Research Article

Design and Characterisation of Chloramphenicol Ocular Insert for Ocular Drug Delivery

***Priyanka Khokhar**

Department of Pharmacy, IIMT College of Medical Sciences, 250001, Incholi, Meerut, Uttar Pradesh, India.

ABSTRACT

The purpose of the present work was to develop an ophthalmic drug delivery system using different gelling agents with different mechanisms for ocular inserts of Chloramphenicol, an antibiotic drug. PVA a backing membrane and gelling agent Methyl cellulose were employed for the formation of ocular inserts along with HPMC as a hydrophilic agent. The formulations F1 to F4 and F5 to F8 were evaluated for Uniformity of thickness, Uniformity of weight, Surface pH, drug content, *In vitro* drug release, and Sterility test. The results were found to be satisfactory in terms of surface pH, weight variation, and drug content. The IR study shows polymers compatible with the drug. The *in-vitro* percent cumulative drug release (%CDR) in 10 hours study was 99.97%, 101.9%, 100.45% and 100.2% for formulations F1, F2 , F3 and F4 and was 103.5%, 103.16% ,99.99 %and 105.9% for F5, F6 and F7, F8 formulations respectively. Among these the F3 and F7 formulations showed maximum sustaining effect. Percent drug content of 98.7% and 97.3% was found maximum in the F3 and F8 formulation.

Keywords: Ocular inserts for ophthalmic systems, chloramphenicol, polyvinyl alcohol, methyl cellulose, HPMC

Received 20 Dec 2014 Received in revised form 04 Jan 2015 Accepted 06 Jan 2015

***Address for correspondence:**
Priyanka Khokhar,
Department of Pharmacy, IIMT College of Medical Sciences, 250001, Incholi, Meerut, Uttar Pradesh, India.
E-mail: monikameerut@gmail.com

INTRODUCTION [1]

The eye is a unique organ from anatomical and physiological point of view, in that it contains several highly different structures with specific physiologic function. For instance, the cornea and the crystalline lens are the only tissues in the body in addition to cartilage which have no blood supply, whereas choroid and ciliary processes are highly vascularized and exhibit very high blood flows. The retina with the optic nerve, an extension of the diencephalon of the central nervous system, has a very specific function in the visual perception and transduction phenomena. The eye has special attributes that allow local drug delivery and non- invasive clinical assessment of disease, but it is also a highly complex and unique organ, which makes understanding disease pathogenesis and ocular drug delivery challenging. The specific aim of designing a therapeutic system is to achieve the optimal concentration of a drug entity at the active site for the appropriate duration. Ocular disposition and elimination of a therapeutic agent is dependent upon its physicochemical properties as well as the relevant ocular anatomy and physiology. Ophthalmic inserts offer several advantages like increased ocular residence, accurate dosing, possibility of releasing drugs at a slow, constant rate [2,3].

In the present study, an attempt was made to design and characterize ocular inserts of Chloramphenicol for ocular drug delivery system. Opthalmic ocular inserts of Chloramphenicol was successfully formulated by using different backing membrane and gelling agents viz. poly vinyl alcohol and methyl cellulose with combination of viscosity modifying agent like HPMC. The prepared formulations showed sustained release of drug and improve the bioavailability of Chloramphenicol by increasing the precorneal residence time of formulation. The aim of the present work was to formulate and evaluate the ocular

inserts of ophthalmic drug delivery system of Chloramphenicol is to overcome the disadvantages associated with conventional ophthalmic dosage forms (eye drops and suspensions), to achieve long duration of action and to improve ocular bioavailability.

