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# Design and development of loteprednol etabonate nanodispersion for ophthalmic drug delivery

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**Abstract---**Postoperative inflammation after cataract surgery can prolong visual recovery time, increase the treatment burden and elevate the risk of poor visual outcomes. Corticosteroids are potent anti-inflammatory agents that have been used successfully for decades to treat ocular inflammation. However, the side effects associated with topical corticosteroids including increased intraocular pressure, risk of cataract formation after long-term use, and decreased resistance to infection are of major concerns. Amongst the available topical corticosteroids Loteprednol Etabonate (LE), an ester-based corticosteroid has been selected for studies. The aim of the present study was to develop Loteprednol etabonate loaded nanodispersion for treatment of steroid responsive inflammatory conditions of eye with objectives of reducing the frequency of administration and increasing the solubility of drug. Non-solvent method was used to formulate nanodispersion. The formulation was assessed for particle size and polydispersity index, drug content, surface morphology, isotonicity, test of sterility, *in-vitro* & *ex-vivo* release. Mean particle size and PI of optimized batch was found to be 50±10nm and PI 0.2±0.1. No microbial growth was observed in optimized formulation during sterility testing and the formulation was isotonic when compared with marketed formulation and plain blood cells. The percent drug release at end of 30mins for optimized batch and marketed formulation was found to be 102±1% and 13±1%, respectively at the end of 30 mins. Overall results of present investigation suggest that Loteprednol Etabonate Nanodispersion formulation would reduce dosing frequency, improve therapeutic

efficacy and show greater potential for the treatment of post-operative inflammation after cataract surgery.

***Keywords*---**Loteprednol Etabonate (LE), Nanodispersion, Post-operative inflammation, Ophthalmic

## Introduction

Cataract surgery is the most common surgical procedure in ophthalmology practice, and the number of surgeries is assumed to increase in the future because cataracts are an age-related condition and life expectancy is increasing in most countries.[1] Vision impairment due to cataract inflicts 20 million individuals worldwide and represents nearly half the individuals with blindness. Since visual impairment from cataracts cannot be corrected by spectacle wear, contact lenses or medical treatment, cataract extraction is the only option for patients to clear optical media. As with any intraocular surgery, varying degrees of inflammation occur secondary to mechanical damage from the surgical tissue manipulation and a mild reaction to the foreign intraocular lens (IOL), which may result in significant postoperative inflammation. Postoperative visual symptoms attributed to inflammation include dryness, irritation, and pain, which may delay the postoperative recovery and affect patient satisfaction. Hence, addressing the inflammation is an important part of the postoperative care. [2]

Topical corticosteroids are widely used to address inflammation and improve patient outcomes following cataract surgery. Steroids and non-steroidal inflammatory drugs (NSAIDs) are used in the prophylaxis and treatment of pain and inflammation associated with cataract surgery, either alone or as combination therapy. [3]

Steroid medications used to treat postoperative pain and inflammations are available as topical drop formulations. However, patient compliance with prescribed eye drop regimens is often poor. A number of factors interfere with optimal patient adherence to their topical therapeutic regimens, such as: the complexity of the regimen, side effects (e.g., burning and stinging), forgetfulness (e.g., remembering to take the medication or shake the bottle for suspensions), and lack of manual strength/ dexterity. Complicated tapered dosing schedules, normally associated with topical steroids, may also present a challenge for the patient in terms of applying their medications as prescribed. [3]

Nano-size dispersion, which is an attractive dispersion system compared to the conventional micro-size emulsion system. It has, has been reported as an alternative for overcoming the bioavailability problems of compounds with poor solubility. It is a system consisting of nanosized particles surrounded with emulsifiers dispersed in an aqueous phase. Because of very small particle diameter of the nanosized particles it increases the surface area, thereby enhancing its penetration across cell membrane. [4]

In the current study, amongst the available Topical corticosteroids Loteprednol Etabonate (LE), an ester-based corticosteroid which contains an ester

functionality at C-20 rather than a ketone group, has been selected for further studies. LE lacks serious side effects as shown by other corticosteroids i.e. it does not have an IOP elevating effect and risk of cataract formation. Because of its rapid de-esterification to inactive metabolites, LE appears to have an improved safety profile when compared with other ketone corticosteroids, and it may be more suitable than ketone corticosteroids for the treatment of ocular inflammatory conditions in which long-term therapy is necessary. However, frequency of dosing for LE is quite high i.e four times daily at the beginning of 24 hours and continuing throughout the first 1-2 weeks of the post-operative period. [5]

The current study aims to develop Loteprednol etabonate loaded novel ophthalmic delivery systems for treatment of steroid responsive inflammatory conditions of eye that would exhibit improved bioavailability, reduced dosing frequency and better therapeutic efficacy over the existing marketed formulations. [6]

**Materials**

Loteprednol Etabonate was obtained from local market, Caproyl PGMC and Transcutol P was kindly gifted by Gattefosse, Mumbai, India; Cremophore RH-40 was kindly gifted by BASF, Mumbai; Polyethylene Glycol 400 (PEG 400) was procured from Molychem Pvt. Ltd.; all other chemicals and solvents were procurred from Molychem Pvt. Ltd.

**Methods**

**I. Preformulation Study**

Goal of preformulation study is to determine the necessary physicochemical parameters of drug substance and to establish its compatibility with excipients present in formulation.

**Standardization of Loteprednol Etabonate**

Loteprednol Etabonate was identified by IR spectra and confirmed by its melting point, by comparing the obtained result with standard and were found to be within the limits as per specifications.

**II. Effect of Formulation Matrix on UV Absorbance**

For studying the effect of formulation matrix on UV Absorbance, the UV scan of Loteprednol etabonate, placebo nanodispersion and Loteprednol etabonate loaded nanodispersion were taken and examined for excipient interference, if any.

