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DEVELOPMENT AND EVALUATION OF OPHTHALMIC SUSPENSION CONTAINING CORTICOSTEROID AND ANTIBIOTIC

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ABSTRACTS
In the present study an attempt was made to develop and evaluate the ophthalmic suspension containing corticosteroid drug i.e Prednisolone and Quinolone antibiotic i.e Moxifloxacin. The pH of all formulations was found to be satisfactory in the range of 6.0-6.2, thus there would be no irritation to the patient upon administration of the formulation. The particle size analysis revealed that the particles were in nanometer range and all the formulations showed ideal surface morphology except F2 because after autoclave the particle size of formulation was increased and found to be 17.565 µm which was out of acceptable range. F1 was showed smallest particle size and discrete. The *in vitro* release studies indicated that the formulation F9 showed better effect for desired time and it was found that 120 minutes and 90 minutes for Prednisolone and Moxifloxacin respectively. From the stability studies as per ICH guidelines, it was confirmed that formulations of corticosteroid and antibiotic ophthalmic suspension remained more stable at ambient temperature (25°C) and relative humidity (40%) as compare to other stability conditions.

KEYWORDS: Corticosteroids, Antibiotics, ICH, Surface morphology.

INTRODUCTION
Eye is most interesting organ due to its drug disposition characteristics. Generally, topical application of drugs is the method of choice under most circumstances because of its convenience and safety for ophthalmic chemotherapy. A significant challenge to the formulator is to circumvent (bypass) the protective barriers of the eye without causing permanent tissue damage. Development of newer, more sensitive diagnostic techniques and novel therapeutic agents continue to provide ocular delivery systems with high therapeutic efficacy. Conventional ophthalmic formulations like solution, suspension and ointment have many disadvantages which result into poor bioavailability of drug in the ocular cavity. The specific aim of designing a therapeutic system is to achieve an optimal concentration of a drug at the active site for the appropriate duration.[1,2] Ocular disposition and elimination of a therapeutic agent is dependent upon its physicochemical properties as well as the relevant ocular anatomy and physiology. A successful design of a drug delivery system, therefore, requires an integrated knowledge of the drug molecule and the constraints offered by the ocular route of administration.[3]

ROUTES OF OCULAR DRUG DELIVERY
There are several possible routes of drug delivery into the ocular tissues. The selection of the route of administration depends primarily on the target tissue.

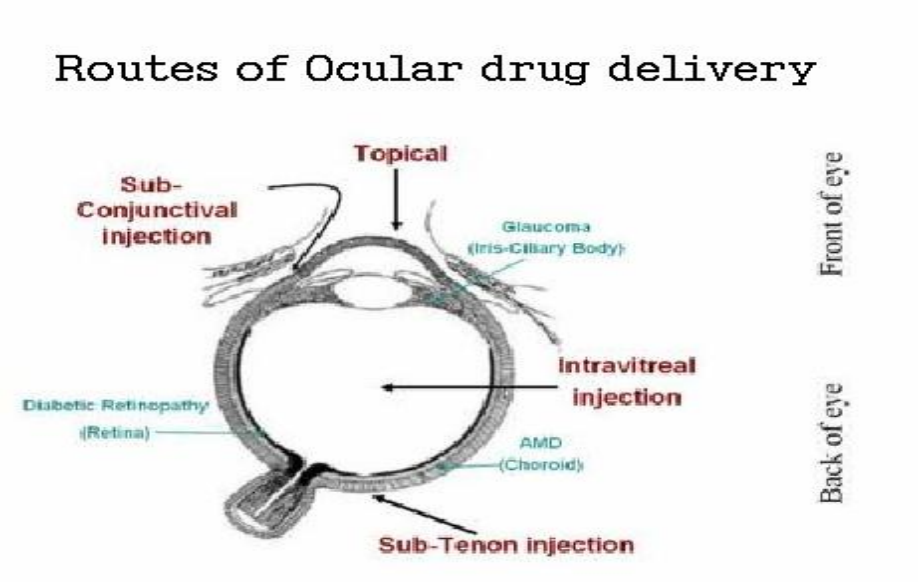


Figure 1: Different Routes for Ocular Drug Delivery.

1. Topical route

Typically topical ocular drug administration is accomplished by eye drops, but they have only a short contact time on the eye surface. The contact and thereby duration of drug action, can be prolonged by formulation design (e.g. gels, gelifying formulations, ointments and inserts).

2. Subconjunctival administration

Traditionally subconjunctival injections have been used to deliver drugs at increased levels to the uvea. Currently this mode of drug delivery has gained new momentum for various reasons. The progress in materials sciences and pharmaceutical formulation have provided new exciting possibilities to develop controlled release formulations to deliver drugs to the posterior segment and to guide the healing process after surgery.[4,5]

3. Intravitreal administration

Direct drug administration into the vitreous offers distinct advantage of more straightforward access to the vitreous and retina. It should be noted; however that delivery from the vitreous to the choroid is more complicated due to the hindrance by the RPE (Retinal Pigment Epithelium) barrier. Small molecules are able to diffuse rapidly in the vitreous but the mobility of large molecules, particularly positively charged, is restricted.[6]

MECHANISM OF OCULAR DRUG ABSORPTION

Drugs administered by instillation must penetrate the eye and do so primarily through the cornea followed by the non-corneal routes. These non-corneal routes involve drug diffusion across the conjunctiva and sclera and appear to be particularly important for drugs that are poorly absorbed across the cornea.

