International Journal of Research in Pharmaceutical sciences and Technology

Formulation and *in-vitro* characterization of erythromycin ocular inserts

M. Samanvitha*[1], Shaik Harun Rasheed[1], S.Y. Manjunath[2]

[1]*Department of Pharmaceutics, Srikrupa institute of Pharmaceutical Sciences, Siddipet- 502277, Telangana, India.*
[2]*Department of Pharmaceutical Chemistry, Srikrupa institute of Pharmaceutical Sciences, Siddipet- 502277, Telangana, India.*

ABSTRACT

Erythromycin has antibacterial activity and especially useful in the treatment of superficial infections involving conjunctivitis and/or cornea caused by organisms. Sustained drug therapies have more advantages than conventional. In the present study, an attempt was made to formulate sustained drug delivery system for Erythromycin in matrix type the formulations for Erythromycin containing 10%, 12%, and 14% w/v of Gelatin & Hydroxy propyl methylcellulose, and 14% , 16%, and 18% w/v for Ethyl cellulose were prepared by solvent casting method and evaluated for their average weight variation, thickness, drug content, in-vitro drug release and stability studies. An increase in average weight and thickness is due to increase in polymer concentration. IR spectrum revealed that there is no incompatibility and no drug-polymer interactions. Gelatin F09, HPMC F15 and EC F21 exhibited maximum average weight 16.66 ± 0.02, 10.81 ± 0.01 & 21.40 ± 0.01 mg respectively and thickness of 0.29 ± 0.01, 0.33± 0.06 and 0.43± 0.02mm respectively. The drug content was found to be 94.48, 92.87 & 90.26% respectively. Formulations containing 16 % and 18% w/v of EC showed sustained and almost complete drug release and dissolved 86.99% and 85.00 % over 14hours period was selected as an ideal formulation. The dissolution data of above formulation were subjected to first order, Higuchi's and peppa's equations. Stability studies conducted for F20 formulation. The formulation showed satisfactory physical stability at 250 C and 400C at 60% and 75% RH respectively. The physical appearance had not changed considerably.

Keywords: Erythromycin; Ethyl Cellulose; Gelatin; Hydroxy Propyl Methyl Cellulose; Opthalmic inserts.

ISSN: 2581-9143
Research Article

Corresponding Author

Name: M. Samanvitha
Email: samanvithamaddi@gmail.com

Article Info

Received on: 22-09-2020
Revised on: 26-10-2020
Accepted on: 01-11-2020

DOI: https://doi.org/10.33974/ijrpst.v2i2.245

INTRODUCTION

Ophthalmic drug delivery is one of the most interesting and challenging endeavors facing the pharmaceutical scientists. The anatomy-physiology and biochemistry of the eye render this organ exquisitely impervious to foreign substances. The challenge to the formulator is to circumvent the protective barriers of the eye without causing permanent tissue damage. The development of newer, more sensitive diagnostic techniques and therapeutic agents renders urgency to the development of maximum successful and advanced ocular drug delivery systems. [1,2,3] The goal of pharmacotherapeutics is the attainment of an effective drug concentration at the intended site of action for a desired period of time. Eye, as a portal for drug delivery is generally used for the local therapy as against systemic therapy in order to avoid the risk of eye damage from high blood concentrations of drug which are not intended for eye.[4,5]

Erythromycin has antibacterial activity and is used in treatment of superficial infections involving conjunctivitis and/or cornea caused by organisms susceptible to Erythromycin. Treatment with conventional drops usually associated extensive drug loss and systemic absorption. This result in poor ocular drug availability and systemic adverse effects, topical administration is preferred over the systemic mode of treating the ocular diseases conditions. [6]

Various drug delivery approaches have been made reported to overcome these limitations of eye drop, in which ocular films are reported to exhibit sustain drug release and improve the corneal residence. In the present study an attempt was made to formulate ocular films of Erythromycin and evaluates their physical properties and in- vitro release profile.

