Research Article

Available Online at: www.ijpir.com

International Journal of Pharmacy and Industrial Research

ISSN Print 2231 – 3648
Online 2231 – 3656

Formulation, Development and In vitro Evaluation of Gatiflaxacin In-Situ Gel

Rubina Apsar Shaik*, Dr. Manichandrika, G. Ramya, K.Rishika, S.Shivani, B.Basanthi Soujanya, V.Soumya, K.Sowmya sri

Department of Pharmaceutics, Bojjam Narasimhulu pharmacy college for women Vinaynagar, Saidabad, Hyderabad- 500059

ABSTRACT

Gatiflaxacin is a fluorinated 4-quinolone antibiotic which is used in the treatment of ophthalmic ailments like infections, inflammations, conjunctivitis, blepharitis, iritis, corneal ulcer etc. Commercially, Gatiflaxacin eye drop solution is available and it is quite easy for the administration. However, the product has drawback of poor bioavailability due to several factors such as tear production, nonproductive absorption, transient residence time, and impermeability of corneal epithelium. In order to improve the bioavailability, residence time and longer duration of action, an attempt was made to formulate in-situ ophthalmic gel of Gatiflaxacin. In present study Carbopol 934 and HPMC, HPMC 15K were used as polymers. Carbopol 934 was used as a pH sensitive polymer and HPMC, HPMC 15K was used as mucoadhesive polymer. All prepared formulations were evaluated. The prepared formulations were evaluated for pH, clarity, viscosity, drug content, gel strength, in vitro drug release, and stability.

Keywords: Gemifloxacin, polymers, Gel strength, Bio availability, In vitro-drug release.

INTRODUCTION

Ocular drug delivery systems are developed to treat eye locally, whereas past formulations are targeted to reach systemic circulation and these are designed to overcome all the disadvantages of conventional dosage forms such as ophthalmic solutions[1]. Most drugs for ophthalmic use like pilocarpine, epinephrine, local anaesthetics, atropine, etc. are weak bases which are generally formulated at acidic pH to enhance stability.[2] But due to their highly ionized form, ocular diffusion is poor. This, coupled with tear drainage, further reduces the rate and extent of absorption.[3]Moreover, if the drug has short half-life, the problems become more complicated. Frequent dosing of large doses of such drugs becomes necessary to achieve the therapeutic objective which often results in corresponding increase in local and systemic side effects[4].So, research on Novel ophthalmic drug delivery systems is in progress to overcome all these disadvantages of conventional ophthalmic dosage forms[5]. This medication is a quinolone antibiotic used for eye infections (such as conjunctivitis).This medication treats only bacterial eye infections. It will not work for other typesof eye infections.[6] Unnecessary use or misuse of any antibiotic can lead to its decreased effectiveness.

Rubina Apsar Shaik
Department of Pharmaceutics, Bojjam Narasimhulu pharmacy college for women Vinaynagar, Saidabad, Hyderabad- 500059, India.

MATERIALS AND METHODS

Gatiflaxacin was collected as a gift sample from Hetero labs, Hyderabad and various excipients like HPMCK15M, Carbopol 934, Benzalkonium chloride and HPMC were purchased from AR chemicals, Hyderabad.

Methodology[7,8]

Compatibility studies of drug and polymers:

Drug polymer interactions were studied by FT-IR spectroscopy. One to 2mg of Gatiflaxacin polymer and physical mixtures of samples were weighed and mixed properly with carbopol to a uniform mixture. A small quantity of the powder was compressed into a thin semitransparent pellet by applying pressure. The IR spectrum of the pellet from 400-4000cm[1] was recorded taking air as the reference and compared to study any interference.

Formulation table of in Gatiflaxacin situ gel composition

Table.No:1 Formulation table for all formulations

Ingridient	F1	F2	F3	F4
Gatiflaxacin	5	5	5	5
HPMC	100	200	300	400
Carbopol 934	100	200	300	400
HPMCK15M	100	200	300	400
Benzalkonium chloride	5	5	5	5
Disodium hydrogen Phosphate	500	1500	1500	1500
Citric Acid	200	200	200	200
H_2O	q.s	q.s	q.s	q.s

Evaluation parameters[9,10,11]

Clarity

The formulations were visually checked for the clarity.

pH

pH of each formulation was determined by using Digital pH meter (Digital pH meter 335). This was previously calibrated by pH 4 and pH 7. The pH values were recorded immediately after preparation.

Measurement of the gel strength

A sample of 50 g of the gel was put in a 50 ml graduated cylinder. A weight of 14.33 g was placed on the gel surface. The gel strength, which is an indication for the ophthalmic gel at physiological temperature, was determined by the time in seconds required by the weight to penetrate 5 cm into the gel. All measurements were performed in triplicate (n=3).

