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Preparation, Optimization And Evaluation Of Dexamethasone Film For Inflammation

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ABSTRACT:

The goal of the current study, which focusses on treating ocular inflammation, is to use ocular films to reduce the frequency of drug administration, achieve controlled release, and increase the therapeutic efficacy of the drug (dexamethasone). According to a factorial design study, multiple combinations containing diverse combinations of polymers, such as HPMC K100M, ethyl cellulose, Carbopol 934, and PVP K30, were designed for different batches of ocular films with a 0.5% w/v concentration via solvent evaporation method. No microbiological growth was discovered in any formulation during sterility testing by direct inoculation method. The drug release for prepared formulations of different batch codes DF1, DF2, DF3, DF4, DF5 and DF6 was found to be 92.6 ± 1.6, 55.1 ± 3.6, 92.3 ± 2.7, 96.1 ± 1.5, 97.9 ± 3.8 & 94.5 ± 4.5 % respectively upto 12 hours. The highest drug release (97.9±3.8) was optimised for ocular films with batch code DF5. Periodically (0.5 to 06 hours) after the sterile formulation was administered, the anti-inflammatory impact was observed in the treated versus control eyes of every rabbit. With just one dose, the inflammation was totally decreased by the optimised batch DF5 of ocular inserts for up to four hours

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KEYWORDS: *Dexamethasone, Ocular films, Solvent evaporation method, Inflammation*

INTRODUCTION

The topical administration of anti-inflammatory drugs, such as non-steroidal (NSAIDs) [1] and steroidal (SAIDs) [2], has been shown in numerous reports to be effective in treating ocular surface and anterior segment inflammation. This includes pain and inflammation following surgery, seasonal allergic conjunctivitis [3, 4], and age-related macular degeneration [5]. Ocular inflammation is recognised as a major eye disorder. Additionally, it has been shown that several immunosuppressive medications, like ciclosporin A (CsA), are effective in treating keratitis linked to dry eye disease (DED) [6, 7]. The fundamental difficulty in the therapeutic management of ocular inflammation is prompt treatment in order to lessen the risk of visual impairment while limiting adverse effects. Topical administration is the most preferred route for the management of ocular inflammations as it is (i) easy to handle, (ii) non-invasive, (iii) rather well-tolerated [1], and (iv) it provides sufficient ocular drug concentrations, while avoiding the systemic side effects associated with oral administration. [3]

Although creating a controlled release formulation for the ocular route has been the most difficult undertaking, pharmaceutical research specialists have found this to be a very creative and fascinating field of study. [5] The eye is a highly sensitive and protected organ due to its particular anatomy and physiology, and its structure prevents drugs from entering the intended site of action. For the treatment of various infections in the cul-de-sac, conventional drug delivery systems such as eye drops, suspensions, and ointments are widely used. However, they cannot be regarded as optimal because most topically instilled drugs do not offer adequate bioavailability due to the wash off of the drugs from the eye through lacrimation and tear dilution [8,9]. In addition, less than 5% of supplied drugs reach the eye because the human cornea, which is made up of epithelium, substantia propria, and endothelium, prevents drug penetration. Alternative techniques (ocular inserts/ films, corneal shield, sol to gel system etc.) are continuously investigated to achieve significant drug absorption into the eye. [10, 11]

High potency is a characteristic of dexamethasone (9-fluoro-11β, 17,21-trihydroxy-16a-methylpregne-1,4-diene-3,20-dione), a synthetic derivative of glucocorticoids. One of the powerful synthetic analogues of systemic cortisol and nearly aqueously insoluble is dexamethasone (DEX) [12, 13]. The great potency and efficiency of dexamethasone sodium phosphate (DEX) has made it stand out among the corticosteroids used in ocular therapy [14]. The drug's molecules bind to glucocorticoid receptors found in different cells to mediate DEX's effect [15].