MATERIALS AND METHODS

Erythromycin was obtained as gift sample from FDC Pharmaceuticals Pvt. Ltd., Mumbai. Hydroxy propyl Methyl Cellulose K4M, Gelatin, Ethyl cellulose, Glycerin, Diethyl phthalate, Benzalkonium chloride, Alcohol, Calcium chloride, Potassium dihydrogen phosphate, Sodium Hydroxide were purchased from SD Fine Chemicals, Mumbai.

Preparation of calibration curve for erythromycin

100 mg of Erythromycin was accurately weighed and transferred into a 100ml volumetric flask and dissolved in simulated tear fluid (Sodium Chloride, Sodium Bi-carbonate, Calcium chloride) and made up to volume to 100ml using simulated tear fluid. From the standard stock solution, concentrations of 3, 6, 9, 12 and 15 µg/ml, solutions were prepared. The absorbance of the diluted solutions was measured at 285 nm against simulated tear fluid as blank.

Drug Excipient Interaction Studies

There is always possibility of drug-Excipient interaction in any formulation due to their intimate contact. The technique employed in this study contact. The technique employed this study was IR spectroscopy.

Preparation of ocular insert

Ocular insert of Erythromycin were prepared by using following polymers Gelatin, Hydroxy propyl methyl cellulose, Ethyl cellulose.

Method for preparation of Gelatin films [7]

The required quantity of gelatin and glycerin were weighed and dissolved in water and the mixture was heated at 600C on a water bath until the entire gelatin was dissolved. The weighed amount of Erythromycin (passed through sieve #400) was added and stirred for 6 hours at 400C on magnetic stirrer to get uniform dispersion. After complete mixing the casting solution (15ml) was poured in clean petri dish. The petri dish was cooled at 100C by placing on ice until the films were gelled. The gelled films were taken out from ice and allowed to dry at room temperature for 24 hours. The dried films thus obtained were cut into required size (8mm diameter) by cork borer and stored till used.

Method for preparation of HPMC films [8]

The required quantity of HPMC were weighed and dissolved in distilled water by gentle stirring on Magnetic stirrer. The required amount of Glycerin was added as plasticizer to above solution under stirring condition. Weighed amount of Erythromycin, previously passed through sieve #400, was added and stirred for 6hrs to get clear solution. After complete mixing, the casting solution15 ml was poured in clean anumbra Petri dish of area 63.64sq.cm. Then the Petri dish was dried at room temperature for 24hrs. The dried films thus obtained were cut into size of mm diameter by cork borer, wrapped in aluminum file and stored till used.

Method for preparation of ethyl cellulose films [9]

Preparation of ethyl cellulose films: Accurately weighed quantity of polymer was dissolved in alcohol containing diethylphalate as plasticizer 40 w/w% of polymer. Weigh and transfer required quantity of Ethyl cellulose to this solution and stir for about 2 hours. Allow to stand overnight and then placed under vacuum to remove air bubbles. The polymeric drug solution 15 ml was then poured into relubricated glass mould and allows to get dried at 50˚C for 6 hours in hot air oven. After drying, the films were removed and cut into circular disc of 8 mm diameter.

Evaluation of the prepared formulations [10, 11, 12]

Uniformity of thickness: Five films were taken from each batch and their individual thickness was measured using micrometer screw gauge.

Uniformity of weight: Five films were taken from each batch and their individual weights were determined by using electronic balance.

Uniformity of drug content: Three films were taken from each batch and individually dissolved or crushed in 5 ml of simulated tear fluid in a beaker and filter it into the beaker.0.5 ml of the filtered solution was taken in 20 ml beaker and diluted to 15 ml with simulated tear fluid. Three reading were taken using Shimadzu-160A UV spectrophotometer at 233 nm.

