International Journal for Pharmaceutical Research Scholars (IJPRS)

V-7, I-1, 2018 ISSN: 2277 - 7873

RESEARCH ARTICLE

Design Development and Evaluation of Ocular Gel containing Gatifloxacin to treat Endopthalamitis

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Manuscript No: IJPRS/V7/I1/00016, Received On: 10/03/2018, Accepted On: 20/03/2018

ABSTRACT

Development of ocular drug delivery system has been major challenging and demanding task for delivery of drug into the eye due to its static and dynamic barriers. Therefore rationale drug delivery has to be developed to overcome the drawbacks of established conventional and nonconventional dosage forms. Most of ocular dosage forms are applied topically and there is no need of crossing the ocular barriers in such cases. Therefore significant therapeutic effect is shown by the drug when given by topical route. Endopthalamitis is inflammation of one or more coats of the eye and adjacent cavities and is an uncommon but potentially sight-threatening condition that varies geographically in incidence and in cause. It is the inflammation involving entire eye. There are two types of Endopthalamitis viz. exogenous and endogenous. The causative organisms are *Staphylococcus aureus S. epidermidis* mainly. Drugs are given intravitreally, systemically and topically. Among them the topical gel are intended to increase patient compliance and promptly release the drug for effective and complete eradication of causative microorganisms is possible. Gatifloxacin having bactericidal action against strains of bacteria and but it is given in treatment of endopthalamitis in the form of ophthalmic solution Therefore ophthalmic gel containing drug PF-127 and PEG was developed and evaluated to overcome the drawbacks of ophthalmic solution as a dosage form.

KEYWORDS

Endopthalamitis, Gatifloxacin, Ocular gel, Pluronic F-12

INTRODUCTION

Endopthalamitis, defined as inflammation of one or more coats of the eye and adjacent cavities, is an uncommon potentially sight-threatening condition that varies geographically in incidence and in cause. Endopthalamitis is inflammation involving the entire eye, meaning that both the front and back portions of the eye are affected. Although the inflammation can be due to various causes, it is generally used to describe an extremely severe infection that has spread throughout the whole eyeball. This type of infection is devastating. Successful treatment of microbial endopthalamitis must take into account the unique challenges posed by the delicate anatomy and physiology of ocular tissues. Inflammation-induced opacity of the cornea, anterior chamber, lens, and/or vitreous impedes formation of a clear image on the retina. Gatifloxacin is an antibiotic of the fourth-generation fluoroquinolone family that like other members of that family, inhibits the bacterial enzymes DNA gyrase and topoisomerase IV.

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Gatifloxacin exhibits stronger antimicrobial activity against gram positive bacteria 2 to 16 times even to 32 times than the first generation to the third generation quinolone drugs it has very strong inhibition effect on pathogenic bacteria which have tolerance to aminoglycoside ,macrolide and other antibiotics and does not crossed drug tolerance with these antibiotics the Gatifloxacin has strong activity against Chlamydia ,mycoplasma since the Gatifloxacin introduces methoxyl group to C8 it overcomes the side effects such as photo toxicity thus the Gatifloxacin more stable in chemical structure and safety also increased. Ocular drug delivery has remained as one of the most demanding task for pharmaceutical scientists. The unique structure of the eye does not allow the drug molecules at the required site of action. Conventional drug delivery systems; which include solutions, suspensions, gels, ointments and inserts, suffer with the problems or disadvantages as well as advantages. Disadvantages or limitations include poor drainage of instilled solutions, tear turnover, poor corneal permeability, nasolacrimal drainage systemic absorption and blurred vision.

MATERIAL & METHODS

Gatifloxacin were supplied as gift sample from Indoco Remedies Mumbai, Pluronic F-127 L. R. were supplied from BASF Mumbai

Equipment used in the formulation of ocular gel for endopthalamitis Electronic balance Shimadzu Japan (Model: AUY220), UV-Spectrophotometer Jasco Japan (Model V-530 & V-630), FT-IR Spectrophotometer Shimadzu Japan (Model FTIR-8400S), DSC Mettler Toledo (Star system), USP Dissolution Apparatus Eletrolab Mumbai (Model TDT-06P), Franz diffusion cell Electrolab Mumbai (Model TDT-08L)

Topical application of eye drops is the most common method of administering drugs to the eye in treatment of ocular diseases. Topical ophthalmic application is considered the preferred way to achieve therapeutic levels of drugs used to treat ocular diseases. to develop better dosage form for ocular drug delivery is major challenge for pharmacologists and scientists due to its unique anatomy and physiology of eye such as static barriers including layers of sclera cornea and retina also blood aqueous blood retinal and blood corneal barriers and dynamic barriers (choroidal conjuctival blood flow) lymphatic drainage system pose a significant challenge for delivery of drug alone or in dosage form.