In order to overcome the issues with traditional ophthalmic dosage forms and achieve a controlled and consistent release of medication, ocular films were prepared using varying concentrations of hydroxyl propyl methyl cellulose (HPMC K100M), polyvinyl pyrollidone (PVP K30), carbopol 934, and ethyl cellulose. Drug permeability through polymeric films is influenced by the polymer's properties, the casting solvent, and the plasticisers employed. In order to decrease brittleness, add flexibility, boost strength, and enhance adhesiveness of the films with surfaces or membranes, plasticisers (phthalate esters, phosphate esters, fatty acid esters, and glycol derivatives) are highly helpful when preparing polymeric ocular films [16, 17].

MATERIAL AND METHODS

Materials: Yarrow Chem Pvt. Ltd., Mumbai, India provided a gift sample of dexamethasone while all the polymers of analytical grade were purchased from different suppliers of India like HPMC K100M from S. D. Fine Chemicals Pvt. Ltd.-Mumbai, PVP K 30 and Ethyl cellulose and PEG from Qualikems fine chem. Pvt Ltd.-Delhi.

Preparation Of Ocular Films: With 0.5 percent w/v concentration of (DF1-DF4), 1.30 percent w/v concentration of (DF5), and 1.44% w/v concentration of (DF6), different combinations were designed for

different batches of ocular films according to a factorial design study. These combinations were created using the solvent evaporation method and contained different combinations of polymers, such as hydroxyl propyl methyl cellulose (HPMC K100M), ethyl cellulose, Carbopol 934, and polyvinylpyrrolidone (PVP). To create a transparent solution, the optimal concentration of particular polymers were homogenised. After the clear solution was ready, 30 millilitres of the solution for six films were pipetted out, and the medication was added. Stirring helped the solution become homogenised. The resultant solution was poured onto the glass ring after it had been placed over the previously lubricated petri plates. The medication solution was used up in one glass ring (5 ml). To facilitate gradual evaporation, an inverted funnel was positioned over the petri plate. Cotton wool was used to plug the funnel's open end. [18, 19] The whole assembly was left undisturbed till the films dried. The film rings were removed from the petri plates once they had finished drying, and a die was used to cut them to the right size.

Table 1: Formulation Chart

Batch Code	Drug (% w/v)	HPMC K100M	Ethyl cellulose	Carbopol 934	Polyvinylpyrrolidone K30	Plasticizer (% w/w)
DF1	0.1	0.5	-	-	-	10
DF2	0.1	-	0.5	-	-	10
DF3	0.1	-	-	0.5	-	10
DF4	0.1	-	-	-	0.5	10
DF5	0.1	0.65	0.65	-	-	10
DF6	0.1	-	0.48	0.48	0.48	10

Physicochemical characterization: The physicochemical properties of the dexamethasone ocular films, including folding endurance, thickness, surface pH, moisture absorption, moisture loss, stability studies, and drug release, were assessed.

The number of folds at a single location needed to split an ocular film into two halves was used to measure the folding endurance of the films. Using screw gauze, the thickness of the recovered films was measured. The film was placed on the anvil so that the area where the thickness is to be measured rests after the basic settings were completed. [20] To determine the film's thickness, the screw was gradually tightened onto the specimen, and the gauze's reading was recorded. By covering them with two drops of distilled water and allowing them to swell, the surface pH of the film was determined. After this the swollen film was taken and pH was determined using pH paper on the surface of the film.

The purpose of the % moisture absorption test was to evaluate the ocular films' physical stability or integrity. After weighing, ocular films were put in a desiccator with 100 millilitres of an ammonium chloride saturated solution. The ocular films were removed and reweighed after three days. [21] The percentage moisture absorption was calculated using the formula:

$$\% \text{ Moisture absorption} = \text{final weight} - \text{initial weight} / \text{initial weight} \times 100$$

The film's integrity was examined at dry conditions using the percentage moisture loss method. Weighed ocular films were stored in desiccators with anhydrous calcium chloride. The ocular films were removed and reweighed after three days, [22] the percentage moisture loss was calculated using the formula:

$$\% \text{ Moisture loss} = \text{initial weight} - \text{final weight} / \text{initial weight} \times 100$$

Stability Study of Optimized Batch of Ocular Film: Using the stability chamber, replicates of ocular films

(packaged in aluminium foil) were stored for 0, 30, 90, and 180 days at a relative humidity of 75% ± 5% at a temperature of 400 ± 2ºC and for 180 days at room temperature. Stability studies were performed on batch code DF5, in accordance with ICH guidelines. The sample was collected after 30, 90, 180 days under accelerated circumstances and 180 days at RT, respectively and assessed. [23, 24]