Swelling index: Three films were weighed and placed separately in beakers containing 4ml of distilled water. After a period of 5 minutes, the films were removed and the excess water on their surface was removed using a filter paper and then again weighed till there was no increase in the weight. The swelling index was then calculated by dividing the increase in weight by the original weight and was expressed as percentage.

In-vitro dissolution studies of formulations using the vial method [13]

The in-vitro dissolution of drug from the different ocular inserts was studied using the vial method. Each insert was placed in 10 ml capacity vials containing 5 ml of simulated tear fluid that was previously warmed at 37±1˚C. These vials were placed over hot plate (maintained at room temperature 37±1˚C) that was positioned on a sieve shaker. Shaker was kept at minimum shaking speed to simulated the blinking of eye. Aliquots of 5ml samples at specific interval of time were withdrawn carefully using pipette and equivalent amount of fresh dissolution fluid was replaced. The aliquots withdrawn were suitably diluted with simulated tear fluid and was analyzed at 285 nm using Shimadzu-160A UV Spectrophotometer against blank.

Table 1: Formulation table

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21
	10% w/v			12% w/v			14% w/v			10% w/v		10% w/v		12% w/v		14% w/v		16% w/v		18% w/v	
Drug (mg)	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
Gelatin (gm)	1.5	1.5	1.5	1.8	1.8	1.8	2.1	2.1	2.1	-	-	-	-	-	-	-	-	-	-	-	-
HPMC(gm)	-	-	-	-	-	-	-	-	-	1.5	1.5	1.8	1.8	2.1	2.1	-	-	-	-	-	-
EC (gm)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2.1	2.1	2.4	2.4	2.7	2.7
Glycerin (ml) (40% w/w of polymer)	0.47	-	-	0.57	-	-	0.67	-	-	0.47	-	0.57	-	0.67	-	-	-	-	-	-	-
Glycerin (ml) (50% w/w of polymer)	-	0.59	-	-	7.1	-	-	0.83	-	-	0.59	-	0.7	-	0.83	-	-	-	-	-	-
Glycerin (ml) (60% w/w of polymer)	-	-	0.7	-	-	0.85	-	-	1.0	-	-	-	-			-	-	-	-	-	-
DEP (ml) (40% w/w of polymer)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.75		0.86	-	0.96	-
DEP (ml) (50% w/w of polymer)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.93	-	1.07	-	1.20
Water (ml)	15	15	15	15	15	15	15	15	15	15	15	15	15	15	15	-	-	-	-	-	-
Alcohol (ml)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	15	15	15	15	15	15
Benzyl Alkonium Choloride (ml)	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012	0.0012