Drug Content

The drug content was determined by taking 1 ml of the formulation and diluting it to 100 ml with distilled water. Aliquot of 5 ml was withdrawn and further diluted to 25 ml with distilled water. Gatiflaxacin concentration was determined at 292 nm by using UV-Visible spectrophotometer

In-vitro Drug Release Study by using P^H 6.8

In vitro release study of the formulated ophthalmic in-situ gel was carried out by using diffusion cell through egg membrane as a biological membrane. Diffusion cell with inner diameter 24mm was used for the study. 1 mL formulation was placed in donor compartment and Freshly prepared 100 mL artificial tear fluid (sodium chloride 0.670g, sodium bicarbonate 0.200g, calcium chloride dehydrated 0.008g, potassium chloride 0.248g, distilled water q.s 100mL.) was placed in receptor compartment. Egg membrane was mounted in between donor and receptor compartment. The position of the donor compartment was adjusted so that egg membrane just touches the diffusion medium. The whole assembly was placed on the thermostatically controlled magnetic stirrer. The temperature of the medium was maintained at 37°C ± 0.5°C. 1mL of sample was withdrawn from receiver compartment after 30 min, 1, 2, 3, 4, 5, 6, 7 & 8 hrs and same volume of fresh medium was replaced. The withdrawn samples were diluted to 10mL in a

volumetric flask with distilled water and analyzed by UV spectrophotometer at 292nm.

Stability studies[12]:

For all the pharmaceutical dosage forms it is important to determine the stability of the dosage form. This will include storage at both normal and exaggerated temperature conditions, with the necessary extrapolations to ensure the product will, over its designed shelf life, provide medication for absorption at the same rate as when originally formulated. The design of the formal stability studies for the drug product should be based on the knowledge of the behavior and properties of the drug substance and formal stability studies on the drug substance.

Storage Conditions

- Accelerated: $40\pm2^0C/75\pm5\%$ RH
- Intermediate: $30\pm2^0C/65\pm5\%$ RH
- Long term: $25\pm2^0C/60\pm5\%$ RH

RESULTS AND DISCUSSION

Drug-Excipient compatibility studies

The physicochemical compatibility of the Gemifloxacin drug and excipients was obtained by FTIR studies.