In-vitro drug release study: The inserts were positioned on a modified Franz diffusion cell that was held at 37 ± 1°C with continuous stirring at 50 rpm. The cellophane membrane was in contact with an isotonic phosphate buffer pH 7.4. 1 ml Sample was withdrawn at different time intervals evaluated for drug concentration spectrophotometrically (Shimadzu UV 1700) at 256 nm. [25]

Sterility testing of optimized batch of ocular film: A batch of optimised ocular films was collected and placed in two distinct sterile nutrient agar petri dishes. As a negative control, one uninoculated nutrient agar petri plate was used (to assess sterility of the medium). As a positive control, one nutrient agar petri dish was infused with an isolated culture of Staphylococcus aureus from the lab. For twenty-four hours, both petri dishes were incubated at 37°C. [26] Results were analysed with positive and negative control petri dishes. The fact that germs grew in the positive control test and did not grow in the negative control test demonstrated that all test equipment was sterile and that aseptic conditions were maintained. Now the sample formulation were placed in the negative control test and incubated at same conditions. There was no growth of microorganism in the samples under test, confirming the sterility of ocular films. These sterile ocular films were considered suitable for in vivo studies. [27, 28]

Sterilization of Optimized Batch of Ocular Film: These formulations were packaged in previously sterilised aluminium foil after being individually sterilised for 90 minutes in a cabinet under aseptic circumstances by subjecting both sides to UV light. [29]

Pharmacological study: The institutional animal ethics committee at the study site prepared and approved the protocol for in vivo studies with rabbits. Prior to the trial, the rabbits were kept in a temperature-controlled room between 20°C and 24°C while being given pellets with a balanced diet. When a 100 microlitre syringe was used to subconjunctivally inject arachidonic acid (05%) into the left and right eyes of six male Albino rabbits weighing 2.5 kg, the amount of inflammation increased in proportion to the dose. Prior to administering the medication (zero-time), and at predefined intervals following the insertion of an ocular film containing dexamethasone into the conjunctival sac of each rabbit's treated right eye, the inflammation was noted with lid closure in both eyes. Its topical therapy of ocular irritation was suggested by dose-response relationships that were shown. Based on the Peyman scale, the lid closure was rated as follows: 0 for entirely open, 1 for two-thirds open, 2 for one-third open, and 3 for fully closed. [30-32]

RESULTS AND DISCUSSION

Glycerin was used as a lubricant during the solvent evaporation method's preparation of the dexamethasone ocular films, which were then characterised based on physicochemical parameters, sterility tests, and in-vitro and in-vivo release investigations. A variety of metrics, including folding durability, thickness, surface pH, percentage of moisture absorption, percentage of moisture loss, and drug release of ketorolac tromethamine, were assessed for each formulation including each polymer. (Table 2)

Table 2: In Vitro Evaluation Of Optimized Batches

Batch Code	Folding endurance (no. of folds)	Thickness (µm)	Surface pH	% moisture Absorption (w/w)	% moisture loss (w/w)	% Drug Release
DF1	74 ± 1.26	5.5 ± 0.1	6.6	6.16 ± 1.4	1.11 ± 0.04	92.6 ± 1.6
DF2	78 ± 1.65	4.9 ± 0.2	7.1	1.94 ± 1.1	0.59 ± 0.05	55.1 ± 3.6
DF3	53 ± 0.59	6.3 ± 0.8	6.6	4.28 ± 1.2	0.48 ± 0.02	92.3 ± 2.7

DF4	43 ± 1.13	6.6 ± 0.4	6.9	6.65 ± 1.4	1.23 ± 0.02	96.1 ± 1.5
DF5	80 ± 0.18	4.8 ± 0.1	7.0	3.12 ± 1.1	0.56 ± 0.04	97.9 ± 3.8
DF6	67 ± 0.73	4.6 ± 0.4	7.3	4.11 ± 1.5	0.69 ± 0.02	94.5 ± 4.5

Values are expressed as mean ± SD (n=5)