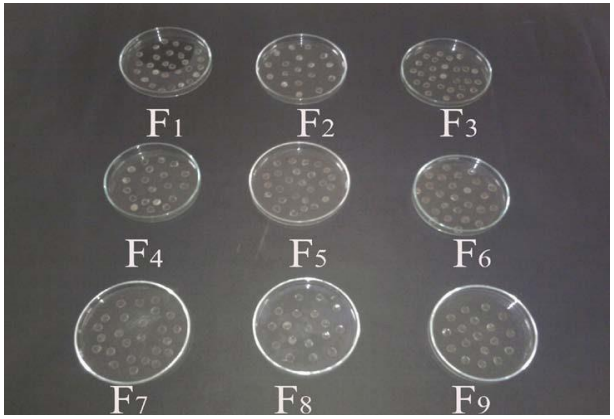

Figure 1: Ocular Inserts of Erythromycin using Gelatin as polymer

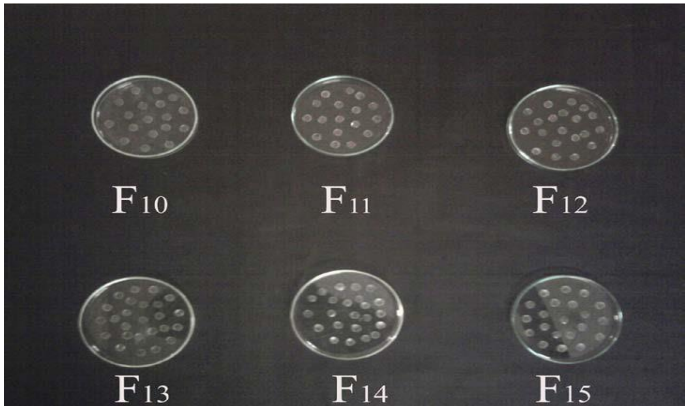

Figure 2: Ocular Inserts of Erythromycin using HPMC as polymer

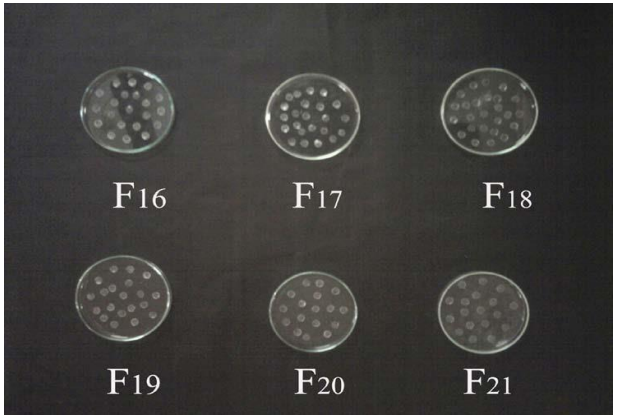

Figure 3: Ocular Inserts of Erythromycin using Ethyl cellulose as polymer

Table 2: Physico-chemical Evaluation of Ocular Inserts

Formulations	Weight in (mg) ± SD	Thickness in (μm) ± SD	Swelling Index (%)	% Drug content
F1	11.1 ± 0.0101	0.19±0.01	1.30 ± 0.0220	98.68 ± 0.03
F2	17.4 ± 0.0121	0.26±0.01	1.85 ± 0.0103	95.33 ± 0.07
F3	12.8 ± 0.0113	0.22 ± 0.07	1.98 ± 0.0111	99.00 ± 0.05
F4	13.2 ± 0.0134	0.27 ± 0.05	2.14 ± 0.0114	98.30 ± 0.05
F5	14.76 ± 0.0212	0.28±0.05	2.18 ± 0.0124	99.41 ± 0.02
F6	18.33 ± 0.0100	0.30 ± 0.03	2.29 ± 0.0231	97.74 ± 0.04
F7	20.66 ± 0.0242	0.31 ± 0.03	2.40 ± 0.0241	93.49 ± 0.05
F8	16.73 ± 0.0112	0.28 ± 0.02	2.83 ± 0.0101	98.55 ± 0.03
F9	16.66 ± 0.0212	0.29 ± 0.01	2.86 ± 0.0114	94.48 ± 0.02
F10	10.8 ± 0.0210	0.25 ± 0.07	1.35 ± 0.0112	99.38 ± 0.21
F11	11.37± 0.0211	0.30 ± 0.04	1.42 ± 0.0224	93.40 ± 0.09
F12	18.53 ± 0.0118	0.29 ±0.02	1.96 ± 0.0218	91.76 ± 0.01
F13	14.59 ± 0.0134	0.31 ± 0.04	2.28 ± 0.0113	93.66 ± 0.02
F14	12.21± 0.0123	0.34 ±0.05	2.32 ± 0.0213	99.79 ±0.01
F15	10.81± 0.0121	0.33 ± 0.06	2.36 ± 0.0311	92.87 ± 0.09
F16	16.52± 0.0102	0.30 ± 0.02	1.37 ± 1.0101	98 ± 0.02
F17	19.31 ± 0.0211	0.38 ± 0.04	1.29 ± 1.0112	98.18 ± 0.01
F18	22.66 ± 0.0211	0.44 ± 0.02	1.22 ± 0.0215	91.32 ± 0.03
F19	20.76 ± 0.0202	0.39 ± 0.01	1.19 ± 0.0312	94.84 ± 0.07
F20	22.66 ± 0.0021	0.43 ± 0.04	1.16 ± 0.0101	96.60 ± 0.07
F21	18.4 ± 0.0031	0.43± 0.02	1.06 ± 0.0108	90.26 ± 0.03