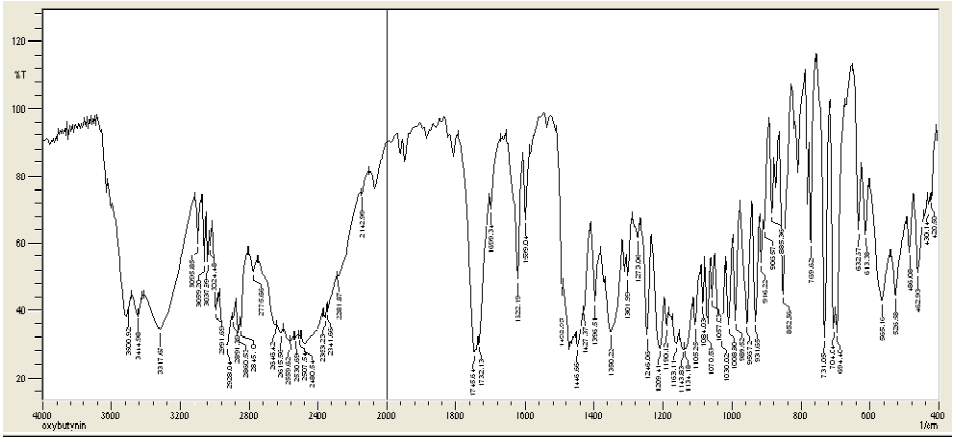

Fig.No:1 FTIR spctra of pure drug of Gatifloxacin

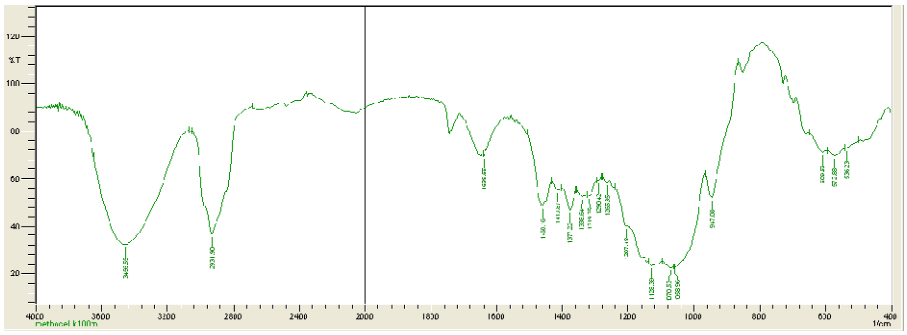

Fig.No:2 FTIR spectra of pure drug with excipients

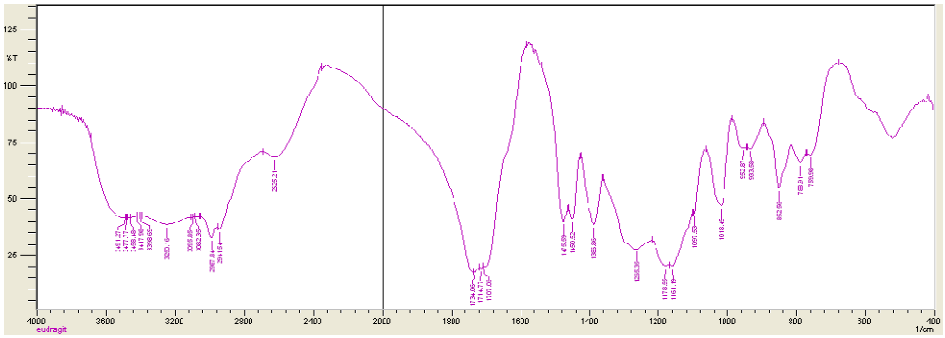

Fig. No: 3 FTIR spectra of pure drug with cellulose acetate phthalate

Evaluation parameters

Clarity test

The formulated all formulation kept under for visual observation. The prepared formulations were found to be free from any suspended particulate matter.

P^H: Table.No:2 Showing results of $_PH$

S.NO:	Formulation code	pH
1	F1	6.50
2	F2	6.53
3	F3	6.56
4	F4	6.54

Discussion

All formulations were performed for pH determination .The all formulations came results within range of pH.(6-7)

Gel strength

Table.No:3 showing results of Gel strength

S .No	Formulation code	Gel strength (SEC)
1	F1	0.65
2	F2	0.70
3	F3	0.80
4	F4	0.90

Discussion

All formulations were performed for gel strength parameter .The formulations results within range of limits(0.5 sec-1min)

Drug content

Table.No:4 Showing results of Drug content

S.No	Formulation code	Drug content
1	F1	89.90
2	F2	90.23
3	F3	96.56
4	F4	94.53

Discussion

All above f1-f4 formulations performed drug content parameter. The high drug content was F3formulation found to be 96.56

In-Vitro dissolution studies

Table.No:5 Showing results of *In-vitro* drug release data

Time in hours	F1	F2	F3	F4
0	0	0	0	0
1	10.5	15.5	29.5	22.56
2	25.2	29.36	55.6	44.62
3	35.3	38.5	60.5	55.83
4	42.6	50.6	72.3	70.26
5	52.2	62.21	87.6	82.87
6	60.5	72.93	92.6	88.38
7	62.16	74.56	94.34	91.26
8	74.5	89.72	99.6	93.71

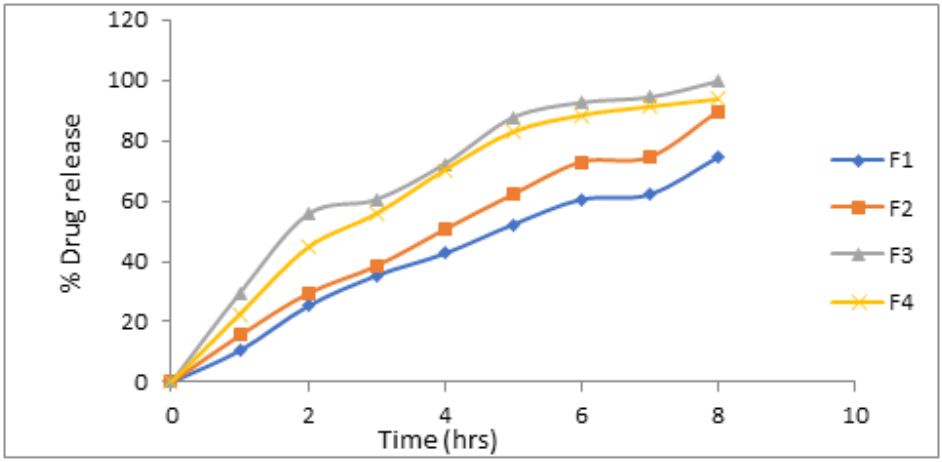

Fig.No:4 All drug release profile data

Discussion

On comparing all formulated drug release profiles the best/optimized formula i.e., F-3 formulation, it was clearly observed that the drug was fit enough with a release of 99.6% within 8 hrs.

a) Stability samples are stored at

- Accelerated: 40±2^{0}C/75±5% RH
- Intermediate: 30±2^{0}C/65±5% RH
- Long term: 25±2^{0}C/60±5% RH

b) Testing Intervals

- Accelerated: Initial, 1month.