The ocular films' physico-chemical properties were influenced by the type of rate-controlling membrane. The most significant ingredient that can influence the mechanical characteristics of the films is the plasticiser, which lowers the polymer's glass-transition temperature. PEG-400 was used for this investigation at a concentration of 10% w/w of total polymer because it produced sufficiently malleable films to enable uniform subdivision into films without shattering the film. HPMC K100M ocular films with EC and PVP K30 rate-controlling membranes were elastic and flexible. Thickness and folding endurance were optimum in all batches and the % cumulative drug release (Figure 1) was evaluated with all six batches, the batch code DF5 was optimized with a maximum drug release (97.9 ± 3.7) having surface pH (7.0), % moisture absorption (3.12 ± 1.1 w/w) and % moisture loss (0.56 ± 0.04 w/w). All the batches of formulations except batch code DF2 shows approximate linearity but batch code DF5 shows desirable cumulative release of drug within 12 hrs

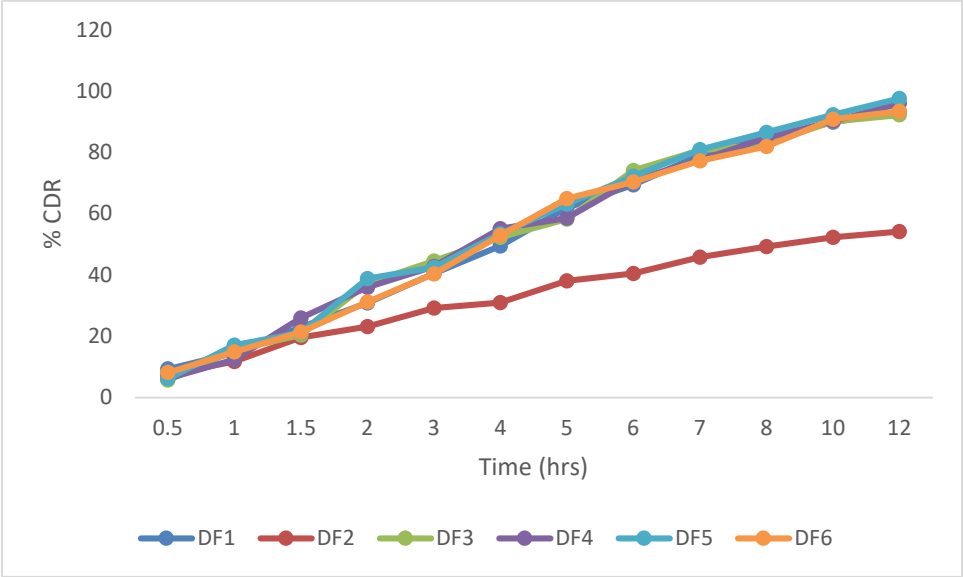

Fig 1: % Cumulative Release of Optimized Batches of Ocular Films of Dexamethasone

Stability study: The stability study was conducted for batch code PEEH with an accelerated study from 0 day to 6 months & up to 6 months at room temperature, based on the physicochemical characteristics and in-vitro comparative release study of all six batches. Folding endurance, thickness, surface pH, % moisture absorption (table 3) and % drug release (figure 2) were further evaluated. The results of the accelerated stability investigations, which were conducted at higher temperatures and humidity levels, showed that the surface pH, folding endurance, and film thickness did not significantly alter. Ocular films could be kept in a study storage area safely. To guarantee formulation stability, moisture-proof packaging and a storage temperature of no more than 40 °C are advised. According to the ICH criteria, the formulations may be awarded a preliminary shelf-life of more than years, as the overall deterioration was less than 5%. During the accelerated stability analysis, the drug release for batch code DF5 was shown to be optimal at various time intervals.

Table 3: Stability Study Of Final Selected Batch DF5

Parameters evaluated	Accelerated Study	Room Temp.