Table 3: In vitro drug release for F1- F9 formulations in Simulated tear fluid

Time (min)	Formulations								
	F1	**F02**	**F03**	**F04**	**F05**	**F06**	**F07**	**F08**	**F09**
30	61.353	64.397	68.193	56.919	59.855	64.799	56.465	58.301	63.242
60	69.409	70.902	77.260	66.599	70.825	76.189	64.890	69.186	73.332
120	96.163	97.127	98.984	95.188	96.259	97.734	91.778	94.009	96.172
180	-	-	-	-	-	-	-	97.796	99.232

Table 4: In-vitro drug release for F10- F21 formulations in simulated tear fluid

Time	Formulations											
(min)	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**	**F16**	**F17**	**F18**	**F19**	**F20**	**F21**
30	54.279	56.111	54.177	55.695	52.111	55.053	24.427	23.720	22.263	21.893	21.958	20.365
60	64.334	68.584	63.279	67.308	63.030	65.725	31.780	28.905	31.807	31.425	29.343	28.901
120	77.902	86.279	69.841	77.167	69.334	76.420	36.122	34.824	35.957	33.137	34.653	33.115
180	91.001	96.129	88.102	90.007	86.875	88.113	37.413	34.976	36.309	34.098	35.402	34.895
240	-	-	96.068	98.325	95.45	97.874	38.950	38.137	39.947	38.354	38.086	37.552
300	-	-	-	-	-	-	41.687	41.016	39.982	38.837	37.926	37.536
360	-	-	-	-	-	-	44.079	43.216	43.783	41.056	42.357	40.662
420	-	-	-	-	-	-	52.113	49.037	51.092	49.235	50.137	49.342
480	-	-	-	-	-	-	61.252	58.124	59.146	59.002	58.053	57.900
540	-	-	-	-	-	-	68.324	63.891	64.024	62.986	62.837	59.496
600	-	-	-	-	-	-	74.903	71.012	73.896	69.670	71.198	67.794
660	-	-	-	-	-	-	81.106	78.982	78.001	76.159	76.854	75.164
720	-	-	-	-	-	-	86.996	83.581	85.785	82.026	84.920	82.111
780	-	-	-	-	-	-	-	-	86.142	85.881	85.721	84.341
840	-	-	--	-	-	-	-	-	88.969	86.432	86.005	85.002

Table 5: Stability studies For F18

	Stored at 25 ^{0}C/ 60 % RH		Stored 40^0 C / 75 % RH	
Time in weeks	**Physical appearance**	**% Drug content**	**Physical appearance**	**% Drug content**
0	+++	95.14	+++	97.12
2	+++	96.54	+++	94.26
4	+++	99.78	+++	96.48
6	+++	98.20	++	95.28
8	++	96.47	++	94.91

Stability Studies: As per ICH guidelines the selected formulations were stored at 25^{0}C/60%RH and 40^{0}C/75/RH for 2 months and evaluated for their physical appearance and drug content at specific period.