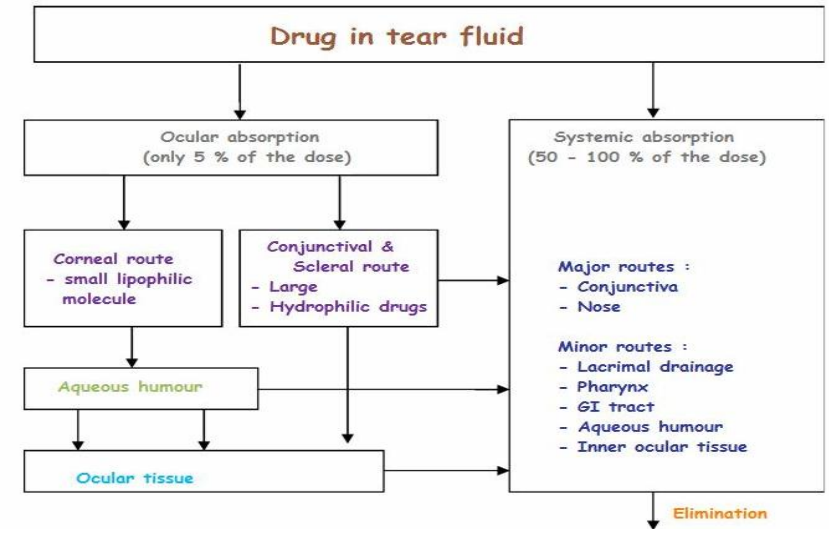


Figure 2: Ocular Drug Absorption.

1. Corneal permeation

The permeation of drugs across the corneal membrane occurs from the precorneal space. Thus, the mixing and the kinetic behavior of drug disposition in tears have a direct bearing on efficiency of drug absorption into the inner eye. The productive absorption of most ophthalmic drugs results from diffusional process across corneal membrane.[7,8]

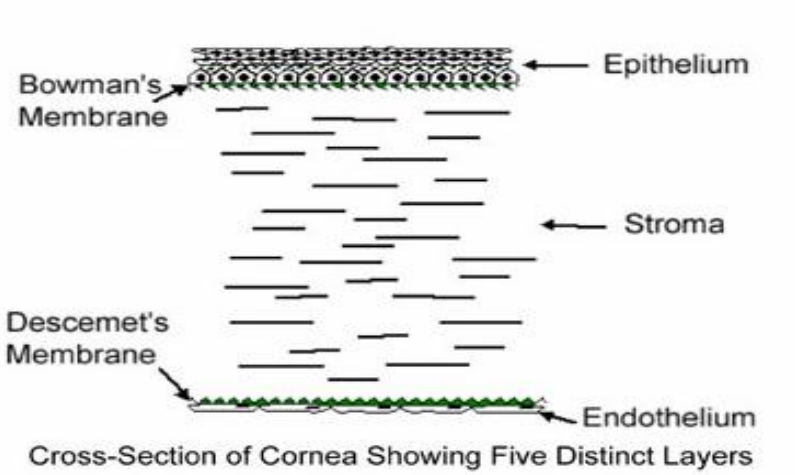


Figure 3: Corneal Membrane Depicting Various Barrieirs to drug Absorption.

The efficiency of absorption process is a function of rate and extent at which the transport processes occur. The flux of any drug molecule across the biological membrane depends on the physicochemical properties of the permeating molecule and its interaction with the membrane. The extent to which the transport or absorption process occurs is also function of physiological mechanism of precorneal fluid drainage or turnover.[9]

In terms of transcorneal drug permeation, the cornea can be considered to consist of three primary layers (epithelium, stroma and endothelium). The epithelium and endothelium contain on the order of a 100 fold greater amount of lipid material than the stroma. Consequently, depending on the physicochemical properties of a diffusing drug, the resistance offered by the individual layers varies greatly.[10,11]

Epithelium, being lipoidal, represents a diffusional barrier offering high resistance to ionic or other aqueous soluble or polar species. In contrast, compounds with relatively low polarity encounter a greater diffusional resistance in the hydrophilic stroma layer. This frequently cited concept of drug permeation across the corneal membrane is referred to as "differential solubility concept".[12,13]

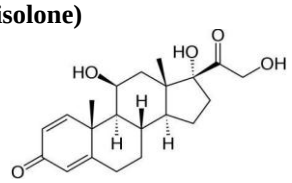
2. Non-corneal permeation

Primary mechanism of drug permeation is the sclera is likely to be diffusion across the intercellular aqueous media in the case of structurally similar corneal stroma. Therefore the possibility of partitioning mechanism cannot be eliminated.

Although like cornea, the conjunctiva is composed of an epithelial layer covering an underlying stroma, the conjunctival epithelium offers substantially less resistance than does the corneal epithelium.[14,15]

DRUGPROFILE

API-1 (Prednisolone)



Drug Category: Corticosteroids (glucocorticoid), anti-inflammatory action.

Appearance: A white or, almost white crystalline powder.

Solubility: Freely soluble in chloroform, sparingly soluble in Acetone, Slightly soluble in methanol, practically insoluble in water.

Pharmacology

- API-1 is a "soft" steroid belonging to a unique class of glucocorticoids.
- It possesses a metabolically labile 17 beta-chloromethyl ester function which was designed in order to be hydrolyzed to an inactive carboxylic acid moiety.
- This inactive metabolite is more hydrophilic and is thus readily eliminated from the body.
- It is used as a topical agent for the treatment of steroid responsive inflammatory conditions of the eye such as allergic conjunctivitis, uveitis and iritis.

