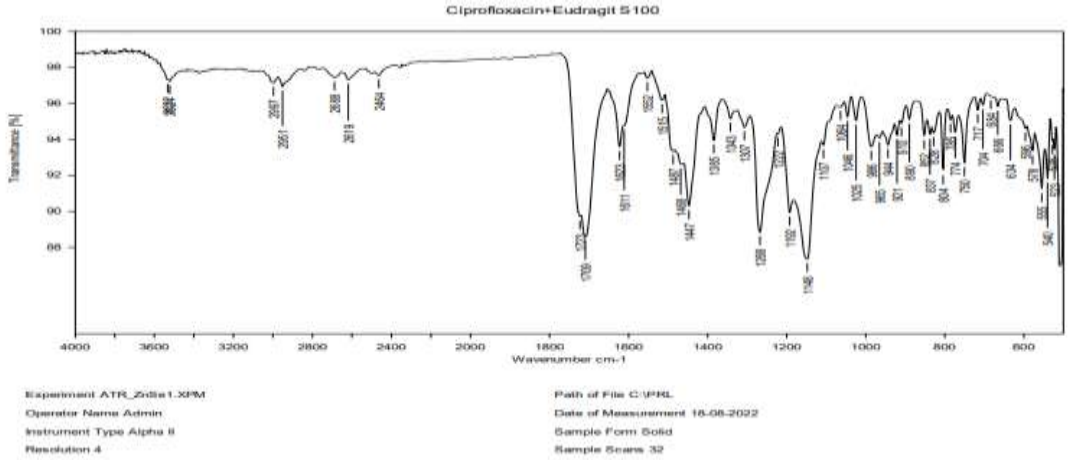


Fig04 FT- IR spectra of ciprofloxacin +Eudragit –s 100

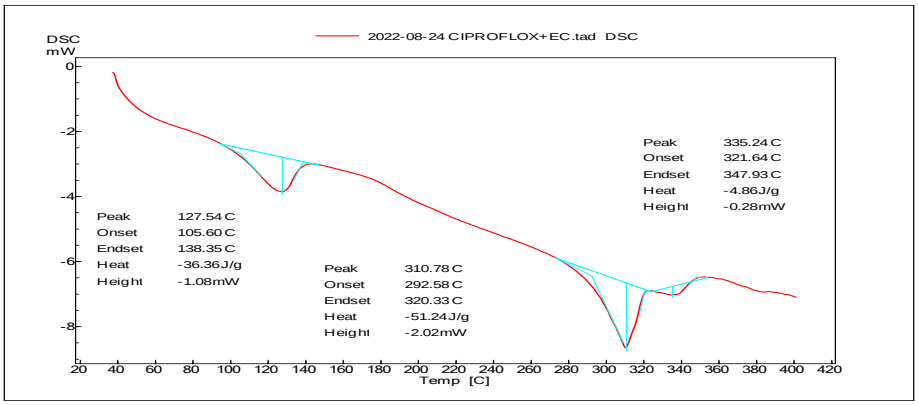
International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1089-1102 www.ijprajournal.com ISSN: 2456-4494

FTIR characteristic peak along with polymer

Table 2 FT-IR Characteristic peak of Pure Drug and excipients

Sl. No	Functional group	IR range	IR Observed peaks (cm^{-1})			
			Ciprofloxacin	Drug + Ethyl Cellulose	Drug+Chitosan	Drug+erudragit
1.	N-H	3100-3010	3054.61	3055.63	3054.62	3054.86
2.	C=O	1685-1666	1677.78	1677.86	1678.57	1677.88
3.	N-O	1550-1500	1509.45	1509.72	1510.64	1509.65
4.	C-N	1250-1020	1236.48	1236.61	1236.75	1236.59

DIFFERENTIAL SCANNING CALORIMETRY (DSC): Thermal behavior of the drug and polymer were studied with the help of DSC and obtained their endothermic peaks are corresponding to its melting point. So therefore, ciprofloxacin appeared in the physical mixture indicating that there was no possible interaction between the drug and the excipients in the microspheres formulation.