**III. Drug-Excipient Compatibility Study by Differential Scanning Calorimeter (DSC)**

DSC of Loteprednol Etabonate, drug loaded formulation and blank formulation was carried out for determining drug–excipient compatibility. The thermal analysis was performed in a nitrogen atmosphere at a heating rate of 10ºC/min over a temperature of 30ºC to 350ºC.

**IV. Analytical method development:**

UV spectrophotometric method for determination of Loteprednol Etabonate at $\lambda_{max}$ 243 nm was developed and standardized in Methanol and Simulated Tear Fluid (STF) pH-7.4. The developed analytical method was employed for

determination of drug content in the formulation as well as in diffusion studies.

**Formulation and Development of Loteprednol Etabonate Loaded Nanodispersion**

**1. Solubility study of drug in various oils, surfactants, co-surfactants and co-solvents** [7]

The selection of the components to be used in formulating Nanodispersion was done based on the solubility of LE in various oils, surfactants & co-surfactants. A visual observation was made for complete solubility of first aliquot (10 mg) of LE in various oils. In oils which showed complete solubility of first aliquot of LE (10 mg), the second aliquot of LE (10 mg) was added followed by heating and subjecting it to cyclomixing for 4-5 mins. This process was repeated for number of times till the oils get saturated with LE. The total amount of LE to make the oil saturated was noted and approximate solubility of LE in oil was determined. Only few promising oils showing appreciable solubility were selected and studied further to measure quantitative solubility of drug in selected vehicles. In a similar manner solubility study for various surfactants, co-surfactants and co-solvent were carried out.

Table 1: List of Oils, Surfactants, Co-Surfactants & Co- Solvents Screened For Solubility of Le

| Drug | Oils | Surfactants | Co-surfactants | Cosolvent |
|---|---|---|---|---|
| LE | Castor oil, coconut oil, tea tree oil, soyabean oil, groundnut oil, sunflower oil, corn oil, sesame oil, cotton oil, Oleic acid, Capmul MCM NF, Campul MCM EP,captex 200,captex 355,captex 355 EP/NF,captex 300, Isopropyl myristate , Caproyl PGMC,Caproyl PEG 860,Caproyl 90,Maisine CC,Miglyol812,Peceol, Linoliec acid, Neobee M-5, Aconon MC8-2 | Cremophor-RH 40, Cremophor EL, Tween20, Span20, Labrafil LWL1349, Labrafil M 1944CS, Labrafil M 2125CS | PEG 400 & PEG 600 | Transcutol P |

**2. Preparation of Nanodispersion**

Loteprednol Etabonate has a high oil/water partition coefficient and so an attempt was made to dissolve it in the oil phase. Therefore, Caproyl PGMC was chosen as carrier oil. Cremophore RH-40, with HLB (hydrophilic-lipophilic balance) value of 16, was selected as emulsifier. To reduce interfacial tension in

order to obtain a stable formation, PEG 400 as co-surfactant together with an emulsifier was used. Transcutol P was selected as a co-solvent was further added for increasing solubility of LE. In this method, LE was dissolved separately in oil, surfactant, co-surfactant and co-solvent. Later quantity equivalent to 1gm of oil: surfactant: co-surfactant: co-solvent was weighed. Caproyl PGMC as carrier oil, Cremophore RH-40 as emulsifier and PEG 400 as co-surfactant with a ratio provided sufficient protection for oil particles. Oil phase was added drop wise to buffer (pH 5) as the aqueous phase in order to produce a nanodipsersion.

Table 2: Ingredients and Activity in Formulation

| Ingredients | Role |
|---|---|
| Loteprednol Etabonate | Drug |
| Caproyl PGMC | Oil phase |
| Cremophore RH-40 | Surfactant |
| PEG 400 | Co-surfactant |
| Transcutol P | Co-solvent |
| Benzalkonium Chloride | Preservative |
| Buffer | Vehicle |

**3. Optimization of Nanodispersion**

Nanodispersion formulation was optimized by changing various factors that would affect its formation.

**i. By changing the amount of co-solvent**

Trials were taken by changing the amount of Co-solvent to check for formation of nanodispersion. Batches that showed good particle size and Polydispersity index were selected further.

**ii. By changing the volume of Formulation**

Volume of final formulation was adjusted in an attempt to further increase the dose of drug.

**Evaluation and characterization of Loteprednol Etabonate Loaded Nanodispersion.**

The prepared formulations were evaluated for pH, drug content, % Transmittance, Particle size, Isotonicity testing, Test for sterility, surface morphology, *in-vitro* Diffusion Study & *ex-vivo* Diffusion Study. [8]

***In-Vitro Diffusion Study of Loteprednol Etabonate Loaded Nanodispersion***

The *in-vitro* diffusion study was carried out using Franz diffusion cell. The receptor compartment was filled with 18 ml of Simulated Tear Fluid pH 7.4. Nanodispersion sample was kept in donor compartment over a dialysis membrane. The aliquot of 1ml was taken in suitable interval of time and analyzed using UV spectrophotometer. .[9]

***Ex-Vivo* Diffusion Study**

In *ex -vivo* diffusion study procedure similar to *in- vitro* release study was followed. To study the permeation across the ocular membrane, goat cornea was used. Whole cornea of goat was be procured and transported to laboratory in normal saline maintained at 4ºC. The goat cornea was washed with saline maintained at

$4^0$C. The washed cornea was then kept in freshly prepared simulated tear fluid pH 7.4 maintained at $4^0$C till use. The study was carried out by using Franz diffusion cell in such a way that corneal side continuously remained in contact with the formulation in the donor compartment. [9]

**Test for Sterility** [10]

1. **Preparation of culture medium**
   a) Nutrient broth was used to detect the growth of microorganism; Nutrient broth was dissolved in water. This solution was sterilized in an autoclave at 15 LBS pressure, 121°C for 30 min. The medium was freshly prepared and allowed to cool just prior to use. It is then transferred to test tube.
   b) SBCD (Soybean casein digest medium) medium was used to detect the growth of aerobic bacteria and fungi. 7.25 g of readymade SBCD was dissolved in 250 ml of purified water and this was sterilized in an autoclave at 115°C for 30 min. The medium was freshly prepared and allowed to cool just prior to use. It is then transferred to test tube.
2. **Procedure**
   Sterile formulation was taken in to laminar airflow sterile formulation removed from vial with the help of syringe.1 ml of formulation is placed in test tube containing culture media. The media was kept for incubation for 7 days. Media was kept for incubation for 14 days. Media was observed every day for microbial contamination and compared with the negative control.