Mechanism of action

- There is no generally accepted explanation for the mechanism of action of ocular corticosteroids.

- However, corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins.
- It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Indication and Uses

As an ophthalmic it is used for the treatment of steroid responsive inflammatory conditions of the eye such as allergic conjunctivitis, uveitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis and selected infective conjunctivitides. As a nasal spray, used for the treatment and management of seasonal allergic rhinitis.

Dosage and Administration: Shake vigorously before using.

One drop instilled into the affected eye(s) four times daily.

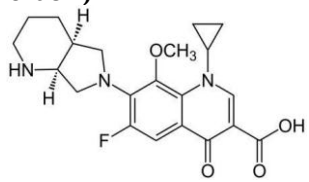
Side Effects: Adverse effects include abnormal vision / blurring, burning on instillation, chemosis, discharge, dry eyes, epiphora, foreign body sensation, itching, injection, and photophobia.

Contraindication: API-1, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia and varicella and also in mycobacterial infection of the eye and fungal diseases of ocular structures. It is also contraindicated in individuals with known or suspected hypersensitivity to any of the ingredients of this preparation and to other corticosteroids.

How to Use: 0.5% is supplied in a plastic bottle with a controlled drop tip.

Storage: Store upright between 15°–25°C (59°–77°F). Do not freeze. Keep out of reach of children.

API-2 (Moxifloxacin)



Drug Category: Quinolones Antibiotics (Anti-infective).

Appearance: A pale yellow or bright yellow, crystalline powder.

Solubility: Freely Soluble in glacial acidic acid, Slightly soluble in water; methylene chloride and methanol; practically insoluble in acetone and dichloromethane.

Pharmacology

- It is a quinolone/fluoroquinolone antibiotic.
- It is bactericidal and its mode of action depends on blocking of bacterial DNA replication by binding itself to an enzyme called DNA gyrase, which allows the untwisting required to replicate one DNA double helix into two. Notably the drug has 100 times higher affinity for bacterial DNA gyrase than for mammalian.
- It is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria.

Mechanism of action

- It acts on DNA gyrase and toposiomerase IV, enzymes which, like human topoisomerase, prevents the excessive supercoiling of DNA during replication or transcription. By inhibiting their function, the drug thereby inhibits normal cell division.

Indication and Uses: It is indicated for the treatment of infections caused by susceptible strains of the following bacteria in the conditions listed below.

Table 1: List of gram-positive and gram-negative bacteria.

CONJUNCTIVITIS

Gram-positive bacteria	Gram-negative bacteria
Staphylococcus aureus	Enterobacter cloacae
Staphylococcus epidermidis	Haemophilus influenzae

Table 2: List of gram-positive and gram-negative bacteria.

CORNEAL ULCERS

Gram-positive bacteria	Gram-negative bacteria
Staphylococcus aureus	Pseudomonas aeruginosa
Staphylococcus epidermidis	Serratia marcescens

Dosage and Administration: The recommended dosage regimen for the treatments are is:

Instill one to two drops every two to four hours in the affected eye(s) for 1-2 days and Instill one to two drops four times daily from 3 to7 days.

Side Effects: The most frequently reported drug-related adverse reaction was transient ocular burning or discomfort. Other reported reactions include stinging, redness, itching, chemical conjunctivitis/keratitis, ocular/periocular/facial edema, foreign body sensation, photophobia, blurred vision, tearing, dryness and eye pain. Rare reports of dizziness and nausea have been received.[16,17]

Contraindication: It is contraindicated in patients with a history of hypersensitivity to quinolones, or to any of the components in this medication.

How To Use: 0.3% is supplied sterile in opaque white LDPE plastic bottles and white dropper tips with beige high impact polystyrene (HIPS) caps.

Storage: Store at 25^{0}C, excursions permitted to15-30^{0}C. Protected from light.

1. Preformulation studies

A. Determination of melting point

Table 3: Reported and observed melting point of API'S.

Name	Reported Wavelength	Observed Wavelength
API-1	228- 232ºC	231.60ºC
API-2	250- 257ºC	257.38ºC

C. IR Spectroscopy

Table 4: Reported and observed IR frequencies of API-1.

Functional Group	Reported Frequencies (in cm-1)	Observed Frequencies (in cm-1)
-OH	**3328**	**3310.50**
-CH	**2921**	**2922.21**
-C-O	**1100**	**1067.16**
-C=O	**1655**	**1607.70**
-CO-O	**1742**	**1749.47**

Table 5: Reported and observed IR frequencies of API-2.

Functional Group	Reported Frequencies (in cm-1)	Observed Frequencies (in cm-1)
-NH	**3124**	**3052.92**
-C=O	**1816**	**1835.60**
-C-F	**1028**	**930.67**
-OH	**620**	**603.52**

Table 26 and 27 Showed that, functional group frequencies of API-1 and API-2 were in the reported range which indicates that the obtained samples of API'S was pure.

D. UV Spectroscopy

Table 6: Reported and observed wavelength of API'S.