Gatifloxacin is used in the different ocular infections such as bacterial conjunctivitis, keratitis and is drug of choice to treat endopthalamitis. It is used in concentration 0.3 to 0.5 % w/v for ocular use in the solution form. Due to use of solution Less than 5 Percent of the dose is absorbed after topical administration into the eye Gels in the tablet form to which fast erosion of gel containing PF 127 and polyethylene glycol. PF 127 has compatibility with the ophthalmic products as compared to established components of ointment bases. It leads to development of advanced techniques for ocular therapy those include particulate delivery system which improves the pharmacokinetic and pharmacodynamics properties of various types of drug molecules.

UV Spectroscopy[4]

Stock solution 100 µg/ml of drug was prepared in phosphate buffer solution pH 7.4 and UV spectrum of 10 µg/ml solution of Gatifloxacin was taken to determine its absorption maxima

FT-IR Spectroscopy

FT-IR spectrum of Gatifloxacin was recorded as potassium bromide powder bed at resolution of 4 cm-1 for its authentication and to study principle peaks using FT-IR spectrophotometer (FT-IR 8400S,Shimadzu).The identified peaks were compared with the principle peaks of reported IR spectrum and the sample was authenticated

Differential Scanning Calorimetry

The DSC was recorded on a METTLER TOLEDO (Star ^{e} SW 920) Gatifloxacin (1.4mg) was heated in crimped aluminum pan with a pierced lid at a scanning rate of 10^{0}c in an atmosphere of nitrogen flow (40ml/min) using

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the range of 40-300 ^{0}C. The DSC was calibrated for baseline using empty pans and for temperature and enthalpy using indium

Preparation of Calibration Curve of Gatifloxacin in Phosphate buffer pH 7.4 by using UV Spectrophotometer

An accurately weighed quantity (100 mg) of Gatifloxacin was added to 100 ml Phosphate buffer pH 7.4 to make stock solution having strength100µg/ml. From stock solution 10 µg/ml solutions were prepared by diluting 1ml of stock solution 1 to 10 and 100 ml. From the above solutions dilution series of 1, 2, 4, 6, 8, 10, 15 µg/ml were prepared. Determined the absorbance of Gatifloxacin at wavelength 285 nm the calibration curve and absorbance of different concentration of Gatifloxacin

Drug Polymer Compatibility Studies

Compatibility studies were performed in order to confirm the drug-excipients compatibility. It mainly included Fourier-transform infrared (FT-IR) and differential scanning Calorimetry. (DSC)

Fourier Transform Infrared (FT-IR) Spectroscopy Study[3]

FT-IR spectra of pure Gatifloxacin and physical mixtures of drug with excipients Pluronic F-127 and PEG 4000 separately in 1:1 proportion were obtained on spectrophotometer (FT-IR 8400S,Shimadzu).using KBr powder bed. The instrument was operated under dry air purge and scans were collected at scanning speed 2mm/sec with resolution of 4cm^{-1} over the region of 4000-400 cm^{-1}. The scans were evaluated for presence of principle peaks of drug shifting and disappearance of drug peaks and appearance of new peaks due to chemical interaction between drug and excipients.

Differential Scanning Calorimetry (DSC) Study[3]

The DSC study was carried out for pure Gatifloxacin solid excipients and tablet .The DSC patterns were recorded on a METTLER TOLEDO (Star ^{e} SW 920) each sample (2-4mg) was heated in an atmosphere of nitrogen flow (40ml/min) within the range of 40-300 ^{0}C. The DSC was calibrated for baseline using empty pans and for temperature and enthalpy using indium excipients.