	0 day	30 days	90 days	180 days	180 days
Folding endurance	80	79.5	77	74	82
Thickness (µm)	4.8	4.8	4.9	4.8	4.9
Surface pH	7.0	7.1	7.1	7.3	7.3
% moisture Absorption (w/w)	3.12	3.14	3.17	3.27	2.92
% Drug Release	97.9	97.23	95.11	94.87	96.11

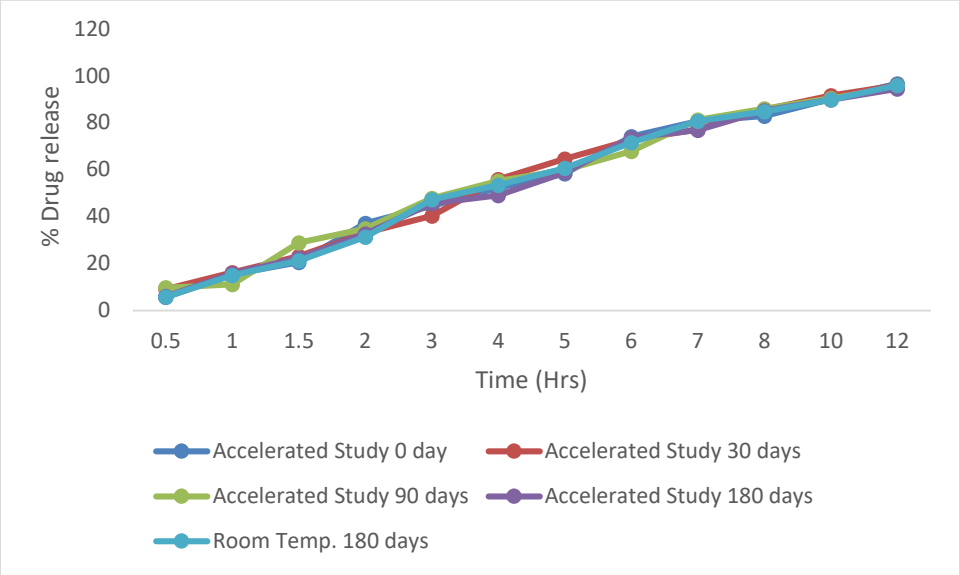

Figure 2: % Drug Release From Batch DF5 During Stability Study

Pharmacological Study: Following the administration of the final optimised sterile formulation, inflammation was observed in both eyes of each animal at regular intervals (0.5 to 06 hours) in the treated eyes compared to the control eyes. The Tukey-Kramer multiple comparison test was employed after a one-way ANOVA to compare the means of the various groups. When compared to the control group, there is a substantial drop ($P < 0.05$ & $P < 0.01$) in the inflammatory scores. The optimised batch DF5 of ocular inserts totally reduced the inflammation up to 4 hours in a single dose, according to the findings shown in Figure 3.

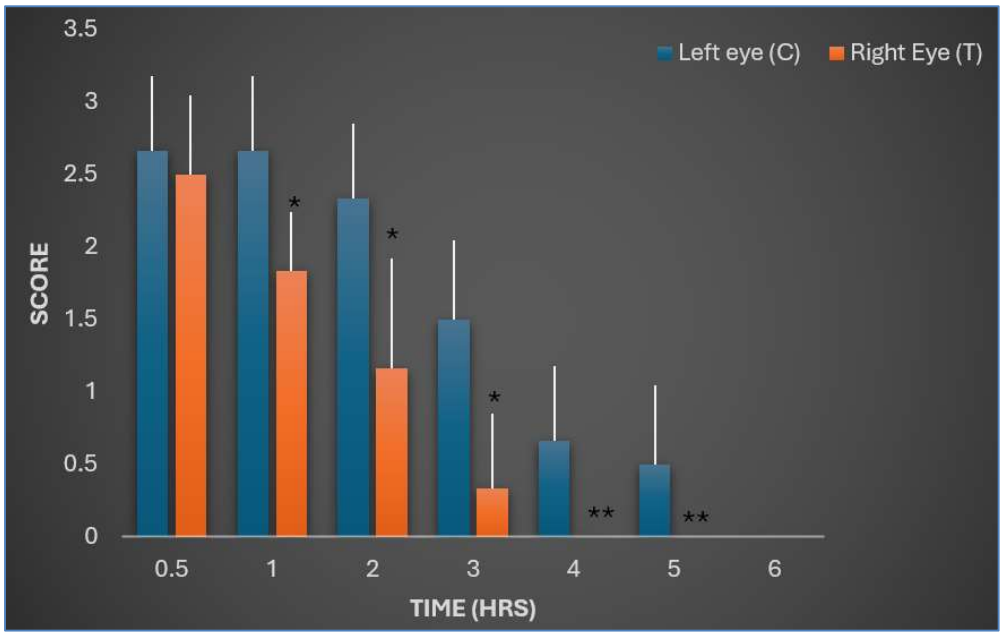

Figure 3: Effect of anti-inflammatory agent (± SD) between control and treated group. (*P < 0.05 & **P < 0.01 vs. control group)