EVALUATION AND CHARACTERIZATION OF THE PREPARED MICROSPHERES.

PERCENTAGE YIELD

It was observed that as the polymer ratio in the formulation increases, the product yield also increases. The low percentage yield in some formulations may be due to microspheres lost during the washing process. A 100% yield could not be achieved principally due to adhesion of microspheres to the stirring rod of the Mechanical stirrer. The percentage yield was found to be in the range of 71.00% to 80.40%. The percentage yield of the prepared Microspheres is recorded.

International Journal of Pharmaceutical Research and Applications
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Table 3: Percentage yield of ciprofloxacin microspheres

Formulation Code	Theoretical Yield(gm)	Percentage Yield (%)
F1	2.0	71.±0.43
F2	3.0	84.±0.61
F3	4.0	75.±0.57
F4	2.0	70± 0.32
F5	3.0	76.±0.54
F6	4.0	82±0.21
F7	3.0	78±0.12
F8	4.0	79±0.39
F9	2.0	80±0.67

DRUG ENTRAPMENT EFFICIENCY

The % of Drug Entrapment Efficiency of all the formulations was in the range of 75.00% to 79.60%. The % drug entrapment efficiency of the prepared Microspheres is displayed in **table no.4.** The drug entrapment efficiency of the prepared microspheres increased progressively with an increase in proportion of the respective polymers.

Increase in the polymer concentration increases the viscosity of the dispersed phase. The particle size increases exponentially with viscosity. The higher viscosity of the polymer solution at the highest polymer concentration would be expected to decrease the diffusion of the drug into the external phase which would result in higher entrapment efficiency. Similarly increasing EC/HPMC ratio shows increased entrapment efficiency of Microspheres. This may be attributed to the rapid hardening of the droplets following increased EC proportion that results in reduced drug diffusion into the aqueous phase. Entrapment efficiency was decreased upon increasing Drug composition. [18]

DRUG ENTRAPMENT EFFICIENCY

Table 4Percentage Drug Entrapment efficiency of ciprofloxacin microspheres

Formulation Codes	**Drug Content (mg)**	%Drug Entrapment Efficiency
F1	75	75.00±0.13
F2	90.5	90.50±0.84
F3	82.6	82.60±0.68
F4	78	78.00±0.56
F5	81.6	81.60±0.67
F6	84.6	84.60±0.43
F7	80.5	80.50±0.62
F8	81.6	81.60±0.12
F9	79.6	79.60±0.21

PARTICLE SIZE ANALYSIS

The prepared hollow microspheres were in a size range suitable for oral delivery. The mean size increased with increasing polymer concentration which is due to a significant increase in the viscosity, thus leading to an increased emulsion droplet size and finally a higher microsphere size. Acyclovir floating microsphere had a size range of 167.5µm to 180.08 µm.

The particle size data is presented in **table no.5**the particle size as well as %drug entrapment efficiency of the microspheres increased with increase in the polymer concentration. It is interesting to note that the increase in particle size is comparable with the increase in entrapment efficiency. Additionally, increasing the polymer concentration and keeping the volume of aqueous phase constant; the viscosity of the aqueous phase would increase leading to the formation of large sized droplets which would result in large size of the micro particles. Higher concentration of polymer in the sample leads to an increased frequency of collision resulting in fusion of semi formed and producing an overall increase in the particle size.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 6 Nov-Dec 2022, pp: 1089-1102 www.ijprajournal.com ISSN: 2456-4494

The particle size distribution of microspheres obtained depends on the size of the emulsion droplets, as well as stirring speed & Stirring time, that are determined by a balance between the dispersive and the surface tension forces. The former tends to disperse the emulsion and the latter causes coalescence. Increasing the dispersive force also decreased microsphere mean diameter, but a broader distribution was obtained, contributing to a higher heterogeneity of the batch. Mean size decreased at higher rotational speeds, thus, an optimal impeller rotational speed was chosen to prepare small microspheres with a narrow size distribution suitable for oral drug delivery. [19]