**Result and Discussion**

**Preformulation Study**
**Standardization of LE**

**i. Fourier Transformation Infrared Spectroscopy (FTIR)**

Characteristic peak of pure Loteprednol Etabonate were observed in below mentioned spectra which confirms the identification of the corticosteroid. FTIR of Loteprednol etabonate is given in figure below.

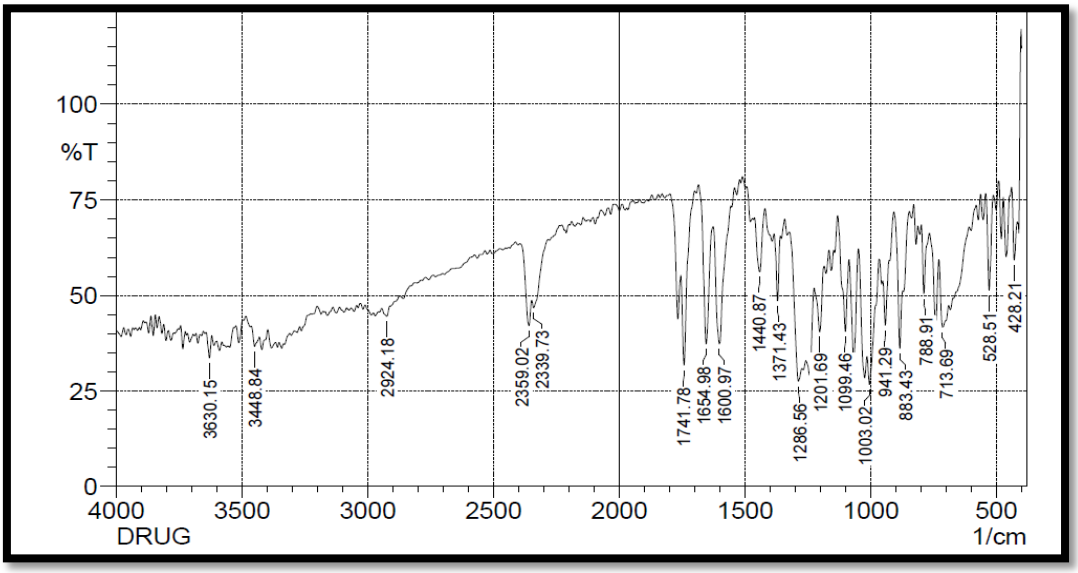



Figure 1: Ftir Spectra of Loteprednol Etabonate

Table 3: Characteristic Stretching Vibrations for Loteprednol Etabonate

| Sr. no | Wavenumber $cm^{-1}$ | Vibrations |
|---|---|---|
| 1. | 1741.78 | C-O ester stretch |
| 2. | 1600 | C=O stretch |
| 3. | 1654.98 | C=C stretch |
| 4. | 883.43 | C-C aromatic stretching |
| 5. | 1286.56 | C-O stretch |

**ii. Melting Point of Loteprednol Etabonate**

Melting point of Loteprednol Etabonate was found to be 237.4 $^0$C.

**iii. Differential Scanning Calorimetry**

The characteristic endothermic peak for Loteprednol Etabonate was obtained at 237.4 $^0$C indicating melting temperature of Loteprednol Etabonate. The DSC thermogram of Loteprednol Etabonate is shown in figure 2.

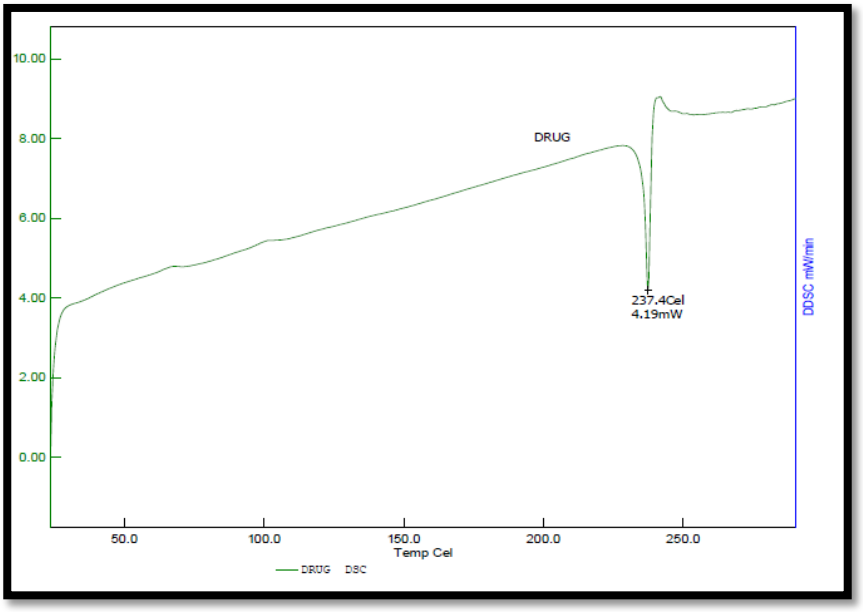



Figure 2: Dsc Thermogram Of Le

**III. Drug – Excipient Compatibility Study by Differential Scanning Calorimetry**

The DSC thermogram of plain Loteprednol Etabonte showing endothermic peak at 237.4 $^{0}$C was compared to that obtained with Loteprednol Etabonate loaded nanodispersion. The absence of melting endothermic peak of LE at its melting temperature suggests that drug was entrapped in oil globules. DSC thermogram of Loteprednol Etabonate, Loteprednol Etabonate loaded formulation and Placebo formulation is shown in figure 2, figure 3 & figure 4 respectively.