Name	Reported Wavelength	Observed Wavelength
API-1	**245 nm**	**244.60 nm**
API-2	**294 nm**	**294.20 nm**

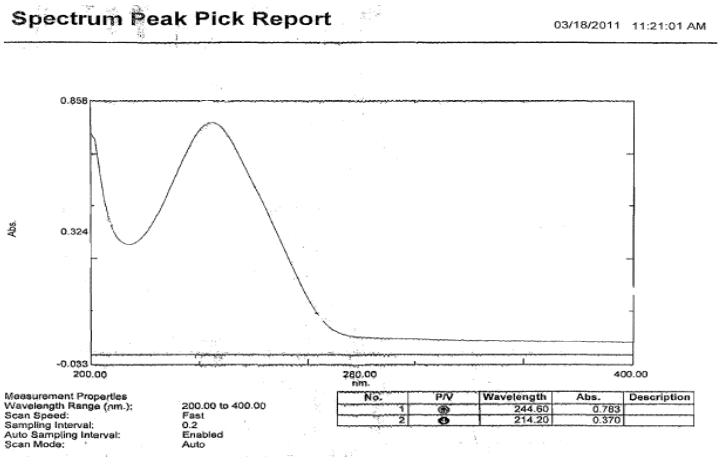


Figure 4: UV spectrum of API-1 in 0.1N HCl.

B. Solubility

API-1 was found to be freely soluble in ethyl alcohol, slightly soluble in acetone and practically insoluble in water.[18,19]

API-2 was found to be freely soluble in glacial acetic acid and slightly soluble in water, methanol.

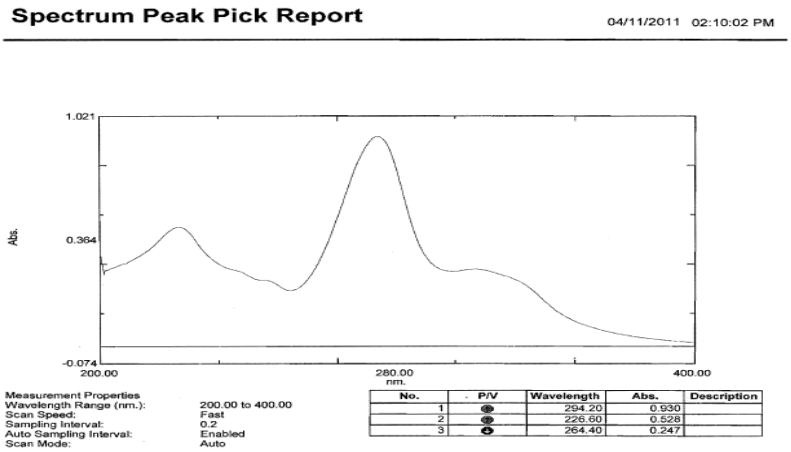


Figure 5: UV spectrum of API-2 in 0.1N HCl.

E. Loss on Drying

After drying 1.0 g of samples of API-1 and API-2 at 60^0C for 3 hours in hot air oven. It was found that weight of sample reduced to 0.82 g and 0.92 g. Sample passed the criteria for loss on drying (NMT 0.5% and NMT 0.2%). respectively.

- **Compatibility studies**

Preformulation studies were carried out to study the compatibility of pure drug API-1 and API-2 with disodium edetate, povidone K-30, citric acid and trisodium citrate prior to the preparation of ophthalmic suspension.[20,21,22]

The individual IR spectra of the pure drugs and the combination spectra of the drugs and other excipients are shown in the **Figure 16-22**, which indicate no interaction between API'S and excipients when compared with infrared spectrum of pure drug as all functional group frequencies were present.[23,24]

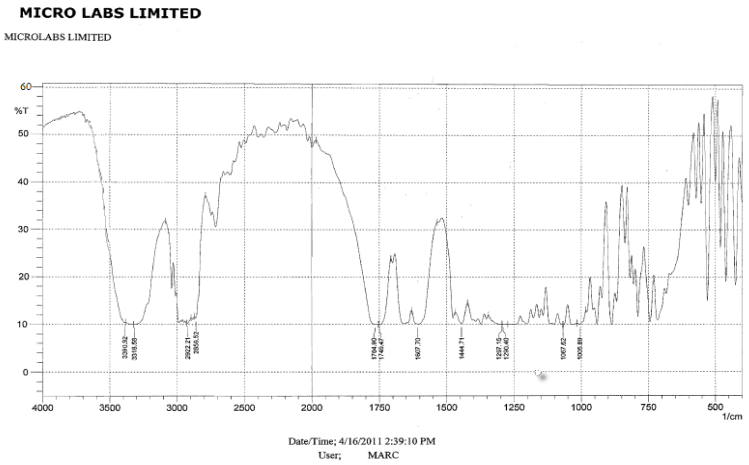


Figure 6: FT-IR spectrum of API-1.

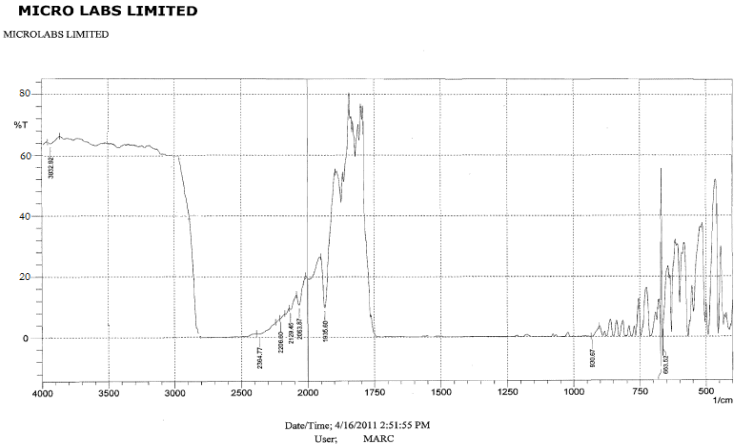


Figure 7: FT-IR spectrum of API-2.