PARTICLE SIZE ANALYSIS

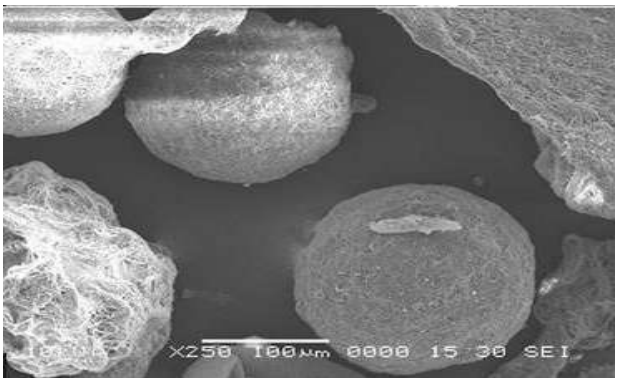
Table 5 Particle Size data of Formulations F-1 to F-9

Formulation Codes	Particle Size (µm)
F1	145.56±0.18
F2	158.2±0.47
F3	130.8±0.13
F4	138±0.25
F5	130.75±0.17
F6	131±0.32
F7	138±0.52
F8	145±0.28
F9	131±0.13

SHAPE AND SURFACE MORPHOLOGY

Morphology of the microspheres was investigated by Scanning electron microscopy (SEM). The photographs of the optimized formulations taken by scanning electron microscope are shown in the Figure

The results of SEM revealed that the microspheres were discrete and spherical in shape with a rough outer surface morphology which might be due to surface associated drug. Surface topography of optimized formulation was carried out. SEM study showed that pores were found on the surface of microspheres which indicates that drug is released by diffusion mechanism.



DEGREE OF SWELLING

The swelling index behavior of the floating microspheres was measured by studying its weight gain. To determine the Swelling index the microspheres were kept dissolution apparatus using the dissolution medium 0.1N HCL at $37\pm0.5°c$. After 0.5, 1, 2, 3, 4, 5, and 6 h, each microsphere from the dissolution apparatus was withdrawal, blotted with tissue paper to remove the excess water, and weighed on the analytical balance. The experiment was performed in triplicate at each time point. [20]

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Table 6 Degree of Swelling of ciprofloxacin microspheres

Formulation Code	Average Swellability	%Swelling	±SEM
F1	1.09	109	0.029
F2	0.84	84	0.0230
F3	0.72	72	0.0233
F4	1.24	124	0.0115
F5	1.06	106	0.0066
F6	0.92	92	0.0033
F7	1.36	136	0.0176
F8	1.08	108	0.0218
F9	0.96	96	0.0133

IN-VITRO DRUG DISSOLUTION STUDIES

The In-vitro dissolution of ciprofloxacin from the prepared Microspheres exhibited a biphasic mechanism. The release of ciprofloxacin from the Microspheres was characterized by an initial phase of (higher release), which was due to the presence of drug particles on the surface of the microspheres followed by a second phase of moderate release. The initial burst effect may be attributed a desired effect to ensure initial therapeutic plasma concentration of the drug. The biphasic pattern of release is a characteristic feature of matrix diffusion kinetics. The initial burst effect was considerably reduced with increase in polymer concentration. The fact that increases in the polymer concentration resulted in better incorporation efficiency could be the reason for the observed decrease in burst effect, since the amount of surface associated drug decreases with an increase in entrapment efficiency. The formulations F5 & F96containing respectively showed the maximum release 87.83 % and 91.94 %, respectively, compared to other formulations at 10 h. As the polymer to drug ratio was increased the extent of drug release decreased. A significant decrease in the rate and extent of drug release is attributed to the increase in density of polymer matrix that results in increased diffusion path length which the drug molecules have to traverse. The release of the drug has been controlled by swelling control release mechanism. Additionally, the larger particle size at higher polymer concentration also restricted the total surface area resulting in slower release the cumulative drug release was significantly decreased with increase in the EC proportion. The reason for this retarded drug release may be due to the increased proportion of the hydrophobic polymer EC that increases the polymer matrix density and thus result in increased diffusional path length, leading to a decrease in drug release from the Microspheres. The results obtained in the Invitro drug dissolution studies are tabulated as shows the release kinetic profile of the formulations and comparison of % CDR of all the formulations were presented.[21]