Table 6: Calibration Curve Data of Erythromycin in Simulated tear fluid

S.No	Conc.(µg/l)	Absorbance
1	0	0
2	3	0.023
3	6	0.045
4	9	0.065
5	12	0.085
6	15	0.103

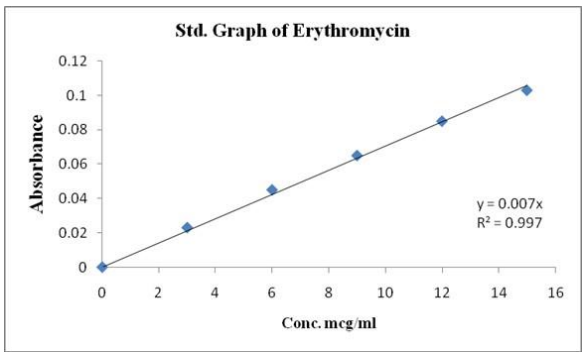

Figure 4: Calibration Curve of Erythromycin in Simulated tear fluid

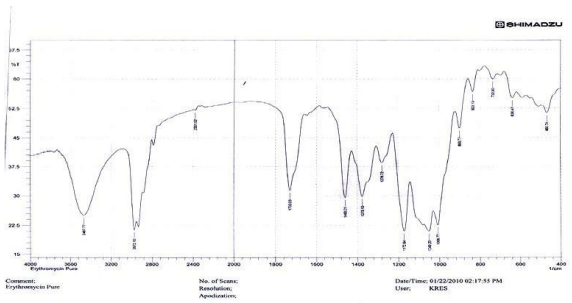

Figure 5: FT-IR of Erythromycin pure drug

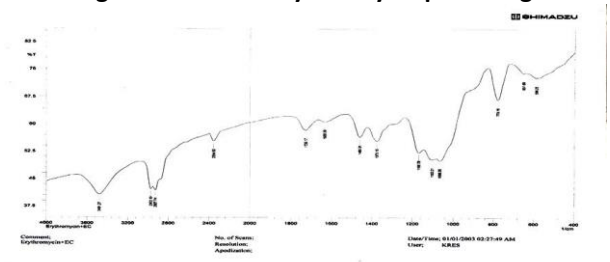

Figure 6: FT-IR Study for Erythromycin+ EC

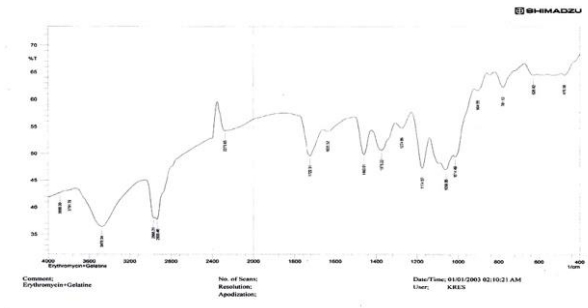

Figure 7: FT-IR Study for Erythromycin+ Gelatin

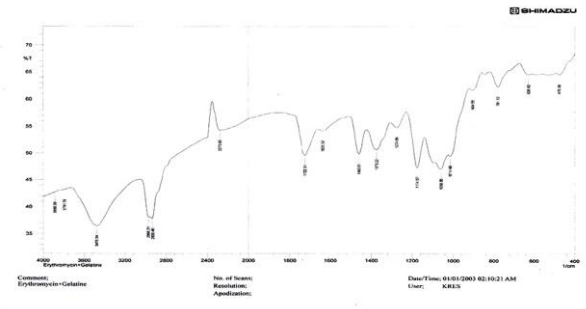

Figure 8: FT-IR Study for Erythromycin+ HPMCK4M

RESULTS AND DISCUSSION

Characteristic absorption bands of Erythromycin seen in the IR spectra of pure drug were also seen in the IR spectra of prepared formulations, indicating that there was no interaction between drug and formulation components. The thickness of the formulations determined by micrometer screw gauge varied between 0.19±0.01 to 0.440±0.02 mm showed that the thickness was uniform and the formulation did not produce any irritation when placed in the cul de sac since they were not thick enough to produce irritation. Uniformity of weight determined by electronic balance results showed that the weights of formulation were between 11.10±0.01 to 22.66± 0.02mg.