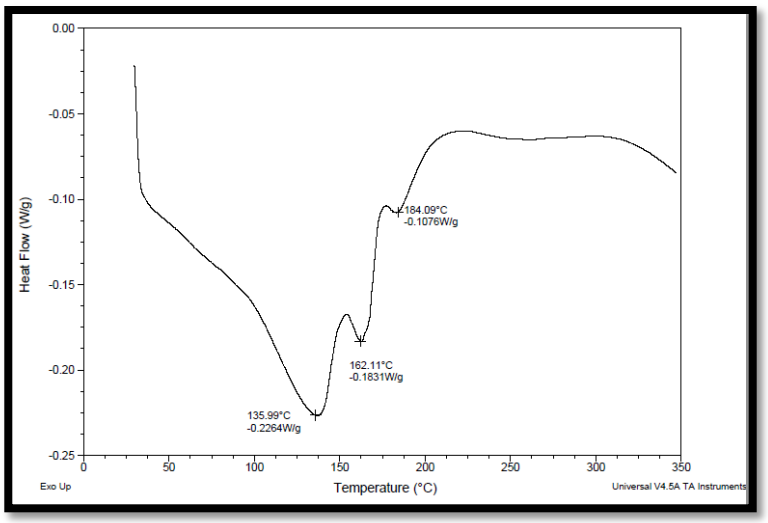



Figure 3: Dsc Thermogram Of Loteprednol Etabonate Loaded Formulation

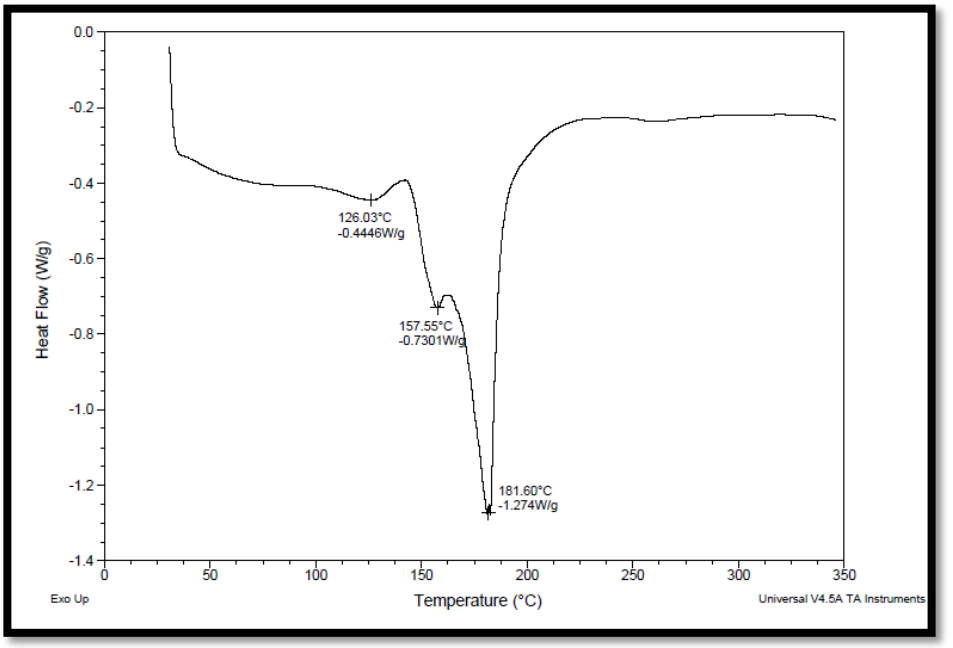



Figure 4: Dsc Thermogram Of Placebo Formulation

### 3. Effect of Formulation Matrix on UV absorbance

For examining interference in absorbance of Loteprednol Etabonate in formulation system, the UV scan of drug loaded formulation and placebo formulation were taken and compared. No interference was observed in case of placebo nanodispersion. The overlay spectra of and drug loaded nanodispersion and placebo nanodispersion is shown in figure 5.