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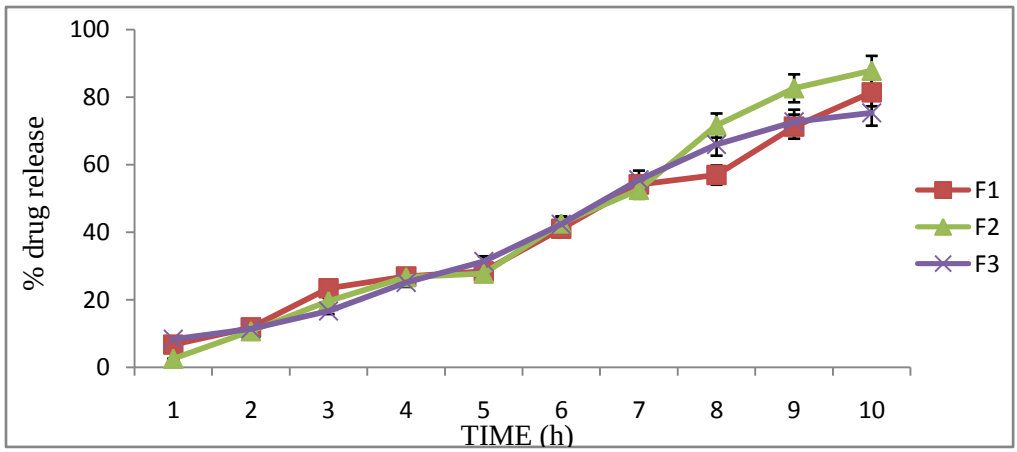
Table 07: In-vitro Drug Dissolution data of F1to F9 Formulations

Time(h)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	6.75 ±0.43	2.520 ±0.43	8.32 ±0.40	5.62 ±2.13	7.65 ±0.15	6.52 ±0.10	5.2±1.02	4.33 ±0.03	4.87 ±0.10
2	11.80 ±0.32	10.66 ±0.65	11.35 ±0.45	13.16 ±1.12	12.26 ±0.12	14.29 ±0.35	8.74 ±1.23	8.92 ±0.04	7.68 ±0.35
3	23.40 ±1.32	19.55 ±0.96	16.62 ±0.12	18.43 ±2.63	20.24 ±0.15	24.09 ±1.02	15.28 ±0.23	14.03 0.08	14.23 ±1.02
4	26.92 ±1.52	26.67 ±0.32	25.08 ±1.23	24.41 ±2.34	29.86 ±0.52	31.24 ±0.13	27.08 ±1.01	25.91 ±0.56	25.23 ±0.50
5	28.43 ±0.98	27.72 ±1.01	31.33 ±0.32	32.01 ±2.12	35.22 ±2.62	36.61 ±0.50	38.20 ±2.17	38.33 ±1.06	36.74 ±1.54
6	41.03 ±3.63	42.58 ±1.13	42.36 ±0.65	40.10 ±2.76	42.66 ±0.33	47.22 ±0.53	43.15 ±3.02	43.60 ±1.40	42.52 ±1.02
7	54.15 ±2.50	52.54 ±1.56	55.49 ±0.12	52.54 ±2.26	53.30 ±0.52	71.99 ±1.40	55.10 ±3.12	50.58 ±2.67	50.65 ±1.40
8	56.93 ±2.32	71.60 ±2.10	65.97 ±0.45	63.23 ±0.39	68.29 ±1.23	85.26 ±1.52	61.63 ±4.20	54.95 ±2.43	71.58 ±0.52
9	71.27 ±3.59	82.63 ±0.15	72.67 ±0.78	76.25 ±0.67	84.57 ±0.25	88.67 ±1.02	71.80 ±2.45	61.75 ±1.6	85.43 ±1.40
10	81.38 ±1.5	87.83 ±1.17	75.32 ±0.19	83.67 ±0.76	88.17 ±2.33	92.99 ±1.40	82.16 ±1.54	68.18 ±0.03	91.94 ±0.03