Discussion

The optimized formulation kept for under accelerated stability studies (30 days) There is no degradation for 30 days no change in the drug release and drug content parameters.

Table.No.6: Showing results of stability data for optimized formulation (F3)

S.No	Test	Initial	30days
1	Drug release	99.60	99.43
2	Drug content	96.56	96.45

SUMMARY & CONCLUSION

In the present work, formulation and characterization of Gatiflaxacin containing using different polymers. All the formulations were evaluated for drug content, gelling capacity, In vitro dissolution studies. Hence Gatiflaxacin was chosen was as a model drug with an aim to develop a sustained release system for 8 hrs. A Standard concentration of Gatiflaxacin was prepared in 6.8 phosphate buffer and absorbance was measured at 292 nm. Gatiflaxacin showed good linearity between 10-50mcg/ml with coefficient of 0.999.FTIR study of pure Gatiflaxacin and formulation showed that they are in no drug polymer interaction. Various evaluation parameters were studied for the formulation like pH, drug content, gelation temperature, gel strength, in vitro drug release studies.

- Before going to develop the formulation, a detailed product literature review was carried out.
- The pH of the given formulations was found to be within range of limits
- The %drug content values were found to be in the range of 96.56%.
- The Gell strength were found to be in the range of limiting time within 1 min.
- *In-vitro* dissolution studies Gemifloxacin insitu gel of F1-F4 formulations are prepared by incorporating carbaol934, hydroxyl propyl methyl cellulose as polymers in different formulations and Benzalkonium chloride as a preservative in varying concentrations.
- The formulation F3 showing drug release of 99.60 % .

CONCLUSION

F1 to F4 formulations were done by using Carbopol 934, HPMC used as polymers in different formulations. All the formulation is carried out all evaluation tests like drug content, ph determination, gelling strength. The results are found to be within the range of limits. Finally, in this study formulation and characterization of in situ oral gelling system containing Gatiflaxacin. All the physical parameters of the pure drug was calculated and *In-vitro* drug release properties F3 showed almost identical good cumulative drug release profiles.

REFERENCES

1. Peppas N, Langer R. New challenges in biomaterials. Science1994; 263:171520.
2. Zhidong L, Jaiwei L, ShufangN,. Study of an Pharma alginate- HPMC based in situ gelling ophthalmic delivery system for gatifloxacin. Int J., 2006; 315: 12- 7.

3. S. Cohen, E. Lobel, A. Trevgoda, Y. Peled. A novel in situ-forming ophthalmic drug delivery system from alginates undergoing gelation in the eye. J. Control. Release., 1997; 44: 201–208.
4. B. Srividya, R.M. Cardoza, P.D. Amin. Sustained ophthalmic delivery of ofloxacin from a pH triggered in situ gelling system. J. Control Release., 2001; 73: 205–211.
5. Wen-Di Ma, Hui Xu, Chao Wang, Shu-Fang Nie, Wei-San Pan, Pluronic F127-gpoly(acrylic acid) copolymers as in situ gelling vehicle for ophthalmic drug delivery system, int. j. of pharmaceutics, 2008; (350): 247-256
6. Jothi M, Harikumar SL and Geeta Aggarwal, In-situ ophthalmic gels for the treatment of eye diseases, International Journal of Pharmaceutical Sciences and Research, 2012; 3: 1891-1904.
7. Geraghaty P, Attwood D, et al. An investigation of parameters influencing the Bioadhesive properties of Myverol 18-99/ water gels. Biomaterials, 1997; 18: 63-7. 17. Motto F, Gailloud P, et al., In-vitro assessment of new embolic liquids prepared from
8. Podual K, Doyle III FJ, Peppas NA. Dynamic behavior of glucose oxidase-containing microparticles of poly (ethylene)- grafted cationic hydrogels in an environment of changing pH. Biomaterials, 2000; 21: 1439-50.
9. Sawhney AS, Pathak CP, Hubbell JA, Hill JL, Desai NP. Photopolymerizable biodegradable hy). drogels as tissue contacting materials and controlled release carriers.US Patent 5410016. 1995.
10. Qiu Y, Park K, Environment-sensitive hydrogels for drug Delivery. Adv Drug Deliv Rev., 2001; 53: 321-39.
11. Hoffman A.S., Afrassiabi A, Dong L.C. Thermally reversible hydrogels: II. Delivery and selective removal of substances from aqueous solutions. J. Control. Release., 1986; 4: 213–222.
12. Miyazaki S, Hirotatsu A, Kawasaki N, Wataru K, Attwood D. In situ gelling gellan formulations as vehicles for oral drug delivery. J Control Rel 1999;60:287-95
13. Mikkelson TJ. Ophthalmic drug delivery. Pharm Tech 1984;8:90-8.