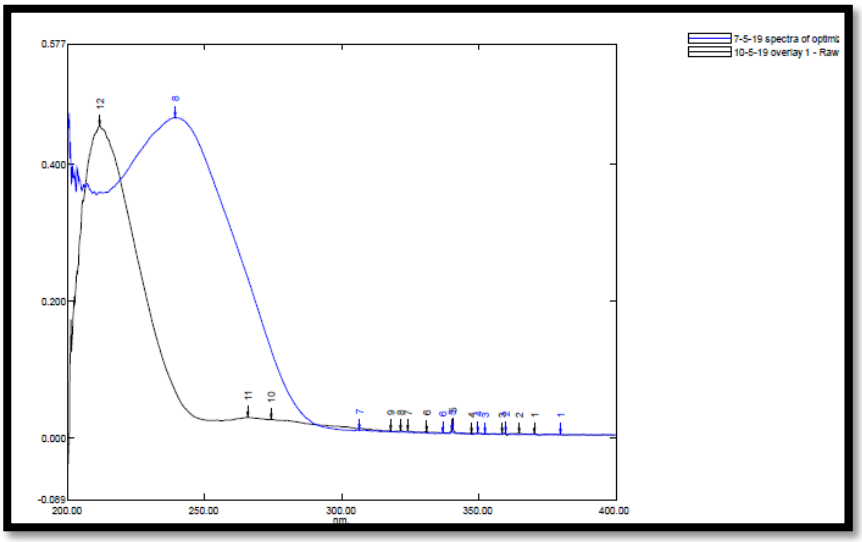



Figure 5: Overlay Spectra Of Drug Loaded And Placebo Formulation

**Formulation and Development of Loteprednol Etabonate Loaded Nanodispersion:**

**1. Solubility study of drug in various oils, surfactants, co-surfactants and co-solvents**

Based on literature survey, different oil, surfactants, co-surfactants were screened in preliminary trials to determine approximate solubility of LE in each different phase by visual observation. Amongst different oils that were screened LE showed good solubility in Tea tree oil & Caproyl PGMC and were able to solubilize an appreciable quantity of LE as compared to other oils. Tea tree oil showed excellent solubility of LE i.e. more than 50 mg/gm but it was not used in further trials as it is reported to show irritation to eyes. Based on the approximate solubility, Caproyl PGMC was then chosen as the oil phase. From the different surfactants and co-surfactants that were screened LE showed good solubility in Cremophore RH-40 and PEG 400, so these were selected as the surfactant and co-surfactant. Finally in order to further increase the solubility of LE, co-solvent was also used.

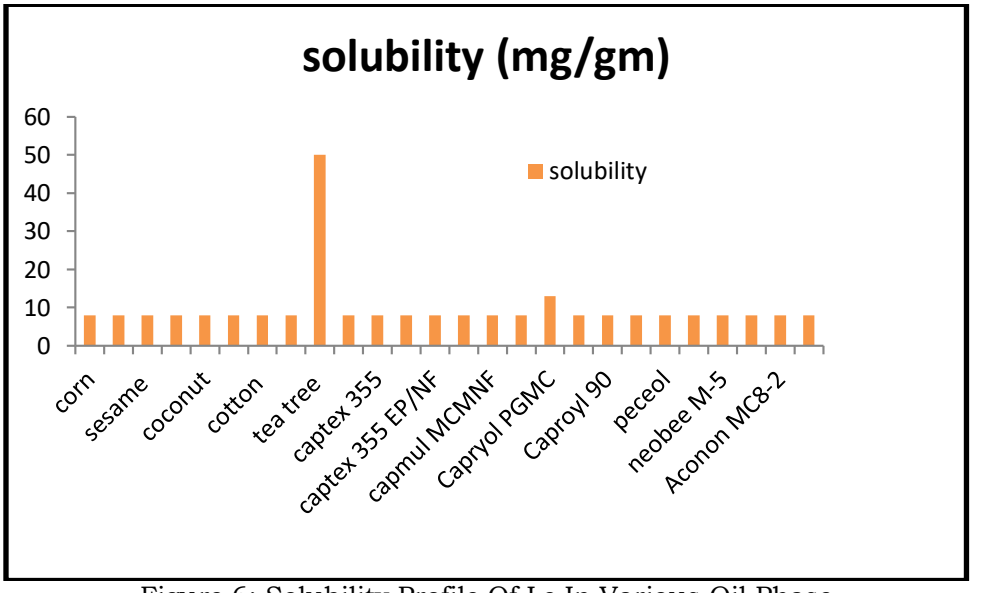



Figure 6: Solubility Profile Of Le In Various Oil Phase

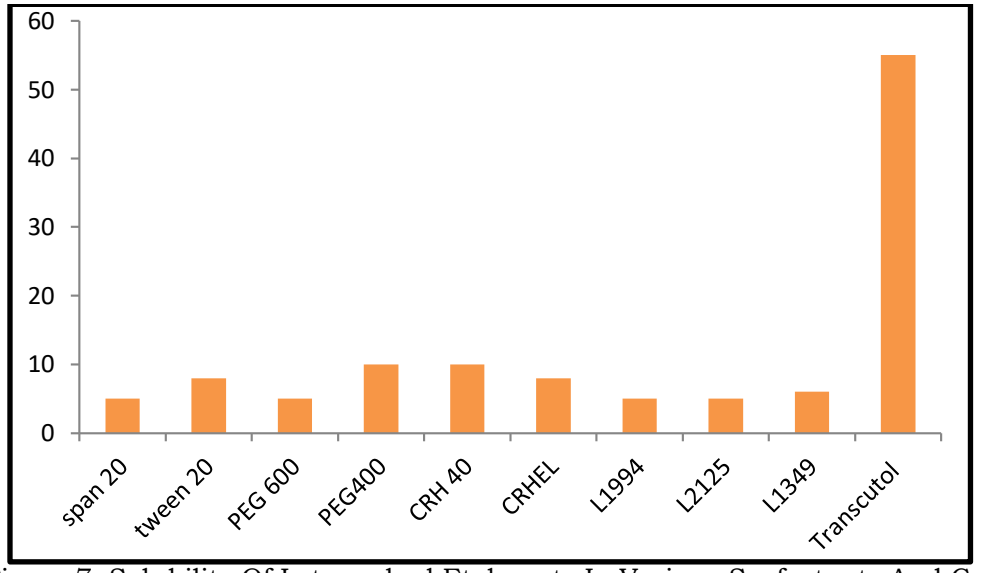



Figure 7: Solubility Of Loteprednol Etabonate In Various Surfactants And Co-Surfactants

**2. Preparation of Nanodispersion**

Different systems of this combination were prepared by varying concentration of selected oil, surfactant and co-surfactant. All the systems were evaluated for formation of nanodispersion by diluting 1 gm of each mixture by 50 ml of buffer (pH 5) in volumetric flask. Buffer of pH 5 was used in order to stabilize the formulation for a longer period of time. The obtained nano dispersion was allowed to stand for 2 hr. and evaluated for their Particle size and Polydispersity index (PI) was noted. Systems that showed particle size less than 1000nm clear and transparent or slightly bluish solutions were considered as nanodispersion producing systems, while the systems which produced white or non-clear turbid emulsion are considered as coarse emulsion producing systems.