Formulation and Development

Preparation of Preliminary Batches

The tablet blend was prepared by accurately weighed powder mass of the drug, Pluronic F-127 and polyethylene glycol were mixed as per required for preparation of the tablet. Firstly this tablet blend was evaluated for the various tablet properties such as bulk density, tapped density etc. Then this prepared tablet blend were compressed under rotary tablet machine for the 100mg tablets were prepared from this powder blend and compressed under 2 ton compression pressure and then this tablets were evaluated for the physical tests of the tablet.

Evaluation of Preliminary Batches

All the preliminary batches were evaluated for tablet properties as tablet was prepared.

Physical Evaluation of Preliminary Batches

Friability of Tablets

Friability is measured of mechanical strength of tablets. Roche friabilator is used to determine the friability by following procedure. A pre weighed (n=10) tablet is placed in the friabilator (LABINDIA, Mumbai, India). Friabilator consist of a plastic chamber that revolves at 25 rpm, dropping the tablets at a distance of 6 inches with each revolution. The tablets are rotated in the friabilator for 4 minutes for 100 revolutions. At the end of test, tablets are reweighed; the loss in the weight of tablet is the measure of friability and is expressed in percentage as; eq^n

$$\text{Friability (\%)} = \frac{\text{Initial weight-Final weight}}{\text{Initial weight}} \times 100 \text{---eq}^n 1$$

Weight Variation of Tablets

According to I.P. procedure for uniformity of weight, twenty tablets are taken and their weight is determined individually and collectively on an electronic weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory

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method of determining the drug content uniformity.

Preparation of Tablet to Gel Form

The gel of above prepared tablets of Gatifloxacin were prepared by the cold method described by[8] was adopted for preparation of PF-127 gel for this the tablet containing Gatifloxacin, polyethylene glycol and PF-127 was placed into the test tube containing 0.5 ml of distilled water and it was well stirred. This solution kept in the refrigerator at 4°C until clear solution was obtained. Then this solution was kept at room temperature and slight increase in temperature until the clear transparent gel was formed.

Design of Factorial Batches

Preparation of Factorial Batches

A 2^2 factorial design was used in order to investigate the joint influence of 2 formulation variables. In this design 2 factors were evaluated each at 2 levels and experimental trials were performed at all four possible combinations. The amount of drug and PEG were selected as independent variables. The in vitro release and gelation was selected as response variables .The experimental variables and their coded levels with actual values.

Table 1: Factorial design for Preparation of Batches

Batches code	Variable level in coded form	
	X_1	X_2
F1	+	+
F2	+	-
F3	-	+
F4	-	-

Table 2: Translation of coded levels

Code	Low (-)	High(+)
X_1 = Amount of PEG	5	10
X_2 = Amount of drug	1.2	3

Table 3: Composition of formulation

Formulation	Drug (mg)	PEG (mg)	PF 127 (mg)	Total weight of tablet (mg)
F1	3	10	87	100
F2	1.2	10	88.8	100
F3	3	5	92	100
F4	1.2	5	93.8	100

All factorial batches having composition this powder blend were evaluated for bulk properties and for physical properties of tablets.

Preparation of Gel

Three tablets from each factorial batch F1 to F4 were placed into separate test tubes containing 0.5 ml phosphate buffer solution. Then each test tube was kept in refrigerator at 4 ^{0}C until clear transparent solution was produced. Then these test tubes were kept at actual room temperature until transparent and easily spreadable gel was formed.

Evaluation of Gel

pH Determination

The pH of each gel was determined using pH meter .the electrode was first calibrated with pH 4.0 and pH 7.0 solutions and then readings were recorded on pH meter

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To Determine Gelation Time

Gelation time is defined as time taken for the transformation of free flowing sol to non-flowing gel at the particular temperature which is 37^0C for this study. It is determined by following method. [8]The solution formed after tablet dissolved in buffer solution in test tube it was kept in refrigerator and temperature maintained was 4^0C. Then this refrigerated solution was kept in water bath by increasing temperature up to 37^0C. Previously refrigerated test tube was immersed in the above water bath and time was noted from the moment of placement in the water bath with the help of stopwatch. The time taken to convert sol into gel, which was said to occur when the meniscus would no longer move upon tilting through 90^0, was taken as gelation time.