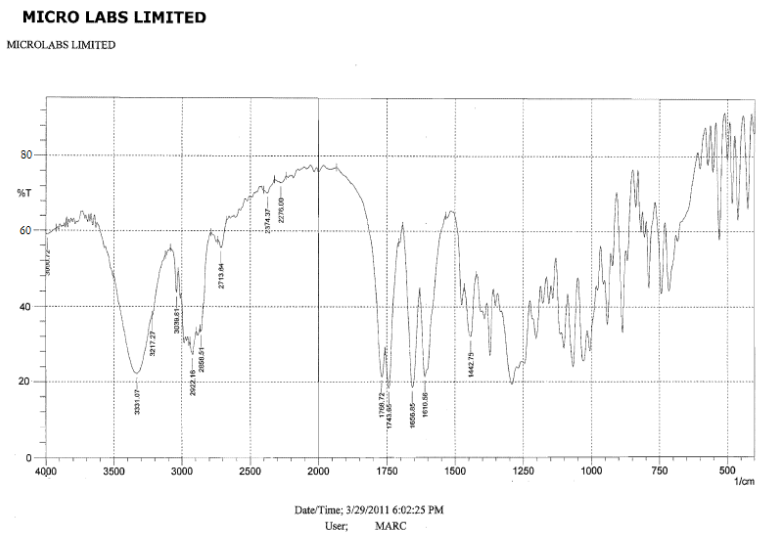


Figure 8: FT-IR spectrum of API-1 + API-2 combination.

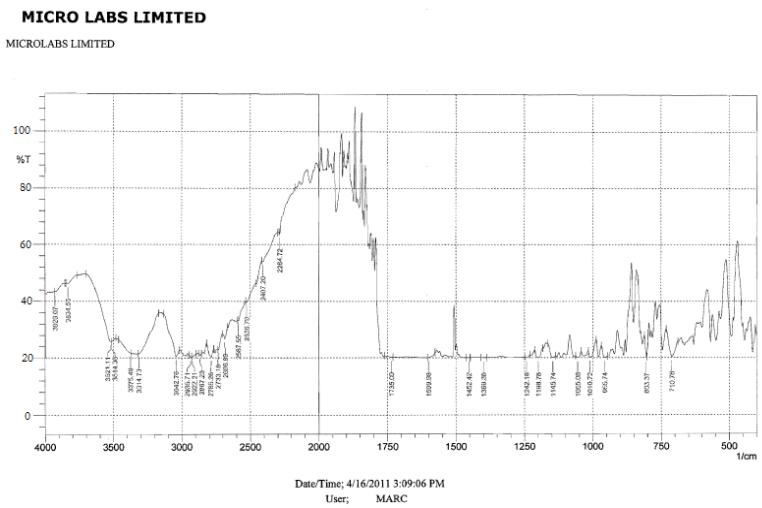


Figure 9: FT-IR spectrum of API-1 + API-2 + Disodium edetate.

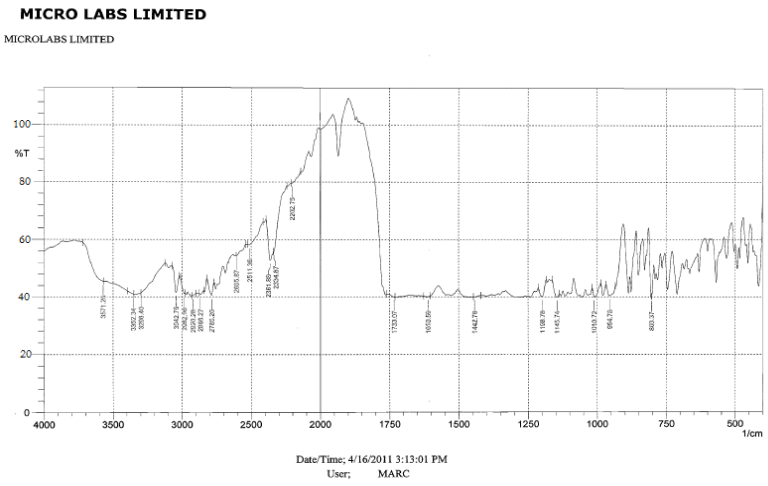


Figure 10: FT-IR spectrum of API-1 + API-2 + Povidone K-30.

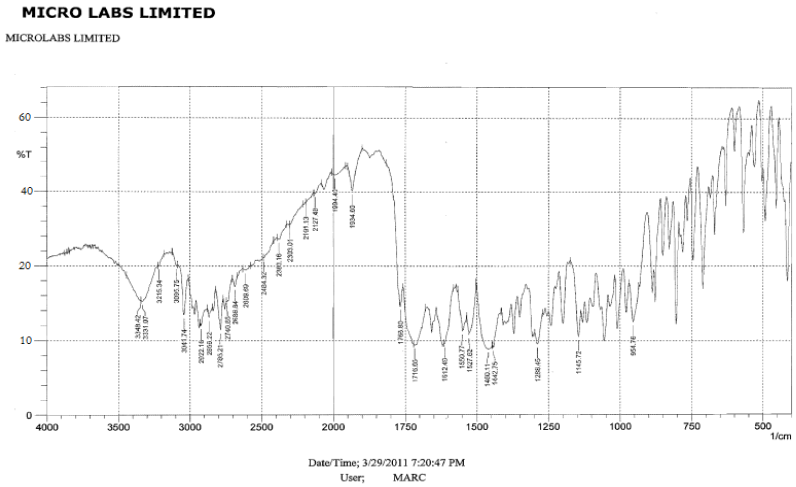


Figure 11: FT-IR spectrum of API-1 + API-2 + Citric acid.