The drug content of the formulations was determined and results showed that the drug content in all formulation was found to contain 90.26±0.03 % to 99.79±0.01 % of Erythromycin. The swelling index of formulations was between 1.30±0.02 to 2.86±0.01 and showed that there was no much variation in the water absorption properties of formulation. In vitro dissolution studies were carried out using procedure as mentioned in section IV methods, the release profile of the formulation is shown in the table 3 & 4.

The release of the drug from formulations F1, F2, F3 containing 10% Gelatin was found to be 96.16%, 97.12% & 98.98% at the end of 2nd hr respectively, the release of the drug from formulation F4, F5 & F6 containing 12% Gelatin was found to be 95.18%, 96.25% & 97.73% at the end of 2nd hr respectively. The release of the drug from the formulations F7, F8, F9 containing 14% Gelatin was found to be 91.77%, 97.79% & 99.23 % at the end of 3rd hr respectively. The release of the drug from the formulations F10 & F11containing 10% of HPMC K4M was found to be 91.00% & 96.12% at the end of 3rd hr respectively. The release of the drug from the formulations F12 & F13containing 12% HPMC K4M was found to be 96.06% & 98.32% at the end of 4th hr respectively. The release of the drug from the formulations F14 & F15 containing 14 % HPMC K4M was found to be 95.45% & 97.87% at the end of 4th hr respectively.

Similarly, The release of the drug from the formulations F16 & F17 containing 14% EC was found to be 86.99% & 83.58% at the end of 12th hr respectively. The release of the drug from the

formulations F18 & F19 containing 16 % EC was found to be 85.78% & 82.02% at the end of 12th hr respectively. The release of the drug from the formulations F20 & F21 containing 18% EC was found to be 84.92% & 82.11 at the end of 12th hr respectively.

From the dissolution studies it is concluded that as the concentration of gelatin increases, drug release from the formulation decreases. The formulation with gelatin as polymer showed complete release of drug in 2 to 3hrs. As the concentration of glycerin in formulation is increased drug release was increased, which could be attributed to its high rate and extent of swelling. This finding was also supported by results of swelling studies where the highest swelling index was exhibited by the formulation containing highest concentration of glycerin, indicating that increase in water soluble plasticizer (glycerin) content results in faster swelling and release from ocular inserts.

As the concentration of HPMC increases, drug release from the formulation decreases. The formulation with HPMC as polymer showed complete release of drug in 3 to 4hrs. As the concentration of glycerin in formulation is increased drug release was increased, which could be attributed to its high rate and extent of swelling. This finding was also supported by results of swelling studies where the highest swelling index was exhibited by the formulation containing highest concentration of glycerin, indicating that increase in water soluble plasticizer (glycerin) content results in faster swelling and release from ocuserts.

As the concentration of EC increases, drug release from the formulation decreases. The finding was also supported by the result of swelling studies where the lowest swelling index was exhibited by the formulation containing highest concentration of ethyl cellulose; this is due to the hydrophobic nature of ethyl cellulose.

The release data were also subjected to model fitting analysis to know the mechanism of drug release from the formulation by treating the data according to zero, first order, Higuchi's and peppa's equation. The results are shown in the table.24 & 25. The linearity and slope indicate that the release of drug from the films have followed First order model and non fickian nature. The Higuchi plots reveled that the release of drug to be by diffusion controlled mechanism.

From the above discussions it can be concluded that formulation containing EC 14, 16 and 18 % w/v i.e, F16, F18 and F20 has achieved the objectives of increased contact time, prolonged release, and decreased frequency of administration and thus may improve the patient compliance.