To Determine Sol-Gel Transition Temperature

The sol-gel transition temperature is defined as temperature at which the sol is converted to gel which no longer moves upon tilting the test tube. Gelation was accessed using a modification of the Miller and Donavan Technique.[9] A 5ml aliquot of gel was transferred to test tubes immersed in water bath at 4^0C and sealed with aluminum foil. The temperature of water Bath was increased in increment 1^0C per min. The samples were then examined for gelation, which was said to occur when the meniscus would no longer move upon tilting through 90^0 meniscus.

In Vitro Release Study of Gatifloxacin containing Poloxamer Gel by Membrane Less Diffusion Method[10]

The method adopted to carry out in vitro release study as per need. 5 ml of each formulation was placed into 10 ml test tubes the gels were allowed to set in water bath maintained at 37 ^{0}C for 30 min. Dissolution medium (5ml) was carefully placed on the surface of the gel, and the tubes were placed in water bath for the duration of the study At predetermined times of 0, 0.5, 1, 2, 3, 4, 5, 6, 21 and 24 hr. The receptor fluid was removed completely and replaced with fresh receptor fluid (phosphate buffer pH 7.4) the sample solution was diluted and analyzed by UV Spectrophotometer. The in-vitro drug release was studied by using different parameters based on assumption that these conditions affecting release of drug in different conditions such as polymer concentration and PEG concentration.

Regression Analysis

Above formulations as per the levels of the independent factors were prepared and evaluated for the in vitro dispersion time, Polynomial equations for dependent factors have been derived using Design Expert 8.0. To describe the response surface curvature, the design was evaluated by 2FI model, Polynomial equation for full factorial design is,

$$Y=b_o+ b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 +b_{22}X_2^2\text{---------- Eq 2}$$

Where, Y is dependent variable, b_o arithmetic mean response of all batches, and b_1 estimated co-efficient for factor X_1. The main effects (X_1 and $X_{2)}$ represent the average result of changing one factor at a time from its low to high value. The interaction term (X_1X_2) shows how the response changes when 2 factors are simultaneously changed. The polynomial terms X_1^2 and X_2^2 are included to investigate non-linearity

Sterility Test

The sterility test was performed according to Indian pharmacopeia. Direct inoculation method was used; 2 ml liquid from test container was removed with sterile pipette or with a sterile syringe or a needle. The test liquid was aseptically transferred to fluid thioglycolate medium (20ml) and soya bean-casein digest medium (20ml) separately. The liquid was mixed with media. The inoculated media were incubated for not less than 14 days at 30 °C to 35°C in the case of fluid thioglycolate medium and 20°C to 25°C in the case of soya bean-casein digest medium

Stability Study

Stability studies were carried out by storing the optimized formulation at various temperature conditions like was stored at ambient conditions, 30 ± 2° / 65 ± 5% RH and 40 ± 2° /

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75 ± 5% RH for period of three months and the formulations were evaluated for Gelling time, Gelling temperature, pH, in vitro release.

RESULTS AND DISCUSSION

Drug Analysis

Physical Appearance

Physical appearance of Gatifloxacin was examined by various organoleptic properties color pale yellow, crystalline powder odorless

Determination of Melting Point

Capillary fusion method was used to determine the melting point of Gatifloxacin. The melting point was recorded and compared to literature value. Experimental value 182-185°C, Literature value 180-188°C

UV Spectroscopy

The UV spectrum of Gatifloxacin was obtained in phosphate buffer pH 7.4 which shows λ_{max} (absorbance maxima) at wavelength 285 nm which matches reported $\lambda_{max.}$ (USP)

Fourier Transform Infrared Spectroscopy

The observed peaks of procured Gatifloxacin were matching with reported principle peaks thus, Gatifloxacin was pure drug.

Differential Scanning Calorimetry

The thermal analysis indicated that the DSC scan of the drug presented a sharp endothermic peak at 190^{o}C corresponding to its melting transition temperature. The sharp endothermic peak shown indicated that the Gatifloxacin was in pure form. Broad endothermic peak at 80-90^{o}C was due to evaporation of water of crystallization.

Preparation of Calibration curve of Gatifloxacin in Phosphate buffer pH 7.4 by using UV Spectrophotometer

The Calibration curve of Gatifloxacin was prepared in Phosphate buffer 7.4 the absorbance at λ max 285 nm for different concentrations of Gatifloxacin and The regression coefficient was found to be 0.997.