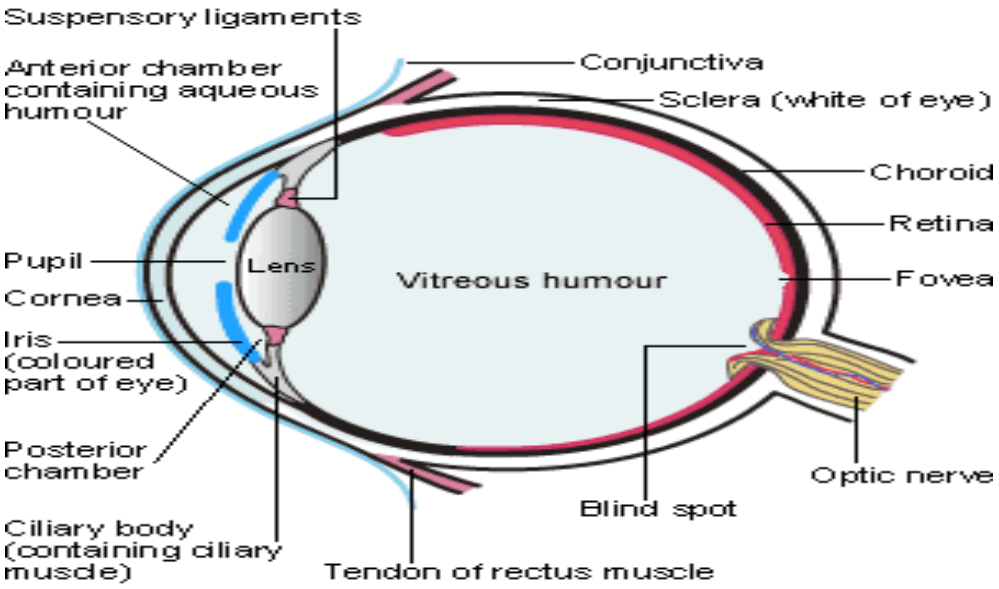

Figure 1: Structure of an eye ball

MATERIAL AND METHODS

Material

Chloramphenicol (Pure drug) was obtained from Taj Pharmaceuticals Ltd. Mumbai, India as a gift sample. Polymers such as HPMC, MC and PVA were obtained from R.K Enterprises Chemicals, U.P, and India as gift samples.

Preparation of Ocular film [4]

The various ocular inserts were being prepared by solvent casting technique under aseptic condition. The calculated amount of powdered polymers was dispersed in cold water with stirring and the prepared dispersion was then left in a refrigerator overnight. The clear solution was obtained gelled at room temperature. The calculated amount of drug was then mixed with 5 drops of glycerol in a small beaker. The final formulation contained with equal amount of polymers and drug. The gel mass was then transferred to a Petri dish, and then allowed to dry in an oven maintained at 50 **°c** until a constant weight was reached. A flexible film was obtained. The dried film was then cut into circular inserts (1.2 cm) using a cork borer. The amount of polymers and drug shows in (**Table 1**).

Table 1: Formulation table of chloramphenicol ocular inserts

Ingredients (W/W)%	F1	F2	F3	F4	F5	F6	F7	F8
Chloramphenicol	40	40	40	40	40	40	40	40
Polyvinyl-alcohol	20	20	20	35	25	5	35	25
Methyl cellulose	25	10	20	20	20	20	5	15
Hydroxy propyl methyl cellulose	10	25	20	5	15	35	20	20
Glycerol	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Water (Q.S)	20	20	20	20	20	20	20	20

Evaluation of prepared ophthalmic film

Drug-excipient interaction studies [5]

Drug- excipient interaction studies were carried out by infrared spectroscopy and ultraviolet visible spectroscopy. The FT-IR spectrum of pure drug and Physical mixture of pure drug and polymers were analyzed to check the incompatibility between the pure

drug and polymers using JASCO FTIR-4100 by potassium bromide method.

Physicochemical evaluations

The ophthalmic film of Chloramphenicol were evaluated for physico-chemical characteristics such as thickness, weight variations, percentage moisture absorption, percentage moisture loss, surface pH and drug contents. The ophthalmic films were evaluated for film thickness by optical microscopy technique. The ophthalmic films were kept vertically standing and thickness measured using the eye piece micrometer. The film thickness was measured at three different points along the film in triplicate and the mean thickness values were calculated· [5]. Determination of average weight and weight variation was carried out by individually weighing 10 films in an electronic balance [6]. For percentage moisture absorption test ophthalmic films were weighed and placed in a desiccator containing 100 ml of saturated solution of Sodium chloride. After three days the ophthalmic inserts were taken out and reweighed, the percentage moisture absorption was calculated [7]. For determination of percentage moisture loss ophthalmic films were weighed and kept in a desiccator containing Anhydrous calcium chloride [8]. After three days the ophthalmic inserts were taken out and reweighed, the percentage moisture loss was calculated. The surface pH of ophthalmic film was determined by allowing them to swell in a closed petridish at room temperature for 30 minutes in 0.1 ml double distilled water. The swollen devices were removed and placed on pH paper to determine the surface pH. After 60 seconds the colour developed was compared with the standard colour scale [9]. For determination of drug content the ophthalmic film was transferred into a graduated glass stopper flask which contained 10 ml of phosphate buffer pH 7.4. It was closed and shaken vigorously. The solution was then filtered. 1ml of filtrate solution was taken and diluted to 5ml with phosphate buffer pH 7.4 and solution was analyzed by using UV spectrophotometer at 254 nm. The procedure was repeated for three times and average of three ophthalmic inserts was calculated [9].

