AMERICAN JOURNAL OF PHARMTECH RESEARCH
Journal home page: http://www.ajptr.com/

Formulation and Evaluation of Gemifloxacin Mesylate Microspheres by Ionotropic Gelation Method

K. Nagasree[*1,2], G.V. Chowdary[3],C.B. Mahendra kumar[1]
1.St.mary's College of Phramacy, Secunderabad, Telangana state, India.
2. Jawaharlal Nehru Technological University, Kukatpally, Hyderabad-500072, Telangana, India.
3.Harizon College of Pharmacy, Keesara, RR Dist, Telangana state, India.

ABSTRACT

Gemifloxacin mesylate loaded microspheres were prepared by Ionotropic gelation technique with different drug to carrier ratio. All the microspheres were characterized for particle size, scanning electron microscopy, FTIR study, DSC, percentage yield, drug entrapment, stability studies and for *in vitro* release kinetics and found to be within the limits. Among all the formulations S8, was selected as optimized formulation based on the physic chemical and release studies. In the *in vitro* release study of formulation S8 showed 95.92%, after 12 h in a controlled manner, which is essential for anti ulcer therapy. The innovator Gemiflox conventional tablet shows the drug release of 95.23% within 1 h. The drug release of optimized formulation S8 followed zero order and Higuchi kinetics indicating diffusion controlled drug release.

Keywords: Gemifloxacin mesylate, gelatin, microspheres, scanning electron microscopy, release order kinetics.

*Corresponding Author Email: nagasree18@gmail.com
Received 10 December 2015, Accepted 11 January 2016

Please cite this article as: Nagasree K *et al.*, Formulation and Evaluation of Gemifloxacin Mesylate Microspheres by Ionotropic Gelation Method. American Journal of PharmTech Research 2016.

INTRODUCTION

Advances over the last decade in site-specific and/or controlled drug delivery systems are contributing to new and/or improved drug therapies. Drug delivery is becoming an increasingly important aspect in new product research and development in the pharmaceutical industry[1]. Oral drug administration is by far the most preferable route for taking medications. However, their short circulating half life and restricted absorption via a defined segment of intestine limits the therapeutic potential of many drugs. Such a pharmacokinetic limitation leads in many cases to frequent dosing of medication to achieve therapeutic effect. This results in pill burden and consequently, patient complains. Rational approach to enhance bioavailability and improve pharmacokinetic and pharmacodynamic profile is to release the drug in a controlled manner and site specific manner[2].

Microspheric drug delivery has advantage over various other dosage forms like we know for lungs disease now a days aerolised drugs are used for local delivery of drugs but it has disadvantage of shorter duration of action so for sustained release and reducing side effects and hence to achieve better patient compliance microspheres can be used. It also has advantage over liposomes as it is physicochemically more stable. Moreover the microspheres are of micron size so they can easily fit into various capillary beds which are also having micron size[3].

For the treatment of chronic diseases it is important to take medication several times, this may lead to fluctuating drug level in body. In order to avoid frequent drug administration and maintenance of therapeutic drug level in body it is essential to administer drug by a sustained release system. Drugs with short elimination half life are most suitable for sustained release formulations. Sustained delivery of drugs can be achieved by microspheres formulation[4]. The microsphere requires a polymeric substance as a carrier and a core material[5, 6]. Microspheres have been widely accepted as a mean to achieve oral and parenteral controlled release[7, 8, 9].

Gemifloxacin mesylate is an oral broad-spectrum quinolone antibacterial agent used in the treatment of acute bacterial exacerbation of chronic bronchitis and mild-to-moderate pneumonia. It has low bioavailability of 71% and half life of 7h[10]. The aim of present work is to design and in vitro evaluation of Gemifloxacin microspheres to enhance its bioavailability and prolonged drug release in the body.

MATERIALS AND METHOD

Materials:

Gemifloxacin mesylate pure drug was generous gift from Hetero Drugs Ltd**,** Hyderabad, India.

Sodium alginate was obtained from Pruthvi Chemicals, Mumbai. Pectin, Gelatin and Calcium chloride was received from MSN Labs Ltd. Hyderabad. All other chemicals used were of analytical grade.

Formulation of Gemifloxacin mesylate microspheres:

Gemifloxacin mesylate microspheres were prepared using polymers sodium alginate and calcium chloride by Ionotropic gelation method. Different formulation trials of Gemifloxacin mesylate were prepared using different concentration of polymer and cross linking agent. Total 14 formulations were developed using sodium alginate and calcium chloride in different concentrations. In this method weighed quantity of Gemifloxacin mesylate was added to 100ml sodium alginate solution and thoroughly mixed at 500 rpm. Resultant solution was extruded drop wise with the help of syringe and needle into 100ml aqueous calcium chloride solution and stirred at 100 rpm. After stirring for 10 minutes the obtained microspheres were washed with water and dried at 60 degrees 2hours in a hot air oven and stored in dessicater.[11]

Table 1: Formulation trials for Gemifloxacin mesylate normal microspheres:

Formulation code	Gemifloxacin (g)	Sodium alginate	Gelatin (mg)	Calcium chloride
S1	3200	1 %	1000	7%
S2	3200	1.2 %	0.858	7%
S3	3200	1.4%	0.716	7%
S4	3200	1.6%	0.574	7%
S5	3200	1.8%	0.432	7%
S6	3200	2%	0.290	7%
S7	3200	2.2%	0.148	7%
Formulation code	**Gemifloxacin (g)**	**Sodium alginate**	**Pectin (mg)**	**Calcium chloride**
S8	3200	1%	1000	10%
S9	3200	1.2%	0.858	10%
S10	3200	1.4%	0.716	10%
S11	3200	1.6%	0.574	10%
S12	3200	1.8%	0.432	10%
S13	3200	2%	0.290	10%
S14	3200	2.2%	0.148	10%

Evaluation of Gemifloxacin mesylate microspheres:

Particle size:

The 100 microspheres were evaluated with respect to their size and shape using optical microscope fitted with an ocular micrometer and a stage micrometer. The particle diameters of more than 100 microspheres were measured randomly by optical microscope.[12]

Angle of repose:

Angle of repose (Ɵ) of microspheres measures the resistance to particles flow, and is calculated according to fixed funnel standing cone method. Where (Ɵ) is angle of repose, H/D is surface area of the free standing height of the microspheres heap that is formed on a graph paper after making the microspheres flow from glass funnel.