Beer's Lambert's law was obeyed within the concentration range of 0-10 µg/ml the results indicate that there is a linear relationship between concentration and absorbance.

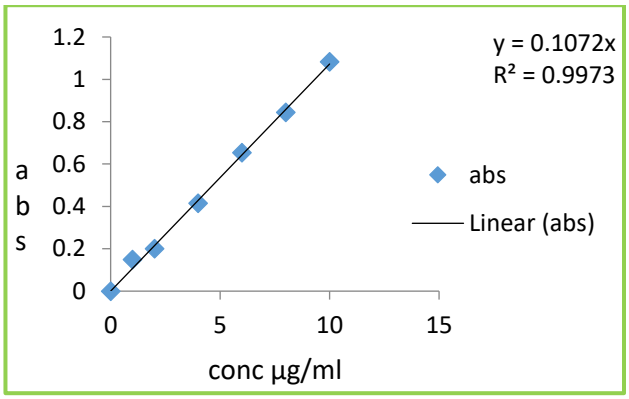

Figure 1: Calibration curve of Gatifloxacin in phosphate buffer 7.4

From the curve it was found that Gatifloxacin obeyed Beer's Lambert's range from 1-10 µg/ml in phosphate buffer 7.4. It shows the linear relationship between concentration and absorbance having correlation coefficient value 0.997.

Drug and Polymer Compatibility Studies

The drug –excipients compatibility studies were performed in order to confirm the compatibility of the drug with the used excipients in the formulation. These studies mainly included FTIR and DSC study.

FT-IR Spectroscopy

IR spectra of Gatifloxacin, Pluronic F-127, and Polyethylene glycol 4000 were recorded.

From the FT IR spectra of Gatifloxacin, physical mixture of drug and excipients it was concluded that there was slight broadening and splitting of O-H and N-H stretching vibrations in physical mixtures of drug with excipients which might be possibly due to interference of moisture. The rest of major peaks were almost identical and unchanged as compared to FTIR spectrum of pure drug, indicated that overall symmetry of the molecule was not significantly affected .Hence there was no chemical interaction between the drug and excipients used for formulation of ocular gel of Gatifloxacin

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Differential Scanning Calorimetry of Excipients Compatibility

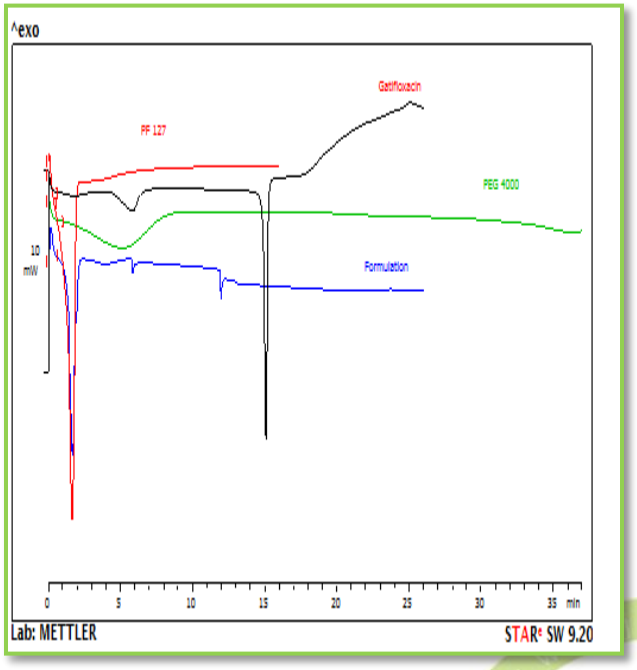

Figure 2: Overlay of DSC of Gatifloxacin, solid excipients and formulation

In the DSC thermo gram of formulation, the disappearance endothermic peak of the drug Gatifloxacin was due to its less proportion as compared to amount of PF 127 or PEG 4000 and its molecular dispersion in the excipients. Endothermic peak at 50°C belonged to PEG 4000 and at 185°C belonged to pure drug which are prominent in their individual DSC spectra.

Absence of any additional endothermic peak suggested compatibility of Gatifloxacin with the excipients selected. Thus from FTIR and DSC studies it was concluded that there was no interaction between the drug and the excipients used in the formulation.