***In vitro* diffusion study** [10]

In vitro diffusion of the drug from different ocular inserts was studied using K-C diffusion cell. In the donor compartment of the cell ocular insert was placed and in receptor compartment isotonic buffer (pH 7.4) is placed. Egg membrane (semi permeable membrane) was placed between both the compartments. The surface of the membrane was in contact with media in receptor compartment. The media in receptor compartment is stirred continuously using a magnetic stirrer and temperature was maintained 37±0.5ºC. At definite time intervals, 1ml of aliquot of solution was withdrawn from receptor compartment and replaced with fresh buffer solution. The aliquots were analyzed spectrophotometrically at 276 nm.

Sterility testing [11]

The sterility testing of formulated films were done according to I. P. Direct inoculation method as described in Indian Pharmacopoeia. Ideal batches of film were used for sterility testing. All the samples were inoculated separately in to ATGM and SBCD media and incubated at 35ºC and 20-25ºC, respectively for 7 days. Similarly unsterilized samples of films were also inoculated separately in to ATGM and SBCD media and incubated at 35ºC and 20-25ºC, respectively for 7 days. A control evaluation was also carried out.

***In vitro* drug release pattern studies** [12]

In order to study the, effect of different concentration and nature of polymers in mechanism of drug release, the obtained in vitro release data was fitted into the Zero order plot, First order plot and Higuchi diffusion models to find the mechanism of release.

RESULTS AND DISCUSSION

The ophthalmic film of Chloramphenicol were prepared by solvent casting technique under aseptic condition and characterized on the basis of interaction studies, physico-chemical characteristics, sterility testing, *in vitro* release study, and *in vitro* drug release pattern studies.

During drug interaction FTIR studies, the spectra recorded were taken as qualitative in order to assess the changes in peak, pattern of peaks etc. No major differences were observed in IR spectra of pure drug and in

physical mixture of drug and polymers. The IR spectral analysis of physical mixture of drug plus polymer showed that all peaks of Chloramphenicol was remaining same as that of pure drug indicating that there was no interaction between drug and polymer.

The physicochemical characteristics of different formulations are shown in (**Table 2**). The ophthalmic films of Chloramphenicol were found to be elastic and flexible. The results indicated that the films shows uniformity of weight and no significant weight variation was observed within the formulations. The minimum standard deviation values revealed that the process is reproducible and capable for giving films of uniform magnitude.

Table 2: Physiochemical evaluation parameters of different formulations

Formulation codes	Uniformity of thickness (mm)	Uniformity of weight (gms)	% Moisture absorption	% Moisture loss	Surface pH	Drug content (%)
F1	0.11±0.005	0.018±0.003	20.13±0.07	10.52±0.38	6.0±0.02	96.86±0.015
F2	0.21±0.001	0.016±0.002	11.1±0.16	12.5±0.60	6.2±0.11	95.9±0.061
F3	0.11±0.002	0.012±0.002	07.9±0.30	16.66±0.31	6.3±0.05	98.7±0.042
F4	0.1±0.001	0.021±0.002	05.5±0.10	15±0.30	6.5±0.11	93.86±0.016
F5	0.21±0.001	0.013±0.005	09.1±0.17	15.4±0.41	6.6±0.01	94.73±0.051
F6	0.35±0.005	0.014±0.006	36.3±0.23	22.2±0.84	6.5±0.02	96.6±0.093
F7	0.13±0.010	0.012±0.001	18.1±0.21	8.33±0.06	6.4±0.02	97.3±0.021
F8	0.31±0.004	0.015±0.002	13.3±0.12	11.1±0.05	6.9±0.01	95.5±0.041