IN-VITRO DIFFUSION DATA & CURVE OF F1-F3 FORMULATION



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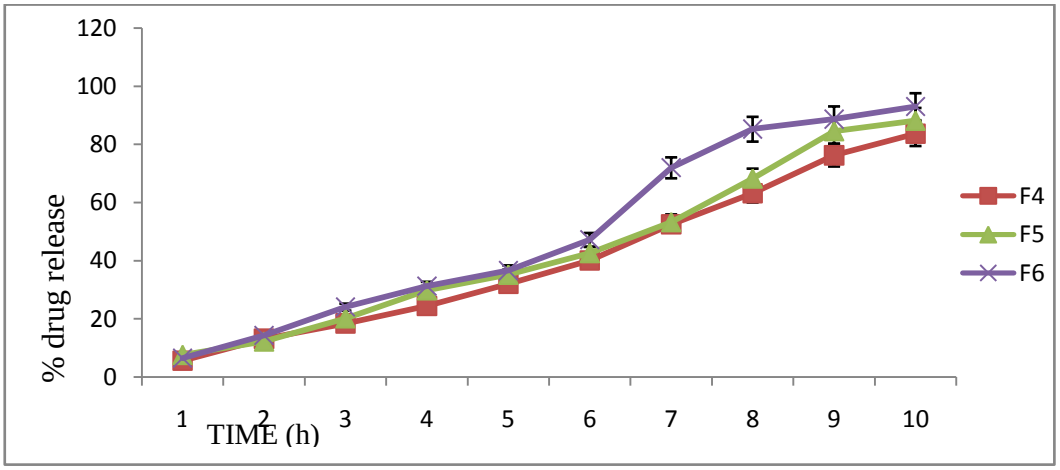
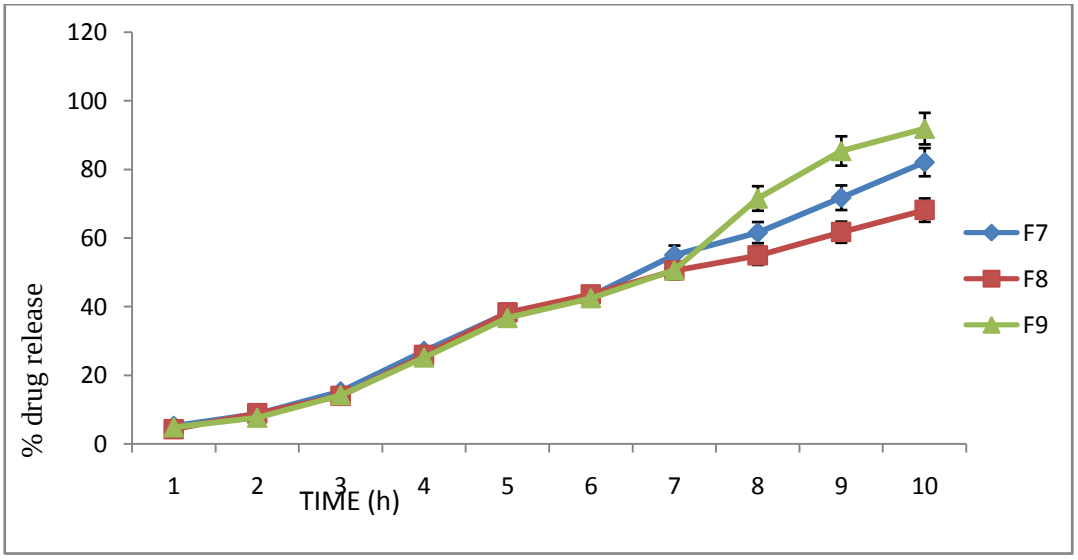
IN-VITRO DIFFUSION DATA & CURVE OF F4-F6 FORMULATION