Formulation and Development

Formulation of mini tablets for ophthalmic use was reported in the literature but may suffer the drawback of patient compliance being invasive drug delivery system. Many gelling systems such as sodium alginate, HPMC and their admixtures had been used to prepare in situ gelling system containing Gatifloxacin. In the present work PF 127 was selected as it will be suitable for other drug also as gelling agent to improve patient compliance i.e. the mode of incorporation of the dosage form proposed to be conversion of tablet to gel before its Para ocular administration. Tablets are most popular unit dosage forms that offer the additional advantage of stability of drug besides its other well-known benefits.

Gelling time is the time required to convert tablet into gel which has significance with respect to instructions to be written on the label .Gelling temperature in the present study has relevance with the feasibility of tablet dosage form to gel at room temperature.

The preliminary batches of tablet which are to be converted into gel after addition of water for injection was prepared according to the procedure reported in and composition of formulation from these results it was concluded that powder flow having good flow properties so the powder blend was compressed into tablets.

Tablets are most popular unit dosage forms that offer the additional advantage of stability of drug besides its other well-known benefits. As compared to semisolid dosage forms, stability of drug in solid dosage form is more particularly when drug is protein. In the treatment of endopthalamitis the drug choices are Vancomycin hydrochloride, Amikacin Ceftazidime, Gatifloxacin etc. Though the present work was aimed at developing ophthalmic gel of Gatifloxacin (from tablet) the excipients are critically selected to prepare these tablets. They are selected in such a way that, not only Gatifloxacin but other drugs like Vancomycin hydrochloride can also be incorporated into this dosage form for effective treatment of endopthalamitis.

From the results it was concluded that powder flow was good so the powder blend were compressed under rotary tablet machine for tablets.

Physical tests of factorial batches

All the factorial batches showed results within the range.

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Evaluation of Gel

pH of Formulation

Table 4: pH of the formulation of the factorial after formation of gel

Formulation	pH
F1	6.1
F2	6.4
F3	6.3
F4	6.3

pH of formulation were in range from 6.1-6.4 it is acidic in nature but the marketed preparation of Gatifloxacin having pH 6.0-6.5.

Gelation Time and Gelation Temp

Gelation time is the time required to form gel of liquid which is refrigerated at 4ºC containing PF 127.

Table 5: Gelation time and gelation temperature of formulations

Formulation	Gelation time (Seconds)	Gelation temperature (ºC)
F1	180±0.26	35±0.23
F2	160±0.15	34±0.54
F3	60±0.32	29±0.12
F4	120±0.85	33±0.63

Represents mean ± SD (n=3)

Gelation time is defined as time taken for the transformation of free flowing sol to non-flowing gel at the particular temperature.

The sol-gel transition temperature is defined as temperature at which the sol is converted to gel which no longer moves upon tilting the test tube.

In vitro Release of the Formulation of the Factorial Batches by Membrane Less Diffusion

Table 6: % Drug release of factorial batches

Formulation	Time (min)	% Drug release
F1	5	17.64±0.23
F2	5	76.18±0.12
F3	5	12.96±0.52
F4	5	23.23±0.36

Represents mean ± SD (n=3)

From the result it was concluded that F2 formulation showed 76.18 % release in the 5 min it contains more amount of PEG therefore due to this increased drug release was reported. Thus PEG increases the drug release and F2 selected as optimized formulation.

Regression Analysis

Above formulations as per the levels of the independent factors were prepared and evaluated for the in vitro dispersion time. Polynomial equations for dependent factors have been derived using Design Expert 8.0. To describe the response surface curvature, the design was evaluated by 2FI model, Polynomial equation for full factorial design is

$Y=32.51\pm14.40X_1-17.21X_2-12.06X_1X_2$ eq^n

Negative sign for the co-efficient of the X_1 indicted that the change in the concentration of the PEG decreased the % release of the drug. From the plot it was observed that with the increase in the amount of PEG there was increase in the % release of the drug also when increase amount of drug there was decrease in the % release of the drug.

Sterility Test

In sterility studies, there was no appearance of turbidity or any odd growth of microorganism. Hence no evidence of microbial growth in formulation.