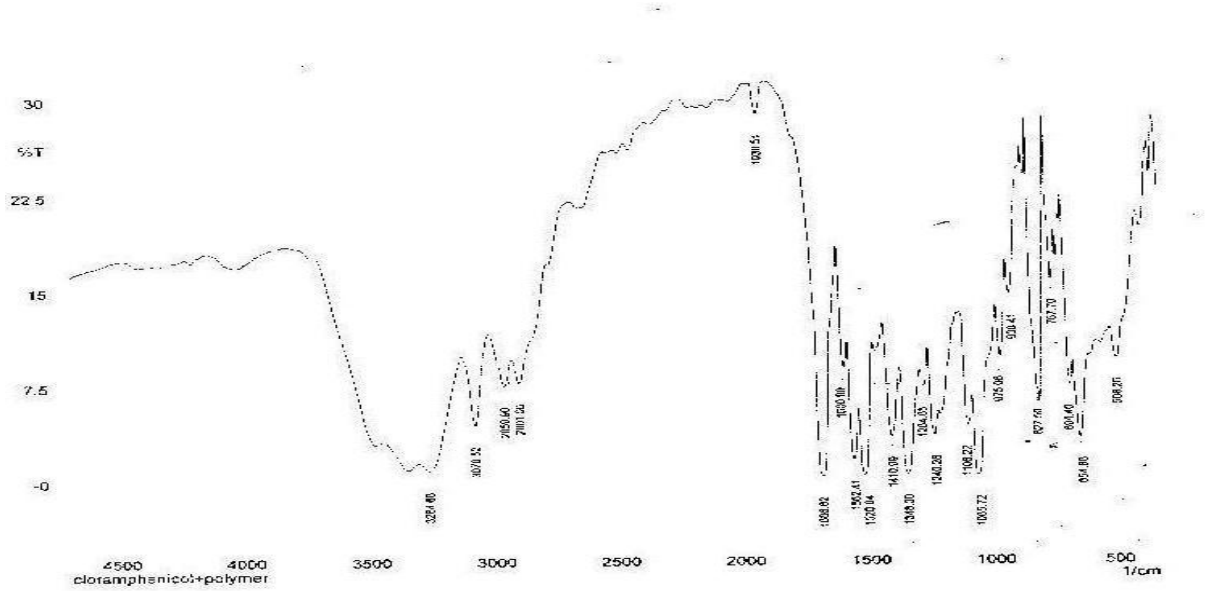

Figure 2: FTIR Spectrum of pure Chloramphenicol with combination of polymers (HPMC, MC, and PVA)

During the % moisture absorption study the results revealed that the moisture absorption is more in films having the high amount of hydrophilic polymer F6 like HPMC while low in films F4 having the less amount of hydrophilic Polymer.

During % moisture loss study the results revealed that the moisture loss was highest in films F6 due to maximum amt. of hydrophilic polymer while lowest in films F7 having low concentration of hydrophilic polymer. It is confirmed that the presence of plasticizers in the form of Glycerol imparts flexibility to the polymers.