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

Bulk density: Volume of the microspheres in the measuring cylinder was noted as bulk density.

$$\text{Bulk density} = \frac{\text{Wt of powder}}{\text{Bulk volume of powder}}$$

Tapped density: Change in the microspheres volume was observed in mechanical tapping apparatus.

$$\text{Tapped density} = \frac{\text{Wt of microspheres}}{\text{Tapped volume of microspheres}}$$

Compressibility index:

Also called as Carr's index and is computed according to the following equation.

$$\text{Carr's compressibility index} = \frac{\text{Tapped density - Bulk density}}{\text{Tapped density}} \times 100$$

Hausner's ratio:

Hausner's ratio of microspheres is determined by comparing the tapped density to the fluff density using the equation.[13]

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Swelling index:

Swelling index was determined by measuring the extent of swelling of microspheres in the given medium. Exactly weighed amount of microspheres were allowed to swell in given medium. The excess surface adhered liquid drops were removed by blotting and the swollen microspheres were weighed by using microbalance. The hydro gel microspheres then dried in an oven at 60 degrees for 5h until there was no change in the dried mass of sample. The swelling index of the microsphere was calculated by using the formula.[14]

Swelling index= (Mass of swollen microspheres - Mass of dry microspheres/mass of dried microspheres) X 100.

Drug entrapment efficiency and % yield:

In order to determine the entrapment efficiency, 10 mg of formulated microspheres were thoroughly crushed by triturating and suspended in required quantity of methanol followed by agitation to dissolve the polymer and extract the drug. After filtration, suitable dilutions were made and drug content assayed spectrophotometrically at particular wavelength using calibration curve. Each batch should be examined for drug content in a triplicate manner.[15]

% Drug entrapment = Calculated drug concentration /Theoretical drug concentration x 100

% yield = [Total weight of microspheres / Total weight of drug and polymer] x 100

***In vitro* drug release studies:**

In vitro drug release studies for developed Gemifloxacin mesylate microspheres were carried out by using dissolution apparatus II paddle type (Electrolab TDL-08L). The drug release profile was studied in 900 ml of 0.01 N HCl at 37± 0.5^0C temperature at 100 rpm. The amount of drug release was determined at different time intervals of 0, 1, 2, 3, 4, 6, 8, 10& 12 hours by UV visible spectrophotometer (Shimadzu UV 1800) at 271nm.[16]

Kinetic modeling of drug release:

In order to understand the mechanism and kinetics of drug release, the result of the *in vitro* dissolution study of microspheres were fitted with various kinetic equations, like zero order[17] (percentage release vs. time), first order[18]. (log percentage of drug remaining to be released vs. time) and Higuchi's model[19]. (Percentage drug release vs. square root of time). Correlation coefficient (r^2) values were calculated for the linear curves obtained by regression analysis of the above plots.

Drug excipient compatibility studies

The drug excipient compatibility studies were carried out by Fourier transmission infrared spectroscopy (FTIR) method, Differential Scanning Calorimetry (DSC) and SEM.

Fourier transform infrared spectroscopy (FTIR)

FTIR spectra for pure drug, physical mixture and optimized formulations were recorded using a Fourier transform Infrared spectrophotometer. The analysis was carried out in Shimadzu-IR Affinity 1 Spectrophotometer. The samples were dispersed in KBr and compressed into disc/pellet by application of pressure. The pellets were placed in the light path for recording the IR spectra. The scanning range was 400-4000 cm^{-1} and the resolution was 1 cm^{-1}.

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry studies were carried out using DSC 60, having TA60 software, Shimadzu, Japan. Samples were accurately weighed and heated in sealed aluminum pans at a rate of 10°C/min between 25 and 350°C temperature rang under nitrogen atmosphere, empty aluminum pan was used as a reference.

SEM studies

The surface and shape characteristics of pellets were determined by scanning electron microscopy (SEM) (HITACHI, S-3700N). Photographs were taken and recorded at suitable magnification.

Stability studies

The stability study of the optimized formulation was carried out under different conditions according to ICH guidelines. The optimized microspheres were stored in a stability chamber for stability studies (REMI make). Accelerated Stability studies were carried out at 40 ^{0}C / 75 % RH for the best formulations for 6 months. The microspheres were characterized for the percentage yield, entrapment efficiency & cumulative % drug released during the stability study period[20.]