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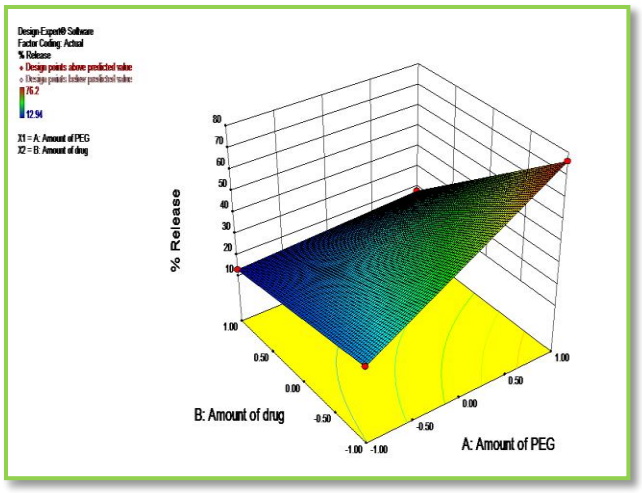

Figure 3: Response surface analysis for percentage release of drug

Stability Studies

For the stability studies different tests were done. In table the results of stability studies are shown. The appearance of the gels remained clear and no significant variation in pH was observed after subjecting the formulations to stability stress.

Table 7: Data showing stability studies of formulation

Sr.no	Temp.	Initial		After 30 days	
		pH	In vitro release	pH	In vitro release
1	30°C	6.4 ± 1.19	76.12 ± 1.35	6.3 ± 1.14	76.13 ± 1.36
2	40°C	6.4 ± 0.25	76.12 ± 0.12	6.3 ± 1.10	76.13 ± 1.23

Sr.no	Temp.	After 60 days		After 90 days	
		pH	In vitro release	pH	In vitro release
1	30°C	6.4 ± 0.23	76.11 ± 1.20	6.3 ± 1.2	76.10 ± 1.02
2	40°C	6.4 ± 0.36	76.12 ± 1.32	6.4 ± 1.36	76.12 ± 1.40

CONCLUSION

Topical formulation of Gatifloxacin was designed and developed with an aim to apply it at Para ocular region.

The excipients selected for this ocular drug delivery system of Gatifloxacin were PF-127, PEG and were found compatible with drug. FT-IR and DSC study of drug excipients compatibility studies showed no interaction between Gatifloxacin and polymers used. PEG was selected because of its capability to alter the properties of self-assembled structures of amphiphilic molecules (e.g. PF127) in solution.

Formulations of mini tablets for ophthalmic use are reported in the literature but may suffer the drawbacks of patient compliance being invasive drug delivery system. The gelling agents such as sodium alginate, HPMC and their admixtures had been used in situ gelling system containing Gatifloxacin. In the present work PF-127 was selected as it will be suitable for other drug also as gelling agent and to improve patient compliance i.e. the mode of incorporation of the dosage form proposed to be conversion of tablet to gel before its Para ocular application.

The powder blends of suitable compositions were prepared and evaluated for bulk density tapped density Carr's index and Hausner ratio. From the results it was concluded that these were considerably good to formulate into tablets.

The gel prepared by dispersing tablet into water for injection was found transparent and spreadable which was good for ophthalmic drug delivery.

A 2^2 factorial design was employed to prepare factorial batches containing two levels of Gatifloxacin and polyethylene glycol as independent variables to optimize the composition of formulation. Factorial batches were evaluated and optimized batch was selected based on the results of evaluation studies.

From the results of evaluation of optimized batch it was concluded that incorporation of PEG increased the drug release and

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spreadability which were in accordance to the purpose of present work.

ACKNOWLEDGEMENT

The authors thank Indoco Pharmaceuticals, Mumbai, for providing Gatifloxacin and BASF for providing Pluronic F-127as gift samples for this work.