CONCLUSION

In the Present research work Erythromycin ocular inserts were prepared using Gelatin, HPMC & EC as base polymer by solvent casting technique. FT-IR spectral analysis showed that characteristic peak of Erythromycin pure drug was retained in the spectra of all the formulations, indicating the intactness of the drug in all the formulations. The prepared ocular insert were evaluated for number of parameters like physical appearance, surface texture, weight uniformity, thickness of ocular insert, swelling index, drug excipient interaction studies, drug uniformity and in vitro drug release. All the prepared ocular insert were of smooth surface and elegant texture. All the prepared ocular insert of Gelatin, HPMC & EC in different concentrations (10, 12, 14, 16 and 18%w/v). The prepared ocular insert were checked visually for its appearance & surface texture. All the prepared patches were of smooth surface & elegant texture. The weights of the ocular insert were in the range of 11.10 ± 0.0101 and 22.60 ±0.0242mg. The thickness of the ocular insert was in the range of 0.19±0.01to 0.44 ± 0.02 mm. Drug content uniformity study showed uniform dispersion of the drug throughout the formulation in the range of 91.32 ± 0.03 to 99.79 ± 0.01%. In vitro drug release studies showed that more than 86% of the drug was released at the end of 12th hrs from EC formulations. The formulations were also subjected to model fitting analysis to know the mechanism of drug release from the formulations by treating the data according to zero, first – order, Higuchi and peppa's equations. The data clearly shows that, all the formulations followed first order and the mechanism of drug release from all batches followed non-fickian diffusion Based on results obtained the formulation F18 has shown the best drug release was tested for stability studies 8 weeks at storage condition of 250 C and 400C at 60% and 75% RH and results reveal that the physical appearance had not changed considerably.

REFERENCES

1. Ammar, H. O., Salama, H. A., Ghorab, M., & Mahmoud, A. A. (2010). Development of dorzolamide hydrochloride in situ gel nanoemulsion for ocular delivery. Drug development and industrial pharmacy, 36(11), 1330-1339.
2. Chrai, S. S., Makoid, M. C., Eriksen, S. P., & Robinson, J. R. (1974). Drop size and initial dosing frequency problems of topically applied ophthalmic drugs. Journal of pharmaceutical sciences, 63(3), 333-338.
3. Robinson JC. (1993), Ophthalmic drug delivery systems. Vol-58 New York; Marcel dekker:29.
4. Hung, O. R., Whynot, S. C., Varvel, J. R., Shafer, S. L., & Mezei, M. (1995). Pharmacokinetics of inhaled liposome-encapsulated fentanyl. Anesthesiology: The Journal of the American Society of Anesthesiologists, 83(2), 277-284.
5. Pal Kaur, I., & Kanwar, M. (2002). Ocular preparations: the formulation approach. Drug development and industrial pharmacy, 28(5), 473-493.

6. Goodman, L. S. (1996). Goodman and Gilman's the pharmacological basis of therapeutics (Vol. 1549). New York: McGraw-Hill.

7. Mundada, A. S., & Shrikhande, B. K. (2006). Design and evaluation of soluble ocular drug insert for controlled release of ciprofloxacin hydrochloride. Drug development and industrial pharmacy, 32(4), 443-448.

8. Jayaprakash, S., Dachinamoorthi, D., Ramkanth, S., Nagarajan, M., & Sangeetha, K. (2006). Formulation and evaluation of Gentamicin sulphate ocuserts. The Pharma Review, 131-34.

9. Kamath, U. R., Singh, U. V., & Udupa, N. (1993). Evaluation of ciprofloxacin hydrochloride ocular preparations. Indian Journal of Pharmaceutical Sciences, 55(4), 148-150.

10. Allen, D. J., DeMarco, J. D., & Kwana, K. C. (1972). Free films I: Apparatus and preliminary evaluation. Journal of pharmaceutical sciences, 61(1), 106-110.

11. Banker, G. S., Gore, A. Y., & Swarbrick, J. (1966). Water vapour transmission properties of free polymer films. Journal of Pharmacy and Pharmacology, 18(7), 457-466.

12. Knaig JL, Goodmann H. J Pharma Sci. 1962;5:77

13. Manvi, F. V., Patil, M. B., Mastiholimath, V. S., & Rathod, R. (2004). Development and evaluation of ocular films of cromolyn sodium. Indian journal of pharmaceutical sciences, 66(3), 309.