RESULTS AND DISCUSSION

Gemifloxacin mesylate microspheres:

Figure 1: **Gemifloxacin mesylate microspheres**

Micromeretic properties of Gemifloxacin mesylate microspheres

Table 2: Micromeretic properties of Gemifloxacin mesylate microspheres:

Formulation code	Particle size (µm)	Bulk density (g/cc^3)	Tapped density (g/cc^3)	Angle of repose	Carr's index	Swelling index
S1	61.12±0.08	0.66	0.69	25˚.74	9.34%	64%
S2	65.29±0.13	0.74	0.72	29˚.67	8.34%	69%
S3	67.43±0.04	0.76	0.73	30˚.54	8.12%	70%
S4	69.67±0.09	0.79	0.73	31˚.15	7.23%	71%

S5	73.45±0.04	0.89	0.75	27˚.93	14.56%	79%
S6	92.45±0.09	0.92	0.76	25˚.21	13.95%	87%
S7	67.45±0.04	0.66	0.59	27˚.93	14.56%	69%
S8	70.45±0.09	0.64	0.76	21˚.45	8.01%	96%
S9	78.45±0.09	0.67	0.62	25˚.54	13.95%	70%
S10	81.23±0.14	0.69	0.64	24˚.91	10.32%	75%
S11	85.12±0.08	0.71	0.66	23˚.74	9.34%	84%
S12	87.29±0.13	0.74	0.68	25˚.67	8.34%	93%
S13	91.43±0.04	0.76	0.73	25˚.54	8.12%	92%
S14	94.13±0.09	0.87	0.78	29˚.15	7.23%	89%

All fourteen formulations were evaluated for various micromeretic and physic chemical parameters and the results are tabulated in Table 2. Among all the formulations S8 shown best results of particle size, bulk density, tapped density, angle of repose, carr's index and swelling index of 70.45±0.09, 0.64, 0.76, 21˚.45, 8.01% and 96% respectively.

Table 3: Percentage drug yield & entrapment efficiency of Gemifloxacin mesylate microspheres.

Formulation code	Percentage yield	Entrapment efficiency
S1	70.00%	69.00%
S2	71.00%	72.00%
S3	81.00%	80.00%
S4	83.87%	83.30%
S5	86.30%	85.20%
S6	91.30%	91.30%
S7	76.00%	74.03%
S8	95.50%	96.90%
S9	81.00%	82.00%
S10	84.00%	83.00%
S11	86.09%	85.00%
S12	87.50%	86.66%
S13	93.30%	91.03%
S14	85.30%	84.88%

The percentage yield and entrapment efficiency of all the formulations were measured by assay method and found to be within the limits. The formulation S8 shows good percentage yield and entrapment efficiency of 95.50% and 96.90% respectively and the results were depicted in

***In vitro* drug release studies**:

Gemifloxacin mesylate microspheres were evaluated for in vitro drug release studies in 0.01N HCL and the results are depicted in Table 4 & 5. The formulation S8 shown best drug release of 95.92**%** within 12h. The drug release was in controlled manner when compared with innovator product Gemiflox immediate release tablet i.e 95. 23 within 1h.

Table 4: *In vitro* cumulative % drug release of Gemifloxacin mesylate microspheres S1-S7 and Innovator product:

Time (h)	S1	S2	S3	S4	S5	S6	S7	Innovator (Gemiflox) 400mg immediate release)
0	0±0	0±0	0±0	0±0	0±0	0±0	0±0	0±0
1	14.23±0.33	15.00±0.33	15.22±0.14	15.62±0.15	14.63±0.33	11.05±0.16	13.23±1.22	95.23±0.12
2	24.80±0.36	25.40±0.45	24.23±0.52	23.01±0.16	32.01±0.16	25.40±0.43	23.34±0.21	--
3	31.38±0.45	30.55±0.45	31.96±0.45	29.11±0.34	37.11±0.32	29.01±0.34	30.08±0.21	--
4	40.10±0.12	38.20±0.34	40.24±0.33	38.24±0.35	44.83±0.14	40.40±0.43	38.90±0.23	--
6	51.60±0.33	52.30±0.12	54.20±0.16	52.83±0.33	57.76±0.18	48.30±0.16	49.91±0.32	--
8	60.30±0.18	63.30±0.32	68.24±0.32	67.03±0.16	64.60±0.11	54.35±0.22	61.20±0.16	--
10	74.60±0.19	69.92±0.16	72.32±0.36	82.62±0.23	75.56±0.23	67.90±0.13	70.10±0.52	--
12	83.50±0.34	85.42±0.32	90.41±0.34	94.36±0.15	85.00±0.44	72.30±0.16	80.20±0.23	--

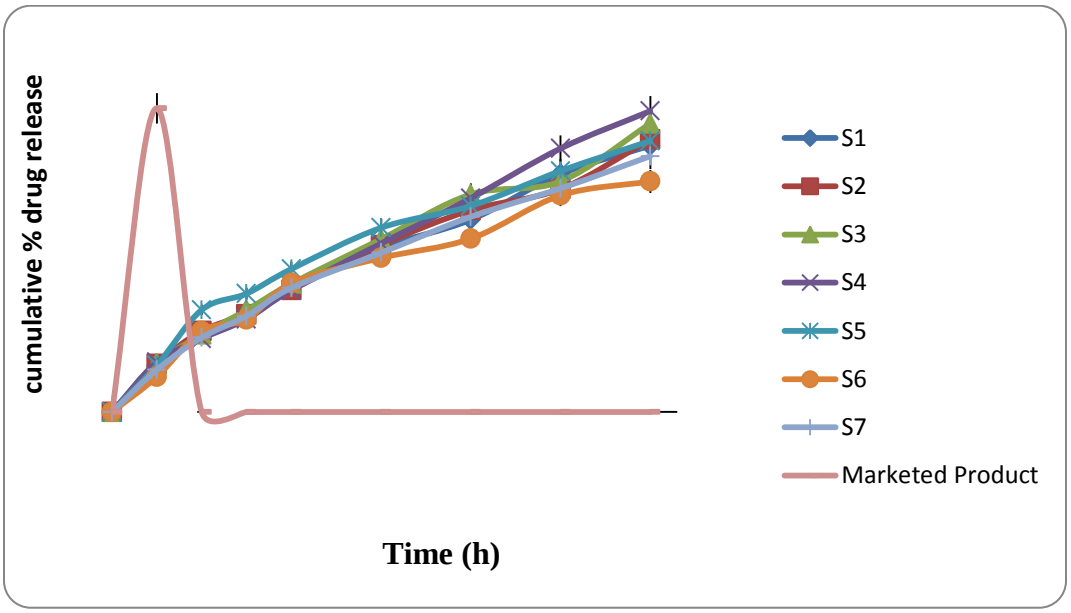

Figure 2: In vitro cumulative % drug release of Gemifloxacin mesylate sodium alginate microspheres formulation