REFERENCES

1. Sadaka, A., Durand, M. L., & Gilmore, M. S. (2012). Bacterial endophthalmitis in the age of outpatient intravitreal therapies and cataract surgeries: Host–microbe interactions in intraocular infection. *Progress in retinal and eye research*, *31*(4), 316-331.
2. Safneck, J. R. (2012). Endophthalmitis: a review of recent trends. *Saudi Journal of Ophthalmology*, *26*(2), 181-189.
3. Gonjari, I. D., Karmarkar, A. B., Khade, T. S., Hosmani, A. H., & Navale, R. B. (2010). Use of factorial design in formulation and evaluation of ophthalmic gels of gatifloxacin: Comparison of different mucoadhesive polymers. *Drug Discov Ther*, 4(6), 423-34.
4. Tripathi, K. D. (2013). *Essentials of medical pharmacology*. JP Medical Ltd.
5. Madhuri, D., Chandraekhar, K. B., Somasekhar, G., Harinadhababa, K., Ramkotiah, M., & Dhandapani, B. (2010). Spectrophothometric determination of gatifloxacin through complexation with surfactant. *International Journal of PharmaSciences and Research*, *1*(2), 84-89.
6. IP 2014. Indian pharmacopoeia, published by the Indian Pharmacopeia Commission central Indian Pharmacopeia laboratory Ministry of health and family welfare Government of India, 1, 52-56.
7. Giovagnoli, S., Tsai, T., & DeLuca, P. P. (2010). Formulation and release behavior of doxycycline–alginate hydrogel microparticles embedded into Pluronic F127 thermogels as a potential new vehicle for doxycycline intradermal sustained delivery. *AAPS PharmSciTech*, *11*(1), 212-220.
8. Schmolka, I. R. (1972). Artificial skin I. Preparation and properties of pluronic F-127 gels for treatment of burns. *Journal of Biomedical Materials Research Part A*, *6*(6), 571-582.
9. Ur-Rehman, T., Tavelin, S., & Gröbner, G. (2011). Chitosan in situ gelation for improved drug loading and retention in poloxamer 407 gels. *International Journal of Pharmaceutics*, *409*(1-2), 19-29.
10. Nie, S., Hsiao, W. W., Pan, W., & Yang, Z. (2011). Thermoreversible Pluronic® F127-based hydrogel containing liposomes for the controlled delivery of paclitaxel: in vitro drug release, cell cytotoxicity, and uptake studies. *International Journal of Nanomedicine*, 6, 151.
11. Harpreet Kaur, Sharnjeet loyee, Rajeev Garg 2016 Formulation and Evaluation of In-situ Ocular gel of Gatifloxacin International Journal of Pharma Research and Health Sciences, 4(5) 1365-1370
12. Garcia Sagrado, F., Guzman, M., Molpeceres, J., & Aberturas, M. R. (1994). Pluronic Copolymers-Characteristics, Properties, and Pharmaceutical Applications: Part II. *Pharmaceutical Technology Europe*, *6*, 38-44.
13. Padma, B., Natuva, D. P., Brahmani, S., Subbarao, K., Anil, B., Sunilbabu Koppula, Ch Baburao. (2012). Ocular Drug Delivery System and Developments, *International Journal of Chemical and Analytical Science*, 3(5), 1413-1418
14. Patel, H. A., Patel, J. K., Patel, K. N., & Patel, R. R. (2010). Ophthalmic drug delivery system–a review. *Der Pharmacia Lettre*, *2*(4), 100-115.
15. Järvinen, K., Järvinen, T., & Urtti, A. (1995). Ocular absorption following topical delivery. *Advanced drug delivery reviews*, *16*(1), 3-19.

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16. Agarwal, K. (2011). In-situ gel formation for ocular drug delivery system an overview. *Asian Journal of Biomedical and Pharmaceutical Sciences*, *1*(4).

17. Maheswara Reddy, C., Firoz, S., Rajalakshmi, R., & Ashok Kumar, C. K. (2011). Design and Evaluation of Chloramphenicol Thermoreversible Insitu Gels for Occular Drug Delivery. *International Journal of Innovative Pharmaceutical Research*, *2*(2), 131-138.

18. Escobar-Chávez, J. J., López-Cervantes, M., Naik, A., Kalia, Y., Quintanar-Guerrero, D., & Ganem-Quintanar, A. (2006). Applications of thermo-reversible pluronic F-127 gels in pharmaceutical formulations. *Journal of Pharmacy & Pharmaceutical Sciences*, *9*(3), 339-58.

19. Schmolka, I. R. (1994). Physical basis for poloxamer interactions. *Annals of the New York Academy of Sciences*, *720*(1), 92-97.

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