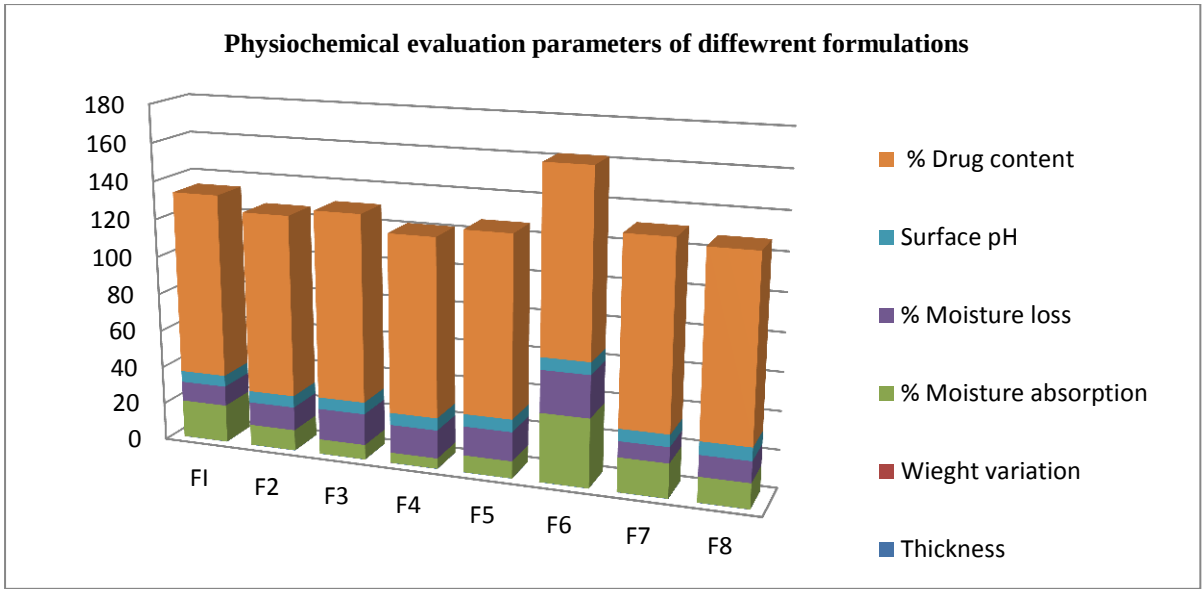

Figure 3: Bar graphs of different evaluation parameters

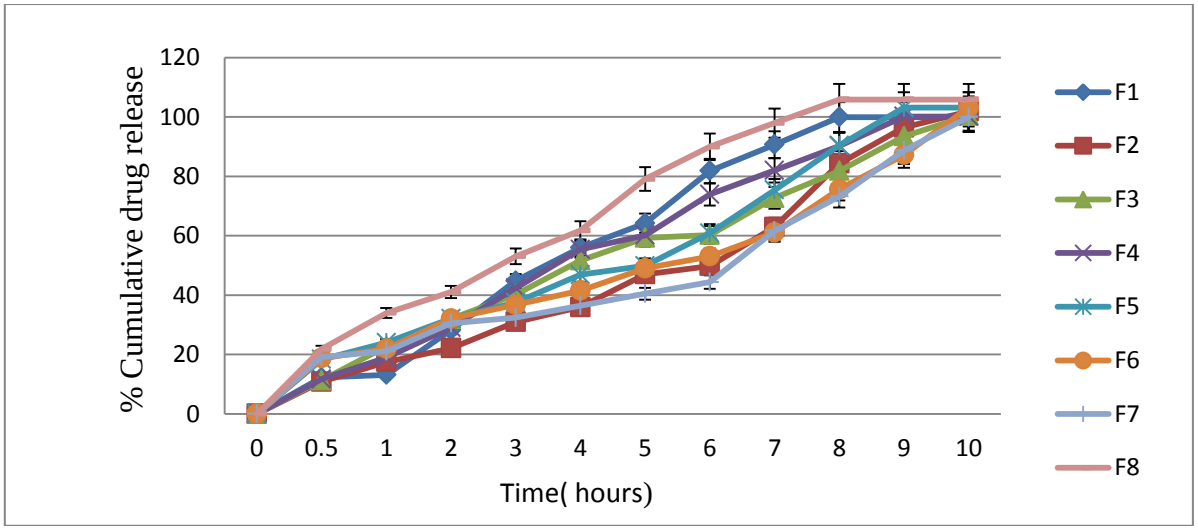

Figure 4: Zero order model

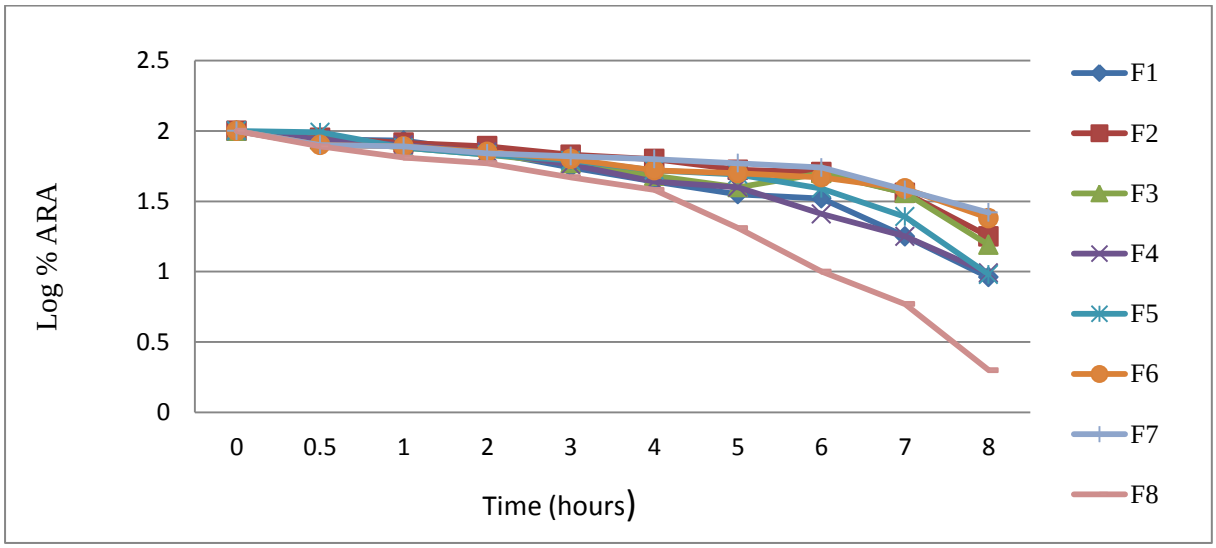

Figure 5: First order plot

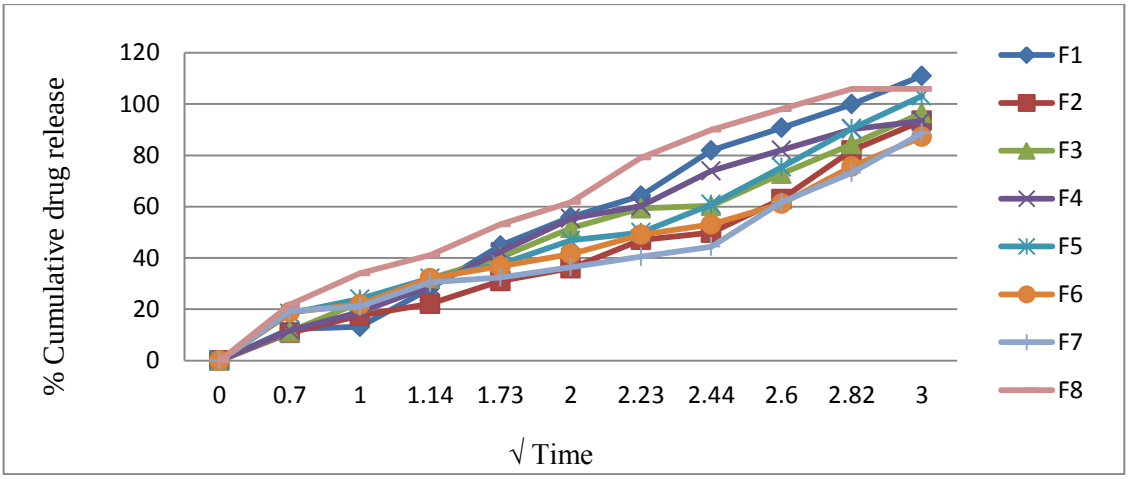

Figure 6: Higuchi model

Table 3: Best fit model

Formulation batch	Zero order plot r^2	First order plot r^2	Higuchi model r^2	Best fit model
F1	0.995	0.910	0.995	Zero order
F2	0.971	0.820	0.986	Zero order
F3	0.994	0.804	0.992	Zero order
F4	0.993	0.910	0.989	Zero order
F5	0.978	0.827	0.994	Zero order
F6	0.986	0.896	0.972	Zero order
F7	0.933	0.896	0.932	Zero order
F8	0.938	0.817	0.978	Higuchi

During evaluating the formulations the surface pH of the prepared films were found between 6 to 7. This shows that the prepared insert would not alter the pH of tear fluid and does not have irritation potential as pH is within the accepted ocular range. The drug content was found to be in the range of 93.86% - 98.72%. No significant difference in drug content was noted when increase in polymer concentrations.

During 10 hours release study the *in vitro* release of Chloramphenicol ocular insert was found in the range of 99.9 % to 105.9% in 10 hours. The formulation FI showed its release in less time period in 8 hrs due to an optimal concentration of polymers present. The formulation F2, F3, F6 and F7 shows high drug release up to 10 hours which may be due to the high compatibility of hydrophilic polymer HPMC as compared to M.C. The in vitro drug release of formulations having the combination of PVA and other two polymers i.e. F4,F5 and F8 showed it maximum drug release of 99.99% within 8 hours, beyond that there was not any further increase in drug release .

Thus it was found that cumulative percent drug release was 99.97%, 101.9%, 100.45% and 100.2% for formulation F 1, F2, F3 and F4 respectively after 10 hours. In vitro release data indicated that the formulation F3 showed better sustained effect than other three formulations.