Table 5: *In vitro* cumulative % drug release of Gemifloxacin mesylate microspheres S8-S14:

Time (h)	S8	S9	S10	S11	S12	S13	S14
0	0±0	0±0	0±0	0±0	0±0	0±0	0±0
1	15.31±0.12	10.10±0.22	13.09±0.12	17.87±0.11	10.34±0.32	14.23±0.22	12.34±0.44
2	22.15±0.22	21.30±0.34	23.09±0.33	23.06±0.32	21.79±0.15	20.12±0.43	25.34±0.54
3	34.19±0.16	35.45±0.45	28.23±0.43	31.05±0.46	31.85±0.76	32.04±0.43	36.12±0.45
4	45.23±0.32	49.89±0.43	42.11±0.17	38.20±0.98	39.90±0.98	44.40±0.88	46.20±0.65
6	58.73±0.14	64.80±0.16	45.39±0.76	49.30±0.78	48.90±0.67	51.00±0.87	52.30±0.78
8	67.46±0.32	73.60±0.54	54.23±0.97	58.30±0.63	63.31±0.43	62.35±0.43	65.30±0.65
10	81.25±0.18	83.85±0.44	67.20±0.33	68.90±0.66	72.22±0.43	74.30±0.57	78.58±0.12
12	95.92±0.15	96.17±0.98	71.34±0.81	73.25±0.98	81.31±0.33	84.50±0.55	86.30±0.11

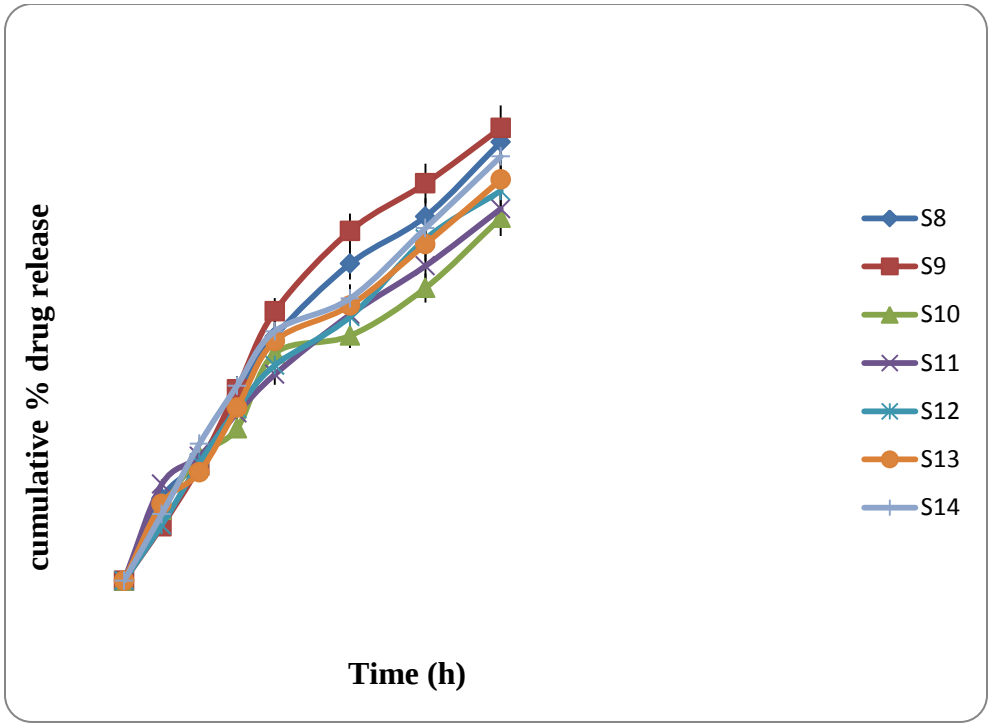

Figure 3: In vitro cumulative % drug Gemifloxacin mesylate sodium alginate release of microspheres formulations

Mathematical modeling of Gemifloxacin mesylate optimized microspheres (S8):

Table 6:Release order kinetics of optimized microspheres (S8)

Formula Code	Zero Order		First Order		Higuchi		Korsmeyer-Peppas	
	R^2	K	R^2	K	R^2	K	R^2	N
S8	0.980	7.625	0.599	0.112	0.965	28.53	0.662	2.113

The *in vitro* release profiles from optimized formulations were applied on various kinetic models. The best fit with the highest correlation coefficient was observed in zero order and Higuchi model,

indicating diffusion controlled principle. Further the n value obtained from the Korsmeyer plots i.e. 2.113 suggest that the drug release from microspheres was anomalous Non fickian diffusion.