Table 4: Formulation Of Nanodispersion By Changing Ratio Of Oil: Surfactant: Cosurfactant

| Sr.no | Batches | % Oil | % Surfactant | % Co-surfactant | % Co-solvent | Particle size | PI |
|---|---|---|---|---|---|---|---|
| 1. | X1 | 32.94 | 40 | 26 | 14 | 31 | 0.208 |
| 2. | A1 | 50 | 45 | 5 | 14 | 44.06nm | 0.323 |
| | A2 | 50 | 40 | 10 | 14 | 1.4nm (unstable) | 4.507 |
| | A3 | 50 | 35 | 15 | 14 | 142.3nm | 0.433 |
| | A4 | 50 | 30 | 20 | 14 | 116nm | 0.658 |
| | A5 | 50 | 25 | 25 | 14 | 3613nm | 0.330 |
| 3. | B1 | 60 | 35 | 5 | 14 | 888.4nm | 0.512 |
| | B2 | 60 | 30 | 10 | 14 | 107.1nm | 0.400 |
| | B3 | 60 | 25 | 15 | 14 | 113.5nm | 0.277 |
| | B4 | 60 | 20 | 20 | 14 | 153.8nm | 0.401 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 4. | C1 | 70 | 25 | 5 | 14 | 124.9nm | 0.295 |
| | C2 | 70 | 20 | 10 | 14 | 1031.1nm | 0.328 |
| | C3 | 70 | 15 | 15 | 14 | 2850.3nm | 0.766 |
| | C4 | 70 | 10 | 20 | 14 | 3041.4nm | 1.490 |
| 5. | D1 | 80 | 17 | 3 | 14 | 2268.2nm | 0.625 |
| | D2 | 80 | 15 | 5 | 14 | 2248.9nm | 0.855 |
| | D3 | 80 | 10 | 10 | 14 | 3358.1nm | 2.240 |

## 4. Optimization of Nanodispersion

Nanodispersion formulation was optimized with respect to amount of cosolvent and volume of water. It was observed that there was decrease in particle size and improvement in PI indicating uniformity of particles as shown in table 5. Volume of formulation in an attempt to further increase the drug loading and was optimized as shown in table 6. Composition of optimized batch **$A2_2$** diluted up to 30 ml with water gave optimum results with respect to particle size and PI.

Table 5: Formulation Of Nanodispersion By Changing Ratio Of Co-Solvent

| Sr.no | Batches | %Oil | %Surfactant | %Co-surfactant | %Co-solvent | | PI |
|---|---|---|---|---|---|---|---|
| 1. | $A1_1$ | 50 | 45 | 5 | 15 | 55.2 | 0.40 |
| 2. | $A2_2$ | 50 | 45 | 5 | 19 | 50.1 | 0.31 |

Table 6: Formulation Of Nanodispersion By Changing The Volume Of Formulation

| Sr.no | Batches | %Oil | % Surfactant | % Co-surfactant | %Co-solvent | Vol. made upto | Particle size(nm) | PI |
|---|---|---|---|---|---|---|---|---|
| 1. | $A2_2$ | 50 | 45 | 5 | 19 | 20 | - | - |
| 2. | $A2_2$ | 50 | 45 | 5 | 19 | 25 | - | - |
| 3. | $A2_2$ | 50 | 45 | 5 | 19 | 30 | 52 | 0.35 |
| 4. | $A2_2$ | 50 | 45 | 5 | 19 | 35 | 51.7 | 0.38 |
| 5. | $A2_2$ | 50 | 45 | 5 | 19 | 40 | 83.8 | 1.54 |
| 6. | $A2_2$ | 50 | 45 | 5 | 19 | 45 | 88 | 0.54 |
| 7. | $A2_2$ | 50 | 45 | 5 | 19 | 50 | 52 | 0.36 |

**Evaluation and characterization of Loteprednol Etabonate Loaded Nanodispersion.**

- **Particle size and Polydispersity Index (PI)**

The most important parameter, which needs to be monitored during nanodispersion formulation is the particle size and size distribution of nanodispersion. The size and size distribution determines there *in vivo* or *ex vivo* performance. For optimized batch the mean particle size was found to be 52±10nm nm for optimized batch and polydispersity index was found to be 0.355±0.1. Low polydispersity index indicates particle size uniformity within the formulation.