The cumulative percent drug release was 103.5%, 103.16%, 99.99% and 105.9% for formulations F5, F6, F7 and F8 respectively after 10 hours. In vitro release data indicated that the formulation F7 showed better sustained effect than the other three formulations.

The formulations which gave good result with highest drug release within 10 hours i.e. F3 and F7 were selected for further studies like sterility testing, Stability studies.

Sterility test were performed on formulations F3 and F7 and was confirmed that the formulations were sterile and method of sterilization i.e. UV Radiation produced sterile formulations. There was no appearance of turbidity and hence no evidence of microbial growth.

CONCLUSION

The ophthalmic films of Chloramphenicol were prepared by solvent casting technique under aseptic condition using different polymers HPMC, MC, PVA. The drug content of the prepared formulation was with the range of 93.86% to 98.70%, so it ensures dose uniformity. The formulation F3 and F7 showed maximum drug content. The ophthalmic drug delivery

System of Chloramphenicol may be effective drug delivery with increased corneal residence time for the treatment of conjunctivitis.

ACKNOWLEDGEMENT

"*Keep your dreams alive", Understand and achieve anything that requires belief in yourself, hard work and dedication.*

I extend my sincere thanks to our Rtn. Yogesh Mohan ji Gupta, Chairman, IIMT Group of Colleges and Rtn. Abhinav Aggarwal, Secretary. General, IIMT Group of Colleges, in acknowledging all the facilities provided to us at institution and enabling to do a work of this magnitude.

I would like to express my most sincere and deep sense of gratitude to my esteemed guide Prof. (Dr) T.S Easwari, M.pharm, PhD, MBA, LLB, Director, IIMT College of Medical Sciences, Meerut, for providing me a very cordial environment. Her discipline, principles, valuable guidance, and the abundant morale support throughout my work will be cherished always.

It is my honour to thank Dr. V. K Shukla, M. Pharm, PhD, PGDDRA, Assistant Director, IIMT College of Medical Sciences, Meerut, who is committed in providing the highest professional and ethical standards of pharmacy to consummate this thesis.

REFERENCES

1. Ross and Wilson 2014, Anatomy and Physiology in Health and illness by Anne Waugh, 12th edition, 196-197.
2. Karthikeyan D., Bhowmick M., Pandey V.P., Nandhakumar J., Sengottuve S., Sonkar, S., Sivakumar T. The concept of ocular inserts as drug delivery systems: An overview. Asian Journal of Pharmaceutics 2008: 460-468.
3. Saettone M.F, Salminen L. Ocular inserts for topical delivery. Advanced Drug Delivery Reviews., 1995, 16: 95-106.
4. Sushil, 2008, Acyclovir ophthalmic inserts/ Asian Journal of Pharmaceutical Sciences vol, 3 (2), 58-67.
5. Tanwar Y.S., Patel D., Sisodia S.S. In vitro and in vivo evaluation of ocular inserts of ofloxacin. DARU. 2007, 15(3) : 139-145.
6. Prasoon 2011 Design and Evaluation of Ocular Inserts For Controlled Drug Delivery of Acyclovir. International Journal of Pharmaceutical & Biological Archives 2(4), 1106-1110.
7. Charoo NA, Kohli K, Ali A & Anwer A 2003. Ophthalmic delivery of ciprofloxacin hydrochloride from different polymer formulations: in vitro and in-vivo studies. Drug Dev Ind Pharm 29(2), 215-221.
8. Srividya B, Cardoza RM & Amin PD 2001. Sustained ophthalmic delivery of ofloxacin from a pH triggered in situ gelling system. J Control Ref 73, 205-211.
9. Patel UL, Chotai NP, Nagda CD, Patel MP & Patel KN 2009. Formulation and in vitro evaluation of moxifloxacin hydrochloride ophthalmic inserts. Int J Pharm Res 1(1) 23-30.
10. Maheswara Reddy C, Firoz S, Rajalakshmi R, Ashok Kumar CK 2011. Design and evaluation of Chloramphenicol thermo reversible In-situ gels for ocular drug delivery 2(2), 131-138.
11. Indian Pharmacopoeia, Ministry of Health and Family Welfare, Govt. of India, New Delhi. 3rd edition, 1996: A- 117 - A- 124.
12. Higuchi, T. Mechanism of sustained-action medication theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J. Pharm. Sci. 1963, 52:1145-1149.