Drug excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy

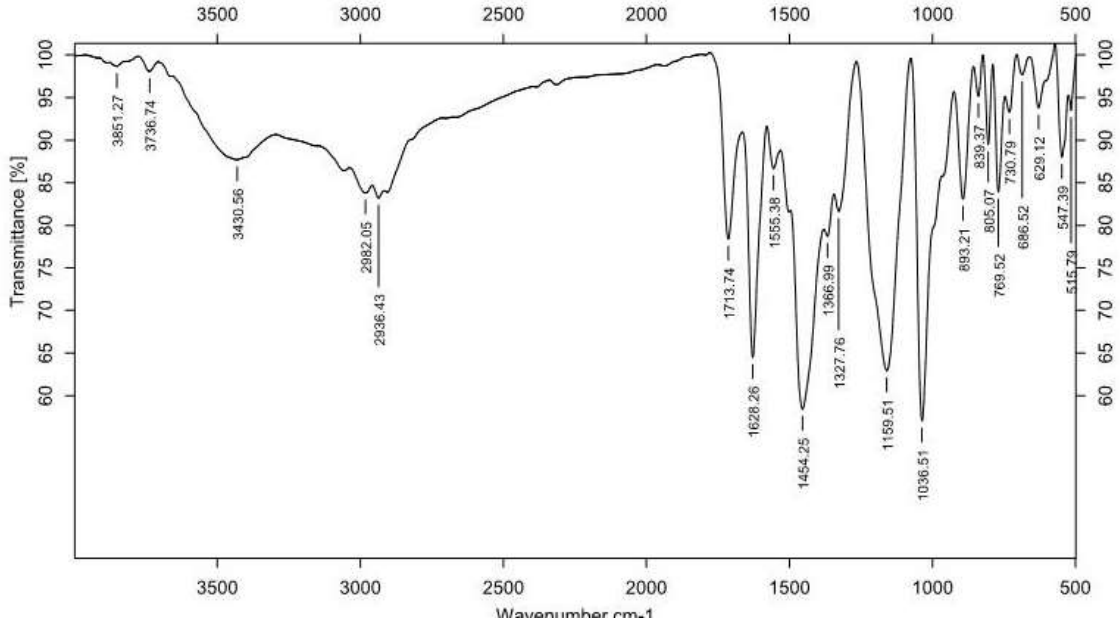

Figure 4: FT-IR spectrum of pure drug Gemifloxacin mesylate

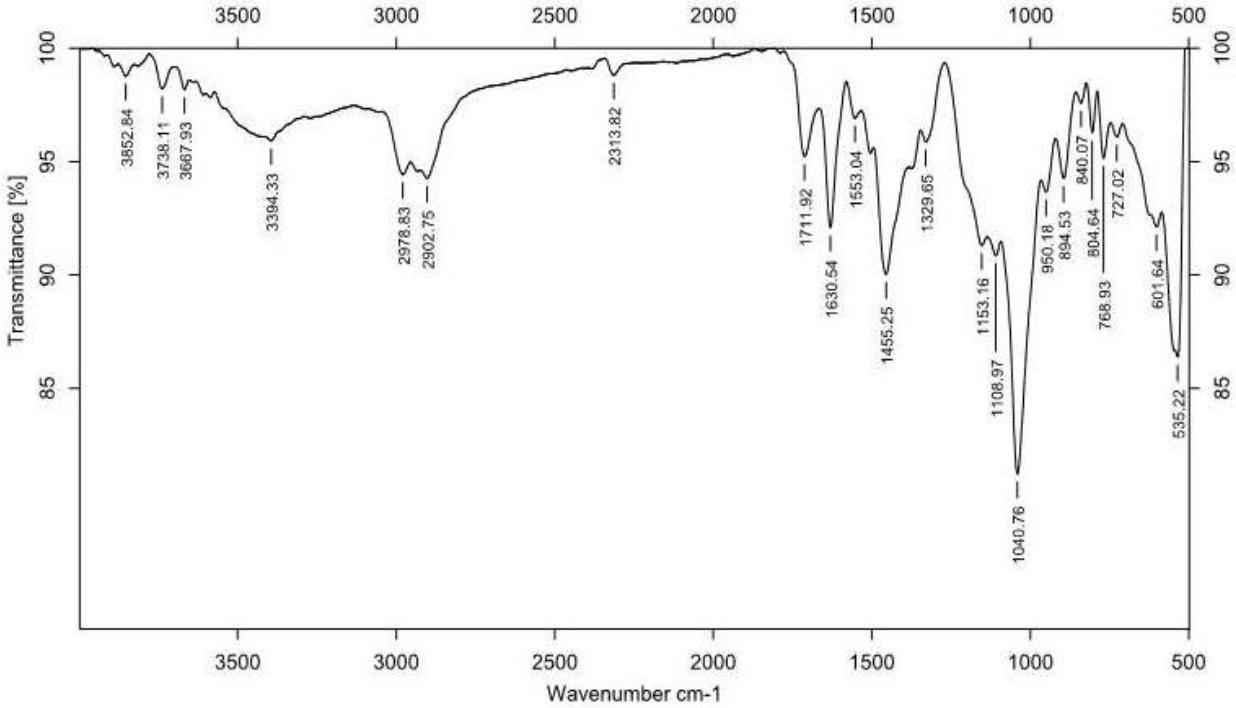

Figure 5: FT-IR spectrum of Gemifloxacin mesylate + Sodium alginate+$CaCl_2$

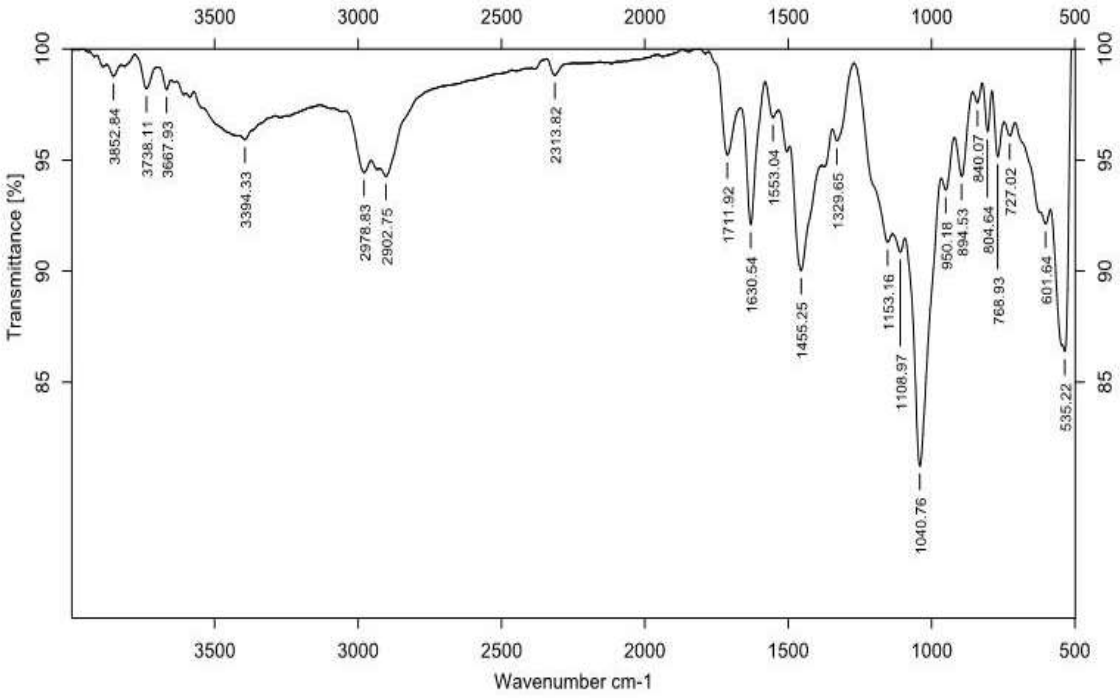

Figure 6:FT-IR spectrum of Gemifloxacin mesylate optimized microspheres (S8)

Drug polymer interaction was checked by comparing the IR spectra of the physical mixture (Figure) of drug with the excipients used with the IR spectrum of pure drug (Figure 4) and optimized formulation (C10) (Figure 6) and results found that there were no possible interaction between drug and polymer (Figure 5).The FTIR spectrum of Gemifloxacin mesylate [Figure] showed peaks corresponding to (C-F) bending at 1036.51cm-^{1} and O–CH3 Bending at 1454.25cm-^{1}, R–COOH Stretching at 1159.51cm-^{1}, N–H Scissoring at 1628.26cm-^{1}, Aromatic–C=O Stretching at 1713.74cm-1, and C–H Rocking at 730.79cm-^{1}. From the FTIR graphs of drug polymer mixture, it was found that the same peaks of the drug are available. Since it proves that there is no incompatibility with the polymers.

DSC Studies:

DSC thermogram revealed that there is no considerable change observed in Gemifloxacin mesylate melting endotherm of pure drug (232.79) (Figure 7) and drug in Gemifloxacin mesylate optimized formulation (S8) (236.36) (Figure 8). It indicates that there is no interaction takes place between drug and other excipients used in the formulation.