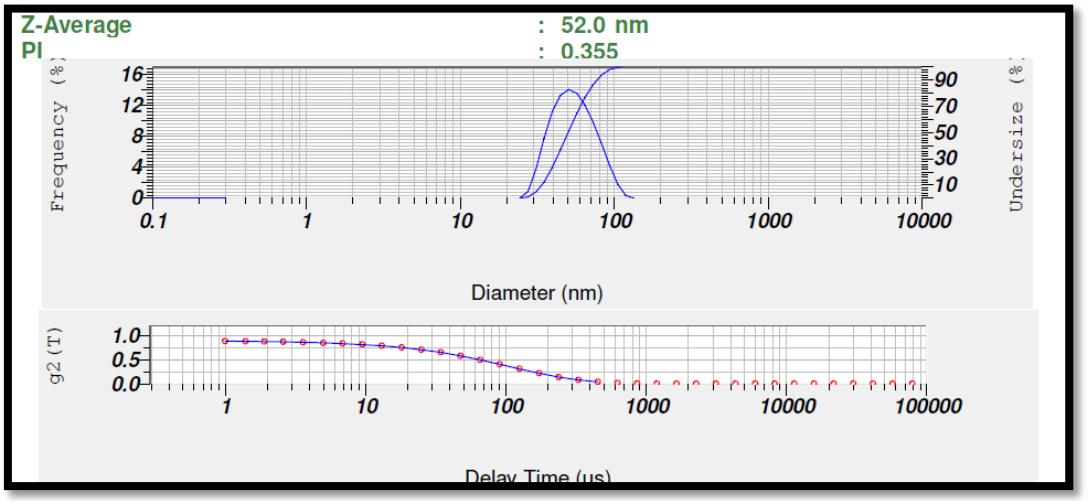



Figure 8: Graph Of Particle Size Distribution Of Optimized Batch

- **Drug content**
  The drug content of Loteprednol Etabonate loaded nanodispersion was found to 97±%.
- **% Transmittance**
  The % transmittance for optimized batch was found to be >70%.
- **Surface Morphology**
  CRYO-SEM was performed on the optimized Loteprednol Etabonate loaded nanodispersion. The results of CRYO-SEM confirm spherical structure of nanodispersion.

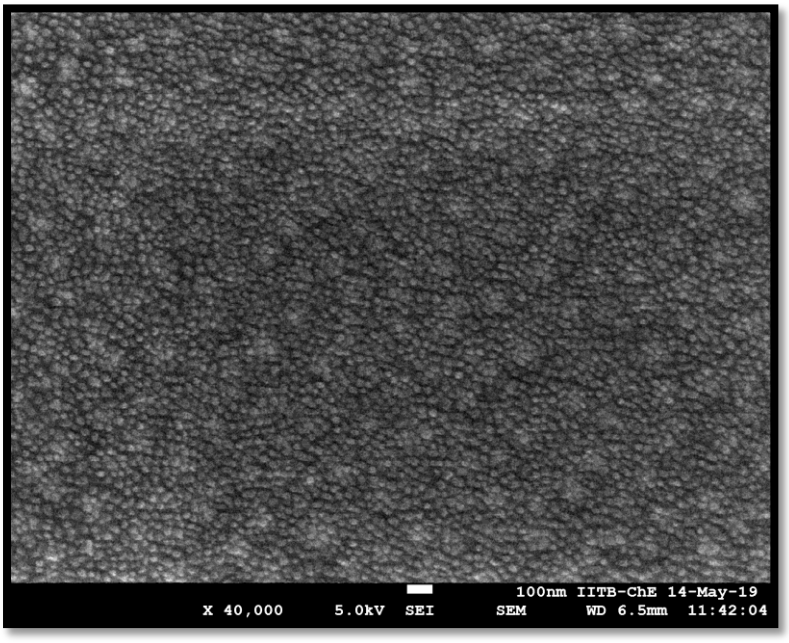
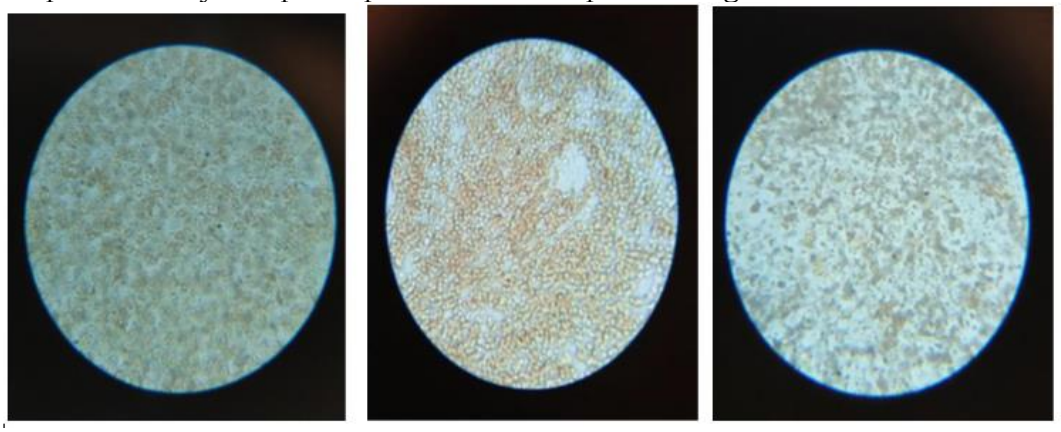



Figure 9: Cryo- Sem Images Of Loteprednol Etabonate Loaded Nanodispersion

- **Isotonicity Testing**
  The optimized formulation was subjected to isotonicity study and exhibited no change in the morphology of blood cells (bulging or shrinkage), which reveals the isotonic nature of the formulation and compared with standard marketed ophthalmic eye drop and plain blood as depicted in figure 10.



A. Plain blood B. Test Formulation C. Marketed preparation

Figure 10: optical microscopic images a. Plain blood b. Test formulation c. Marketed preparation

***In-Vitro Diffusion Study of Loteprednol Etabonate Loaded Nanodispersion***

The % Cumulative Release of optimized batch at the end of 30mins across dialysis membrane for test and marketed formulations was found to be 102.04±1% & 13.86±1 % respectively In vitro release data indicated that test formulation

showed a better effect than the other Marketed formulation. The initial burst release of the drug could be explained by the fact that since it is a nanodispersion the nanosized particle could easily diffuse across membrane resulting into complete diffusion at the end of 30 mins.