IN-VITRO DIFFUSION DATA & CURVE OF F7-F9 FORMULATION



IN-VITRO DRUG RELEASE KINETICS

For understanding the mechanism of drug release and release rate kinetics of the drug from dosage form, the in-vitro drug diffusion data obtained was fitted to various mathematical models such as zero order, First order, Higuchi matrix, Korsmeyer-Peppas model and Hixson-Crowell model. The values are compiled in table 32. The % drug release with data fitting to various kinetic models for optimized microsphere formulations is presented. In formulations F1 and F2, the R values of First order were close to 1. The Dissolution coefficients (n) values ranged between 1.1368 – 1.1278. Since the R values of Higuchi matrix were close to 1 in the formulations F1 to F3. The drug release follows matrix diffusion kinetics and the plot proved linearity; hence it was concluded that diffusion was the main mechanism of drug release from the microspheres.

Table 8 Different kinetic model of ciprofloxacin microspheres:

Formulation code	Kinetic model		Best fit model

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	Zero order (R^2)	First order (R^2)	Higuchi (R^2)	Peppa's (R^2)	N value	
F1	0.9073	0.8187	0.9672	0.9508	1.1368	Higuchi, zero order
F2	0.9899	0.9646	0.9573	0.994	1.0018	Peppa's, zero order
F3	0.9916	0.9785	0.9664	0.9743	0.7967	Peppa's, zero order
F4	0.9941	0.7849	0.9693	0.9985	1.0178	Peppa's, zero order
F5	0.9678	0.8818	0.9523	0.9851	0.9815	Peppa's, zero order
F6	0.9754	0.9799	0.9956	0.8485	1.093	Higuchi, first order
F7	0.9808	0.9388	0.9963	0.9632	0.9237	Higuchi, zero order
F8	0.9678	0.9734	0.9811	0.9912	1.125	Peppa's first order
F9	0.9764	0.9656	0.9929	0.9042	1.1278	Higuchi, zero order

Stability studies:

Swelling index	Encapsulation efficiency	In-vitro drug release studies
84=0.023	90.50%	91.94%

IV. CONCLUSION

In the present work, Microspheres were formulated to deliver Ciprofloxacin via oral route. The results of this investigation indicate that non-aqueous solvent evaporation technique can be successfully employed to fabricate Ciprofloxacin - loaded Microspheres.FT-IR spectra of the physical mixture revealed that the drug is compatible with the polymers used.DSC studies revealed that curves of physical mixtures, which indicates the absence of incompatibility between the drug and each polymer. Micromeritic studies revealed that the mean particle size of the prepared microspheres was in the size range of 145.5 – 131.8µm and are suitable for oral administration.SEM analysis of the microspheres revealed that all the prepared microspheres were discrete, spherical in shape and had ideal surface morphology.Increase in the polymer concentration led to an increase in % Yield and Particle size of the microspheresthe % Drug entrapment efficiency increases with increasing the polymer concentration and also the formulations containing high EC proportion shows good entrapment efficiency. the percentage of particles floated at the end of 10 h than compared with rest of the formulation.The in-vitro drug diffusion decreased with increase in the polymer concentration. The drug diffusion was characterized by an initial phase of higher release followed by a second phase of moderate release.Analysis of drug release mechanism showed that the drug release followed non-Fickian, Super Case –II diffusion and the best fit model was found to be Higuchi and First Order.

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