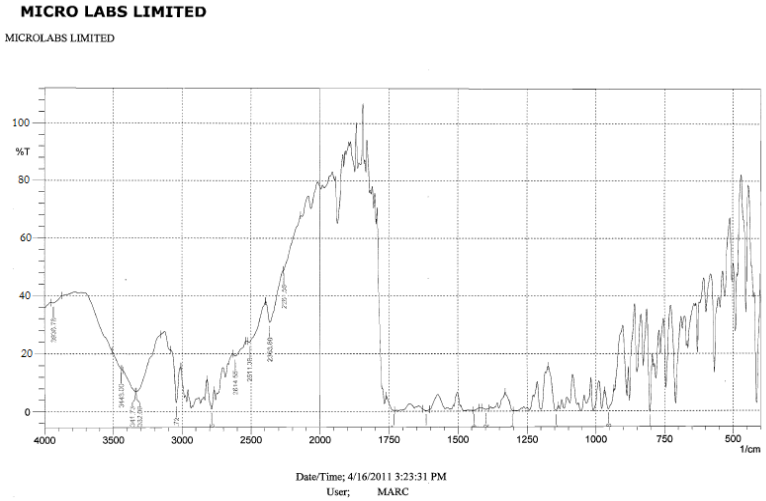


Figure 12: FT-IR spectrum of API-1 + API-2 + Trisodium citrate.

2. Standard calibration curve of API-1 and API-2

Table 29 shows the absorbance of API-1 and API-2 standard solutions containing 2-14 µg/ml of drug in tear fluid (pH 7.4). **Figure 23 and 24** shows a representative standard calibration curve with slope, regression coefficient and intercept respectively. The curve was found to be linear in the range of 2-14 µg/ml at λmax 245 nm (API-1) and 245 nm (API-2). The calculation of the drug content and in-vitro release are based on this calibration curve.[25,26]

Table 7: Standard calibration curve data of API-1 and API-2.

Concentration (µg/ml)	Absorbance at 245 nm	Absorbance at 294 nm
2	0.050	0.137
4	0.094	0.256
6	0.147	0.384
8	0.206	0.491
10	0.257	0.618
12	0.301	0.727
14	0.378	0.825

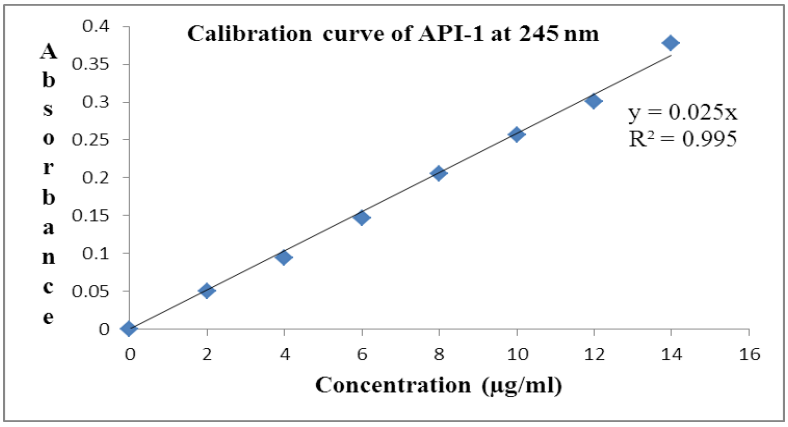


Figure 13: Calibration curve of API-1.

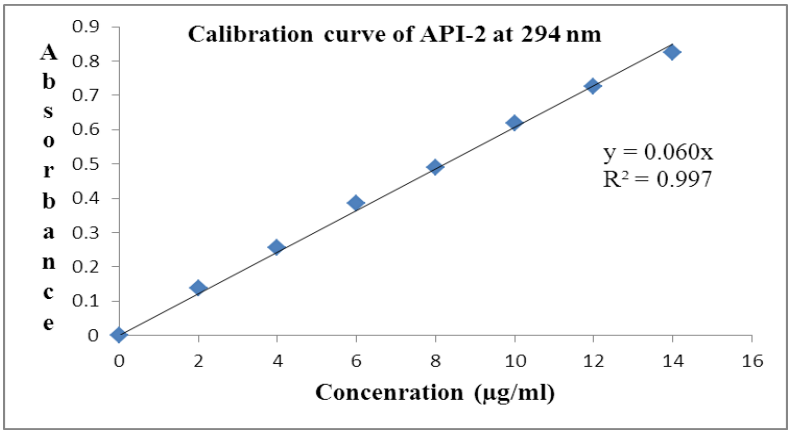


Figure 14: Calibration curve of API-2.

Table 8: Formulation table with ingredients.

Name of the Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Prednisolone	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%
Moxifloxacin	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%	0.3%
Benzalkonium Chloride	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%
Disodium EDTA	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%	0.01%
Citric acid	0.08%	0.08%	0.08%	0.08%	0.08%	0.08%	0.08%	0.08%	0.08%
Trisodium citrate	0.18%	0.18%	0.18%	0.18%	0.18%	0.18%	0.18%	0.18%	0.18%
Glycerin	2.5%	2.5%	2.5%	0.5%	1.5%	2.5%	2.5%	2.5%	2.5%
Tyloxapol	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%	0.01%	0.03%	0.05%
Povidone K-30	0.2%	0.4%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%
Hydrochloric acid	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH
Sodium hydroxide	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH	adjust pH
Water for Injection	Up to 10ml	Up to 10ml	Up to 10ml	Up to 10ml	Up to 10ml	Up to 10ml	Up to 10ml	Up to 10ml	Up to 10ml

3. Evaluation parameters

A. Appearance

The all formulations were found to be off white to pale yellow color redispersible suspension. Terminal sterilization by filtration gives sterile suspension but after sometimes form hard cake at bottom of containers, after shaking cake was dispersed.