CONCLUSION

PEG 400 was used as a plasticiser in the solvent evaporation method to create ocular films of dexamethasone that were made using an excellent film-forming hydrophilic polymer (HPMC K100M) and rate-controlling membranes made of ethyl cellulose and PVP K30. While numerous combinations were used to design varied concentrations, batch code DF5's concentration was transparent, versatile, and smooth. For an optimal batch of ocular film, the following physical-chemical parameters were met: folding endurance, thickness, surface pH, % moisture absorption/loss, stability study, and sterility testing. An in-vitro and an in-vivo investigation showed that the optimal formulation might provide advantages such longer drug release, longer residence times, fewer administration frequency, and better patient compliance with total reduction of inflammation and redness.

REFERENCES

1. Ahuja, M.; Dhake, A.S.; Sharma, S.K.; Majumdar, D.K. Topical ocular delivery of NSAIDs. AAPS J. 2008, 10, 229–241. [Google Scholar] [CrossRef] [Green Version]
2. Behar-Cohen, F. Towards an Optimized Use of Ocular Corticosteroids: EURETINA Award Lecture 2017. Ophthalmologica 2018, 240, 111–119.
3. Schalnus, R. Topical nonsteroidal anti-inflammatory therapy in ophthalmology. Ophthalmologica 2003, 217, 89–98. [Google Scholar] [CrossRef] [PubMed]
4. Wilson, D.J.; Schutte, S.M.; Abel, S.R. Comparing the Efficacy of Ophthalmic NSAIDs in Common Indications: A Literature Review to Support Cost-effective Prescribing. Ann. Pharm. 2015, 49, 727–734. [Google Scholar] [CrossRef] [PubMed]
5. Suresh, P.K.; Sah, A.K. Patent perspectives for corticosteroids based ophthalmic therapeutics. Recent Pat. Drug Deliv. 2014, 8, 206–223. [Google Scholar] [CrossRef] [PubMed]
6. Lallemand, F.; Schmitt, M.; Bourges, J.-L.; Gurny, R.; Benita, S.; Garrigue, J.-S. Cyclosporine A delivery to the eye: A comprehensive review of academic and industrial efforts. Eur. J. Pharm. Biopharm. 2017, 117, 14–28. [Google Scholar] [CrossRef]
7. Deveney, T.; Asbell, P.A. Patient and physician perspectives on the use of cyclosporine ophthalmic emulsion 0.05% for the management of chronic dry eye. Clin. Ophthalmol. 2018, 12, 569–576. [Google Scholar] [CrossRef] [Green Version]