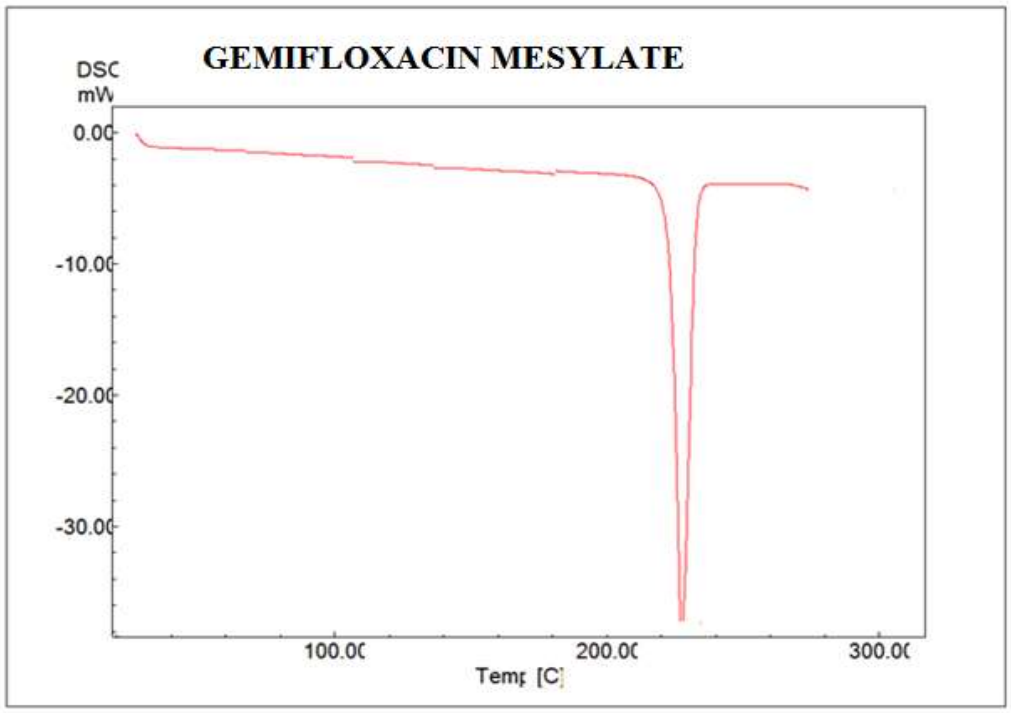

Figure 7: DSC thermogram of Gemifloxacin pure drug

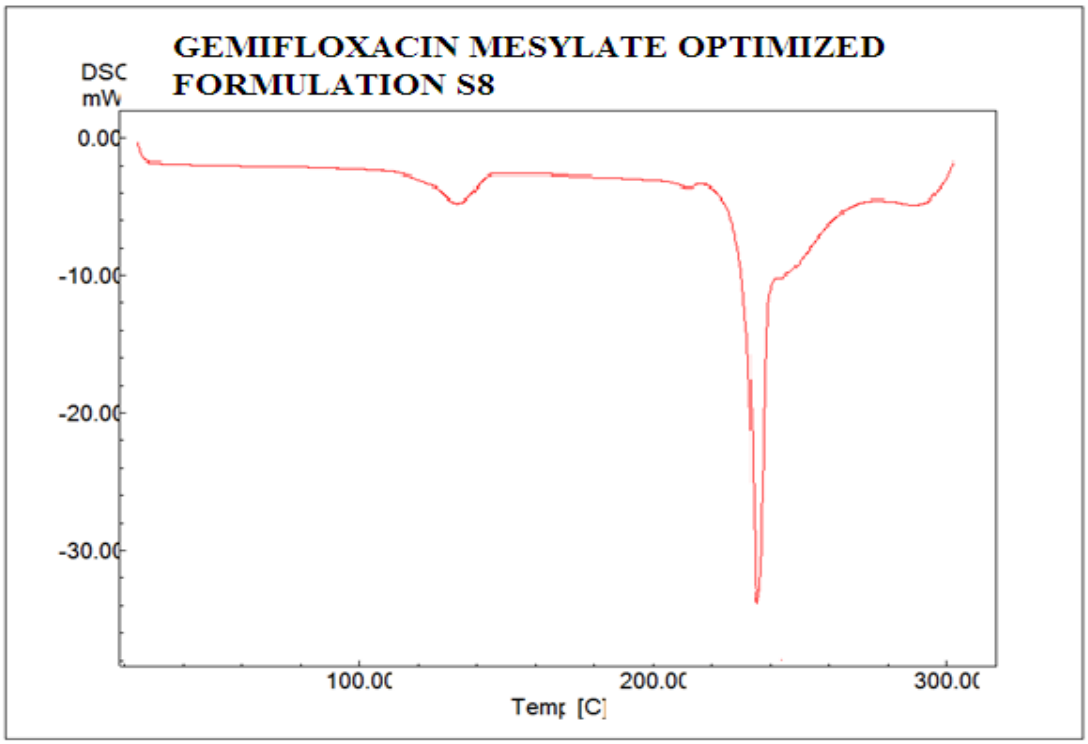

Figure 8: DSC thermogram of Gemifloxacin optimized formulation S8

SEM of Gemifloxacin mesylate microspheres

The external and internal morphology of controlled release microspheres were studied by Scanning Electron Microscopy.

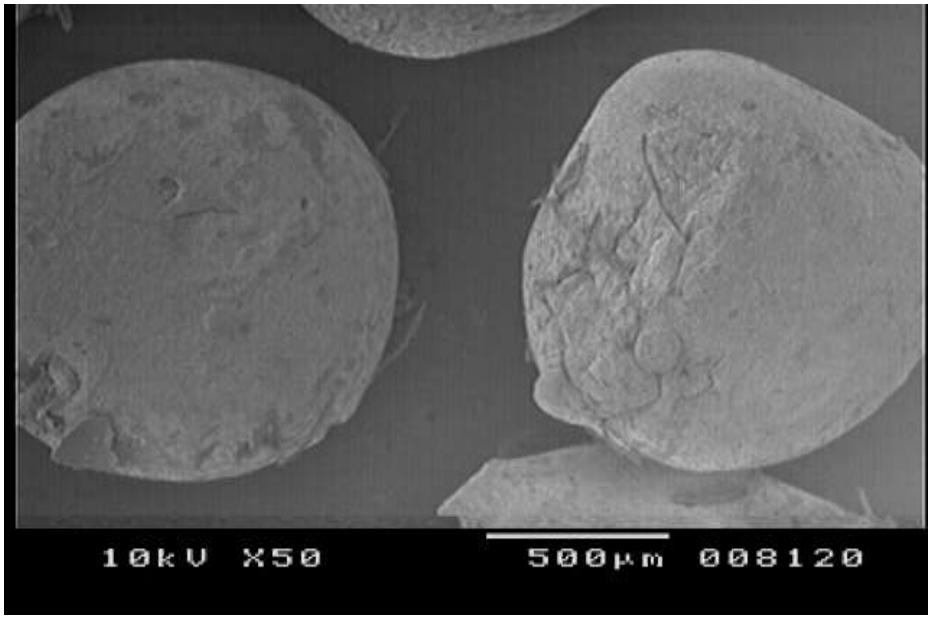

Figure 9: Scanning electron micrographs of Gemifloxacin mesylate microspheres

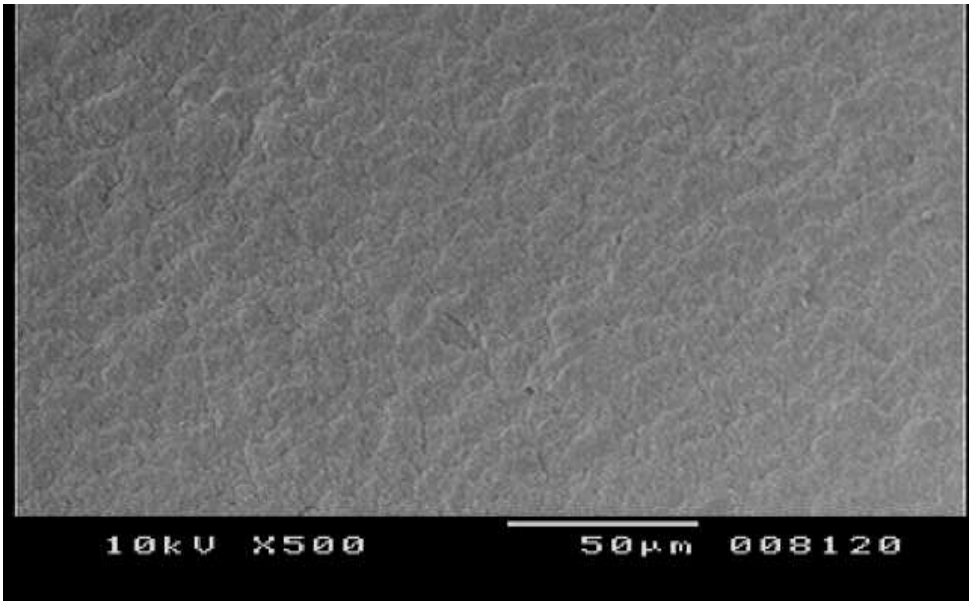

Figure 10: Scanning electron micrographs of Gemifloxacin mesylate microspheres

Morphology of the various formulations of Gemifloxacin mesylate microspheres prepared was found to be discrete and spherical in shape (Figure 9 & 10). The surface of Gemifloxacin mesylate microspheres was rough due to higher concentration of drug uniformly dispersed at the molecular level in the sodium alginate matrices. There are no crystals on surface which states that is drug is uniformly distributed.