Table 7: *in-vitro* percent cumulative release of test and marketed formulation

| Time (mins) | % CR (test) | % CR (formulation) |
|---|---|---|
| 0 | 52.06 | 0.2 |
| 10 | 74.14 | 3.1 |
| 15 | 86.02 | 4.5 |
| 30 | 102.02 | 13.86 |

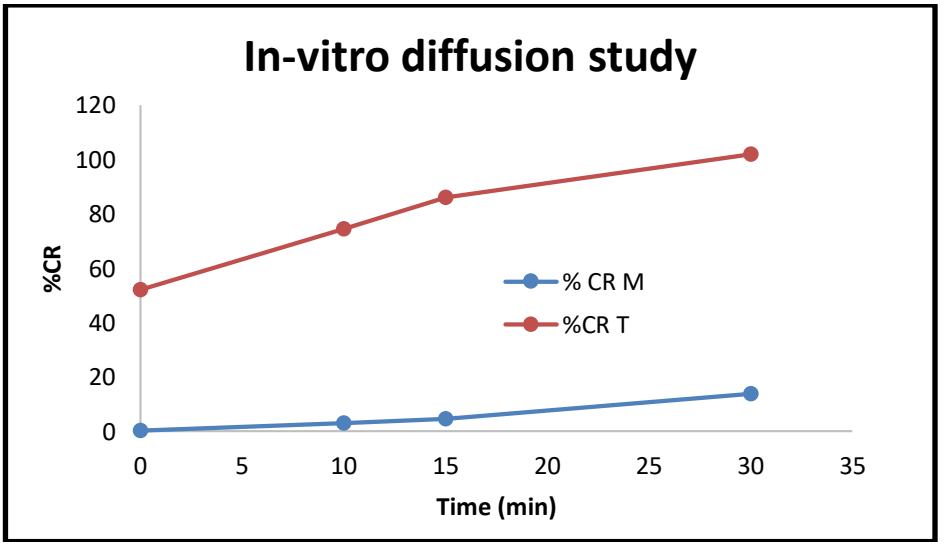



Figure 11: *In- Vitro* Diffusion Profile Of Test And Marketed Formulation

- ***Ex-Vivo* Diffusion Study**

  The ex vivo transcorneal permeation of test formulation and Marketed formulation was conducted on excised goat cornea. The % cumulative release across goat cornea was found to be 14.71±1% and 103.44±10.5 %, respectively. The nanodispersion showed higher permeation across the cornea due to improved solubility and increased drug surface area Thus it can be concluded that nano-sized dispersion can provide better penetration across cornea**.**

Table 8: *Ex-Vitro* Percent Cumulative Release Of Test And Marketed Formulation

| Time (mins) | % CR (test) | % CR (formulation) |
|---|---|---|
| 0 | 55.74 | 0.8 |
| 10 | 77.53 | 4.2 |
| 15 | 87.43 | 6.5 |
| 30 | 103.44 | 14.71 |

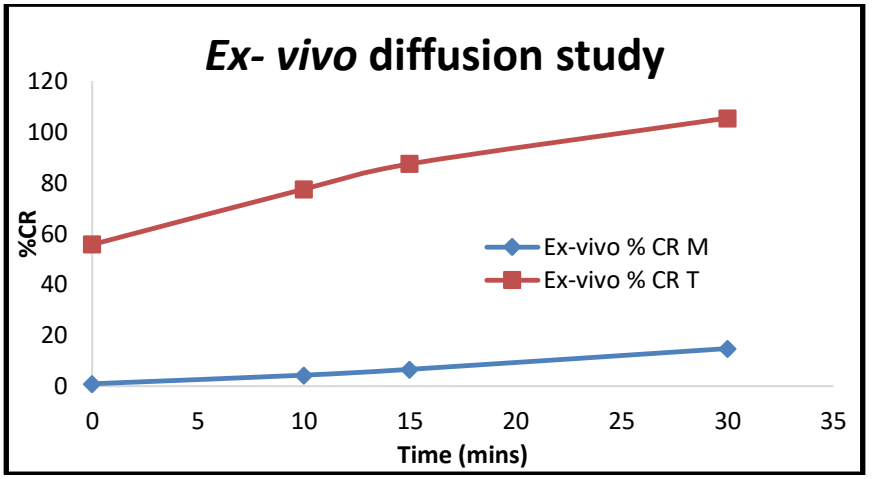



Figure 12: *Ex-Vivo* Diffusion Profile Of Test And Marketed Formulation

- **Test for Sterility**

  Sterility is one of the most vital requirements for an ophthalmic preparation. The tests for sterility are intended for detecting the presence of viable forms of microorganisms in ophthalmic preparations. The principle governing these tests is that if the microorganisms are placed in a medium which provides nutritive material and water, kept at a favorable temperature, the organisms will grow and their presence can be indicated by turbidity in the originally clear medium. In the present study, two media namely, Alternate Thioglycolate medium (ATGM) and soyabean-casein digest medium (SBCD) were used to investigate the presence/absence of aerobic, anaerobic bacteria and fungi, in the formulated nanodispersion

Table 9: Sterility Test Observations In (Soyabean Casein Digest Media) SCDM

| Samples | Day 1 | Day 2 | Day 3 | Day 5 | Day 7 | Day 14 |
|---|---|---|---|---|---|---|
| Negative control | - | - | - | - | - | - |
| Formulation | - | - | - | - | - | - |

✓ Presence of Microbial Growth - Absence of Microbial Growth

Table 10: Sterility Test Observations In Nutrient Broth

| Samples | Day 1 | Day 2 | Day 3 | Day 5 | Day 7 | Day 14 |
|---|---|---|---|---|---|---|
| Negative control | - | - | - | - | - | - |
| Formulation | - | - | - | - | - | - |

✓Presence of Microbial Growth - Absence of Microbial Growth

Since there was no growth in negative control and Formulation that is test solution, Formulation passes the test for sterility hence it was found that formulations were sterile.

**Summary and Conclusion**

In the current study Loteprednol etabonate loaded novel ophthalmic delivery systems for treatment of steroid responsive inflammatory conditions of eye were successfully developed. It has more potential over the existing marketed formulations as exhibited improved solubility and enhanced transcorneal permeation. Overall results of present investigation suggest that Loteprednol Etabonate Nanodispersion formulation would reduce dosing frequency, improve therapeutic efficacy and show greater potential for the treatment of post-operative inflammation after cataract surgery.

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