8. Chien YW: Novel Drug Delivery Systems (Drugs and the Pharmaceutical Sciences). New York: Marcel Dekker Inc., Second Edition 1996.
9. Gaudana R, Jwala J, Boddu SHS and Mitra AK: Recent perspectives in ocular drug delivery. Pharmaceutical Research 2009; 26:1197-1216.
10. Peneva PT: Non-steroidal anti-inflammatory drugs for topical ophthalmic administration: Contemporary Trends. International Journal of Pharmacy and Pharmaceutical Sciences 2015; 7 (9):13-19.
11. Smith SE: Ocular NSAIDs. Therapeutics 2005; 124-127.
12. Schuh S, Coates AL, Binnie R, Allin T, Goia C, Corey M, Dick PT. Efficacy of oral dexamethasone in outpatients with acute bronchiolitis. J. Pediatr. 2002;140:27–32. [PubMed] [Google Scholar]
13. Sweetman SC. Martindale: The Complete Drug Reference. 37th ed. London, UK: Pharmaceutical Press; 2011. pp. 1526–8. [Google Scholar]
14. Sparrow A, Geelhoed G. Prednisolone versus dexamethasone in croup: A randomised equivalence trial. Arch. Dis. Child. 2006;91:580–3. [PMC free article] [PubMed] [Google Scholar]
15. Shimoda H, Taniguchi K, Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, Hirano K, Yamamoto M, Kinosada Y, Itoh Y. Preparation of a fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer chemotherapy. Eur. J. Pharm. Biopharm. 2009;73:361–5. [PubMed] [Google Scholar]
16. Kothawade SN, Deshpande ST, Lunkad AS and Dighe PA: Formulation and in-vitro characterization of Ketorolac Tromethamine ophthalmic inserts. Research Journal of Pharmaceutical Dosage Forms and Technology 2014; 5 (6):311-314.
17. Sankar V, Chandrasekaran AK, Durga S, Geetha G, Ravichandra V, Vijayakumar A and Raguraman S: Design and evaluation of Diclofenac Sodium ophthalmic inserts. Acta Pharmaceutica Sciencea 2006; 48:5-10.
18. Shanmugam S, Valarmathi S, Satheesh KS. Sterility testing procedure of ophthalmic ocusert acyclovir used for treating herpes simplex virus. Asian J Pharm Clin Res 2017 ;10:344-6.
19. Kerur S, Dandgi P, Deshpande P. Controlled release polymeric ocular inserts for delivery of acyclovir. Turkish J Pharm Sci 2010; 7:75-90.
20. Jayaprakash S, James CC, Maria NS, Saisivam S, Nagarajan M. Design and evaluation of keterolac tromethamine ocuserts. Indian J Pharm Sci 2000; 62:334-8.
21. Rao V, Shyale S. Preparation and evaluation of ocular inserts containing norfloxacin. Turkish J Med Sci 2004; 34:239-46.
22. Pawar PK, Katara R, Majumdar DK. Design and evaluation of moxifloxacin hydrochloride ocular inserts. Acta Pharma 2012;62:93-104.
23. Jervis LP. A summary of recent advances in ocular inserts and implants. J Bioequi Bioavai 2017;9:320-3.
24. Kumar KPS, Bhowmik D, Harish G, Duraivel S, Kumar BP. Ocular inserts: a novel drug delivery system. Pharma Innov J 2013;1:1-16.
25. Nageshwara RG and Ramakrishna A: Formulation design and in vitro evaluation of Natamycin ocular insert. International Journal of Pharmaceutical Research and Bioscience 2014; 3(2):687-695.
26. Jervis LP: A summary of recent advances in ocular inserts and implants. Journal of Bioequivalnce and Bioavailability 2017; 9(1);320-323.
27. Prabhakar V, Agarwal S, Chauhan R, Sharma S. Fast dissolving tablets: an overview. International Journal of Pharmaceutical Sciences: Review and Research. 2012;16(1):17.
28. Mandal S, Vishvakarma P, Verma M, Alam MS, Agrawal A, Mishra A. Solanum Nigrum Linn: an analysis of the Medicinal properties of the plant. Journal of Pharmaceutical Negative Results. 2023 Jan 1:1595-600.
29. Vishvakarma P, Mandal S, Pandey J, Bhatt AK, Banerjee VB, Gupta JK. An Analysis of The Most Recent Trends in Flavoring Herbal Medicines in Today's Market. Journal of Pharmaceutical Negative Results. 2022 Dec 31:9189-98.

30. Mandal S, Vishvakarma P, Mandal S. Future Aspects and Applications of Nanoemulgel Formulation For Topical Lipophilic Drug Delivery. European Journal of Molecular & Clinical Medicine. 2023;10(01):2023.
31. Mandal S, Vishvakarma P. Nanoemulgel: A Smarter Topical Lipidic Emulsion-based Nanocarrier. Indian J of Pharmaceutical Education and Research. 2023;57(3s):s481-98.
32. Prabhakar V, Agarwal S, Chauhan R, Sharma S. Fast dissolving tablets: an overview. International Journal of Pharmaceutical Sciences: Review and Research. 2012;16(1):17.