B. pH

The pH of all formulations were found to be satisfactory and were in the range of 6.0-6.2. Sterilization by filtration had no effect on formulations.

C. Viscosity

Table 31 shows the viscosity values obtained for formulations TB-3, TB-4 and TB-5 using Brookfield DV-111+ rheometer at different angular velocity. Formulations were shear thinning and an increase in shear stress was observed with increase in angular velocity. The results obtained from the rheological study of prepared suspensions TB-3, TB-4 and TB-5 revealed that the viscosity decreases as the angular velocity increases.

Generally viscosity values in the range of 1-10 cps significantly improve the contact time in the eye. Higher viscosity values offer no significant advantage and have a tendency to leave a noticeable residue on the lid margin. The rheological profile of prepared suspension of corticosteroid and antibiotics is shown in table.

From the above studies, it was concluded that formulation TB-5 was shown best result and it was comparable to the reported value.

D. Osmolality

Table 32 shows the osmolality value for the formulations TB-6, TB-7 and TB-8 were obtained by using advance osmometer, model 3250. The value of each formulation compared with reported value and select best one.

The osmolality range for ophthalmic suspension is 250-310 mOsm/kg.

From the above result it was concluded that the formulation TB-8 was shown best result and it was comparable to reported value.

E. Redispersability

After storage at 4˚C for 1 week and 40˚ C for 1 week, each container required 6-8 inversions for complete removal of sediment adhere to containers and no any aggregates formed were found by visual observation.

From the above result it was concluded that the formulation TB-11 was shown best result and it was comparable to reported value.

F. Drop size

The drop size was estimated on average weight basis of drops of ophthalmic solution by using the AUW-220, Shimadzu balance.

All the formulations were found to be satisfactory and were in the range of 25-30 mg.

G. Drug Content

Table 9 shows the percent drug content for formulations. The drug content was found to be in acceptable range for all the formulations except TB-12 and was shown that decreased in the assay values of API'S due to terminal sterilization by autoclaved, it occurred due to degradation of API'S. Percent drug content of formulations were listed in following table.

Table 9: Result of assay value of API'S.

Formulation	API-1 (%)	API-2 (%)
F1 to F9 (Autoclave)	82.1	79.1
F1 to F9 (Filtration)	99.0	97.8

H. Preservative Content: Shows the percent preservative content for formulations. The preservative content was found to be in acceptable range for all the formulations except TB-12. Percent preservative.

I. *In Vitro* Release Studies

The release profile of a drug predicts how a delivery system might function and gives valuable insight into its *in vitro* behaviour. The formulations of corticosteroid and antibiotics suspension TB-14 was subjected to *in vitro* release studies. These *in vitro* release studies were carried out using simulated tear fluid (STF) of pH 7.4 as the dissolution medium. The drug release data obtained for formulations TB-14 was tabulated in **Table 36 and 37**. **Figure 27** shows the plot of cumulative percent drug released as a function of time for formulation TB-14. It was found that cumulative percent drug release were 97.86% and 99.56% of API-1 and API-2 for formulation TB-14 respectively after 120 minutes and 90 minutes respectively. The *in vitro* release data indicated that the formulation TB-14 showed better effect for desired time.

Table 10: Result of in-vitro drug release profile of API-1.

Time (min)	Absorbance at 245 nm	Conc. (µg/ml)	Drug release (mg/50ml)	% Drug release	% CDR
15	0.031	1.24	0.62	12.40	12.40
30	0.063	2.52	1.26	25.20	25.44
45	0.096	3.84	1.92	38.40	38.90
60	0.130	5.20	2.60	52.00	52.76
75	0.165	6.60	3.30	66.00	67.04
90	0.202	8.08	4.04	80.80	81.12
105	0.221	8.84	4.42	88.40	90.01
120	0.240	9.60	4.80	96.00	97.86

Table 11: Result of in-vitro drug release profile of API-2.

Time (min)	Absorbance at 294 nm	Conc. (µg/ml)	Drug release (mg/50ml)	% Drug release	% CDR
15	0.058	0.96	0.48	16.11	16.11
30	0.117	1.95	0.97	32.50	32.82
45	0.178	2.96	1.48	49.44	50.09
60	0.240	4.00	2.00	66.66	67.64
75	0.297	4.95	2.47	82.50	83.83
90	0.345	5.75	2.87	95.88	99.56

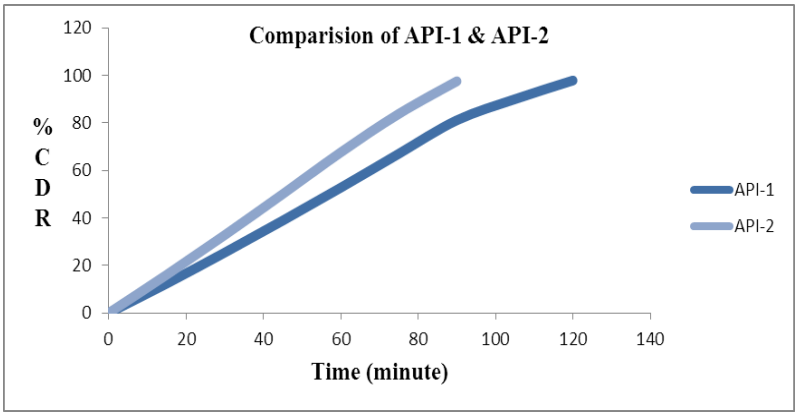


Figure 15: In-vitro dissolution comparision of API-1 and API-2.