Stability studies:

Optimized formulation (S8) was selected for stability studies on the basis of high cumulative % drug release. Stability studies were conducted by performing Percentage yield, %Entrapment

efficiency and *In-vitro* drug release profile for 6 months according to ICH guidelines. From these results it was concluded that, optimized formulation is stable and retained their original properties with minor differences.

CONCLUSION

From the above data, it could be concluded that Gemifloxacin mesylate microspheres exhibited prolonged and controlled release effect compared to Innovator product. Prepared Gemifloxacin mesylate microspheres were characterized for particle size, scanning electron microscopy, FT-IR study, DSC, percentage yield, drug entrapment, stability studies and found to be within the limits. Among all the formulations S8 was selected as optimized Gemifloxacin mesylate formulations based on the physic chemical and release studies. In the *in vitro* release study of optimized formulation S8 showed 95.92% after 12 h in a controlled manner, which is essential for disease like peptic ulcer. The innovator conventional tablet shows the drug release of 95.23 within 1 h.

REFRENCES

1. Anal A. K. Time-controlled pulsatile delivery systems for bioactive compounds. Recent Pat Drug Deliv Formul 2007; 1:73-79.
2. Gattani YS. Floating Multiparticulate drug delivery systems: An overview. Int J Pharma and Biosci 2010; 6(2); 35-40.
3. Prasanth V.V, Akash Chakraborthy M, Sam T M, Rinku M. Microspheres - An Overview. Int J Res in Pharmac and BiomeD Sci 2011; 2(2): 332-338.
4. Nazia K, Md. Irshad A, Anupam K S, Sudhir S G. Fabrication and evaluation of propranolol hydrochloride loaded microspheres by ionic-gelation technique. Der Pharmacia Lettre 2012; 4 (3): 815-820.
5. Sahoo SK, Mallick AA, Barik BB, Senapati PC. Preparation and in vitro evaluation of ethyl cellulose microspheres containing stavudine by the double emulsion method. Pharmazie 2007; 62: 117-121.
6. Chowdary KPR, Koteshwara RN, Malathi K. Ethyl cellulose microspheres of gliplizide: characterization, in vitro and in vivo evaluation. Ind J pharma scie 2004; 66: 412- 416.
7. Leung SS, Robinson JR. Parenteral product. In: Robinson JR, Lee VHL, editors. Controlled drug delivery, fundamentals and applications. 2nd ed. New York: Marcel Dekker Inc; 1987; 448–50.
8. Freeberg S, Zhu XX. Polymer microspheres for controlled drug release. Int J Pharm 2004; 282:1–18.

9. Upadhye K, Bakhle S, Dixit G, Wadetwar R, Deshpande S, Nagulwar V. Preparation and evaluation of gelatin micospheres containing ciprofloxacin hydrochloride. Indian Drugs 2004; 41: 665–9.
10. Mohammed L. H. Formulation and In-vitro evaluation of Gemifloxacin Orodispersible Table. International Journal of Pharma Sciences and Research 2015; 6(2): 386-393).
11. Das M.K. Furosamide loaded alginate microsphere prepared by Ionic cross linking technique: morphology and release characteristics. Ind J Pharma Sci 2008; 70: 77-84.
12. Trivedi P, Verma A M. L, Garud N. Preparation and characterization of aceclofenac microspheres. Asian J. Pharm 2008; 110-115.
13. Ashok T, Harish C, Mukesh P, Arvind D, Chatterjee D. Formulation and evaluation of floating microspheres of atenolol, Panacea J Pharmacy and Pharma Sci 2015: 4(3); 654-679.
14. Rajput G, Majmudar F, Patel J, Thakor R, Rajgor NB. Stomach-specific mucoadhesive microsphere as a controlled drug delivery system. Sys Rev Pharm 2010; 1: 36-44.
15. Deveswaran R, Manavalan R, Madhavan V, Bharath S. Formulation and Optimization of Ketoprofen Microspheres using Response Surface Methodology. Int. J. PharmTech. Res 2010; 2(4): 2319-2326.
16. Shanmugarathinam A, Vidhyeswari D, Puratchikody A. Formulation characterization and in-vitro evaluation of acrylic polymer loaded aceclofenac microspheres, Intl J Pharma and Bio Sci 2011; (2): 253-57.
17. Saparia B, Murthy RSR, Solanki A. Preparation and evaluation of chloroquine phosphate microspheres using cross-linked gelatin for long term drug delivery. Indian J Pharm Sci 2002; 64:48–52.
18. El-Gibaly I. Development and *in vitro* evaluation of novel floating chitosan microcapsules for oral use: Comparison with nonfloating chitosan microspheres. Int J Pharm 2002; 249:7–21.
19. Higuchi T. Mechanism of sustained-action medication: theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci 1963; 52:1145–9.
20. Shanmugarathinam A, Vidhyeswari D, Puratchikody A. Formulation characterization and

in-vitro evaluation of acrylic polymer loaded aceclofenac microspheres, Intl J Pharma and Bio Sci 2011; (2): 253-57.