J. Stability Studies

Prepared formulations TB-12 of corticosteroid and antibiotic suspension was subjected to pH stability and containers compatibility studies at 40°C± 2°C/ NMT 25 % RH, 60°C and 25°C/40% RH for a period of 1 week, 2week, and 1 month.

Table 12: Result of pH stability study.

Product: Corticosteroid and Antibiotic Ophthalmic Suspension (0.5% + 0.3%)										
pH stability data of Batch No.= TB-14										
Description	Off white to pale yellow colour solution.									
Storage condition	**Initial**	**40°C± 2°C/ NMT 25% RH**			**60°C**			**25°C±2°C/40%RH**		
Container type	6.00	BFS	3-piece HDPE	3-piece LDPE	BFS	3-piece HDPE	3-piece LDPE	BFS	3-piece HDPE	3-piece LDPE
1 week		6.09	6.08	6.02	6.10	6.05	5.99	6.00	6.03	5.99
2 week		6.02	5.97	6.01	6.21	6.22	6.02	6.03	6.05	6.00
1 month		6.12	6.15	6.04	6.25	6.24	6.05	6.05	6.09	6.01

From the above data 3-piece LDPE container was better compatible with formulation as compare to 3-piece HDPE and BFS containers. Also the pH remained within desired range for 3-piece LDPE containers.

Also prepared formulations TB-15 of corticosteroid and antibiotic suspension was subjected to stability studies at 40°C± 2°C/ NMT 25% RH, 25°C± 2°C/40% ±5% RH, 30°C± 2°C/65%±5% RH and 60°C for a period of 1 month, 3 month and 6 month as per ICH guidelines. The samples were withdrawn after period of 1 month, 3 month and 6 month and were evaluated for following parameters such as Description, Drug content, Preservative content, pH, Viscosity, Osmolality and Particle size.

The observations are shown in **Table 13**.

Table 13: Result of stability and containers compatibility studies.

Product: Corticosteroid and Antibiotic Ophthalmic Suspension (0.5% + 0.3%)						
Stability data of Batch No.= TB-15						
Description		Off white to pale yellow colored redispersible suspension filled in 5 ml 3-piece LDPE (opaque) containers.				
Stability Condition			40°C± 2°C/ NMT 25 % RH	25°C± 2°C/ 40 % ±5% RH	30°C± 2°C/ 65%±5% RH	60°C
Test parameters		Initial	1 Month	1 Month	1 Month	1 Month
Assay (%)	API-1	101.0	103.1	101.2	101.8	105.2
	API-2	98.8	99.8	98.9	99.2	100.4
Preservative content (%)		110.9	112	111.2	111.9	112.4
pH		6.00	6.84	6.07	6.24	6.98
Osmolality (mOsm)		299	305	300	302	316
Viscosity (cps)		1.92	2.84	2.05	2.22	2.96
Particle size (µm)		5.767	6.481	5.914	6.212	7.324

From the above data 25°C± 2°C/ 40% ±5% RH was shown better result than other stability condition as per specification and also shows better compatibility with 3-piece LDPE containers.

The all formulations were found to be off white to pale yellow color redispersible suspension. Terminal sterilization by filtration gives sterile suspension but after sometimes form hard cake at bottom of containers, after shaking cake was dispersed.

CONCLUSION

In the present study an attempt was made to develop and evaluate the ophthalmic suspension containing corticosteroid and antibiotic.

From the experimental finding, it is concluded that:
The melting point, solubility, IR spectrum and UV spectrum of API'S were found as per specification, thus indicating that the API'S were pure. The individual IR spectra of the pure drugs and the combination spectra of the drugs and other excipient indicated that no interaction between API'S and other excipients when compared with infrared spectrum of pure drug as all functional group frequencies were present. The pH of all formulations was found to be satisfactory in the range of 6.0-6.2, thus there would be no irritation to the patient upon administration of the formulation. The particle size analysis revealed that the particles were in nanometer range and all the formulations showed ideal surface morphology except F1 because after autoclave the particle size of formulation was increased and found to be 17.565 µm which was out of acceptable range. F1 was showed smallest particle size and discrete. All the formulations were shear thinning and an increase in shear stress was observed with increase in angular velocity. All the formulations except F6 and F7 showed osmolality within the range i.e. 250-320 mOsm/kg. The redispersability of all optimized formulations were found to be satisfactory, and it was found to be acceptable value as reported i.e. NMT 10 inversions after shaking. The drug content of the prepared formulation was within the acceptable range and ensures dose uniformity except F9. F9 was shown that decreased in the assay values of API'S due to terminal sterilization by autoclaved, it occurred due to degradation of API'S. The formulation F9 showed maximum drug content i.e. 101% and 98.9% of API-1 and API-2 respectively. The *in vitro* release studies indicated that the formulation F9 showed better effect for desired time and it was found that 120 minutes and 90 minutes for API-1 and API-2 respectively. From the stability studies as per ICH guidelines, it was confirmed that formulations of corticosteroid and antibiotic ophthalmic suspension remained more stable at ambient temperature (25°C) and relative humidity (40%) as compare to other stability conditions.

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