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# Formulation Development of Etoricoxib Cubosomal Gel for Topical Delivery

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## ABSTRACT:
This study aimed to design and evaluate a topical cubosomal gel of Etoricoxib to overcome the limitations associated with its oral administration, particularly gastrointestinal side effects. Cubosomes were prepared using a top-down approach with glyceryl monooleate and poloxamer 407, followed by optimization through a Box–Behnken experimental design. The optimized formulation showed nanosized particles (~347 nm) with high drug entrapment efficiency (86.83%) and satisfactory stability, as confirmed by zeta potential analysis. The optimized cubosomal dispersion was further incorporated into a Carbopol 934 gel and assessed for key parameters such as pH, viscosity, spreadability, and drug content, demonstrating suitability for topical use. Drug release studies indicated a sustained release pattern governed by diffusion mechanisms. In addition, ex-vivo permeation studies revealed improved skin penetration compared to a conventional marketed gel. The findings suggest that the developed cubosomal gel can enhance localized drug delivery while minimizing systemic exposure. This formulation approach offers a promising alternative for effective and safer management of rheumatoid arthritis through topical therapy.

## INTRODUCTION:
Nanotechnology has significantly advanced drug delivery by improving solubility, stability, and targeted action of therapeutic agents. Nanoparticles, typically within the size range of 1–100 nm (and up to 500 nm), possess unique properties due to their high surface area and tunable structure. Among various nanocarriers, cubosomes have gained attention as lipid-based nanoparticles with a three-dimensional bicontinuous cubic structure, enabling the encapsulation of hydrophilic, hydrophobic, and amphiphilic drugs along with controlled drug release.

Cubosomes are biocompatible, stable, and capable of enhancing drug permeation, making them suitable for topical delivery systems. Topical administration offers advantages such as localized drug action, reduced systemic side effects, and improved patient compliance, particularly in the treatment of inflammatory conditions.

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Rheumatoid arthritis is a chronic inflammatory disorder associated with joint damage and increased levels of pro-inflammatory cytokines. Etoricoxib, a selective COX-2 inhibitor, is widely used for its anti-inflammatory effects but may cause adverse effects when administered orally. Therefore, developing a topical delivery system can help minimize systemic exposure.

In this context, the formulation of an Etoricoxib-loaded cubosomal gel represents a promising strategy for achieving controlled drug release, enhanced skin permeation, and improved therapeutic outcomes in the management of rheumatoid arthritis.

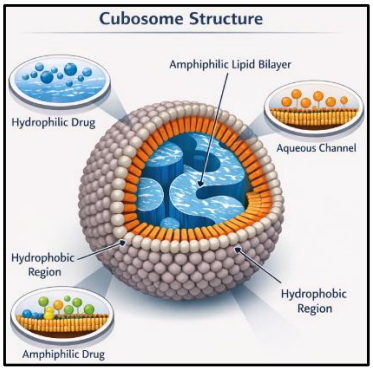


**Fig 1: Structure of Cubosome**

## NEED OF THE STUDY:

Etoricoxib, though effective, causes gastrointestinal side effects such as ulcers and bleeding when administered orally. Being a BCS Class II drug with high permeability, there is a need to control its release to achieve sustained action.

Topical delivery can reduce systemic side effects and provide localized treatment. Incorporation of Etoricoxib into cubosomes can improve drug release, enhance stability, and minimize skin irritation by reducing direct drug contact.

Thus, developing an Etoricoxib-loaded cubosomal gel is essential for controlled, targeted, and safer drug delivery.

## OBJECTIVES:

- To perform preformulation studies of Etoricoxib to assess its physicochemical properties.
- To prepare Etoricoxib-loaded cubosomes using the top-down technique.
- To apply a Design of Experiments (DoE) approach for optimization of the formulation.
- To characterize the developed cubosomes in terms of particle size, zeta potential, and entrapment efficiency.

## MATERIALS AND METHODS:

### 1. Preformulation Studies

### 1.1 Organoleptic Properties

Etoricoxib was evaluated for organoleptic characteristics including color, odor, and appearance.

### 1.2 Melting Point Determination

The melting point of Etoricoxib was determined using the capillary method. The powdered drug was filled into a sealed capillary tube and placed in a Thiele's tube containing liquid paraffin. The temperature at which the drug melted was recorded.

### 1.3 Preparation of Standard Calibration Curve

A stock solution (1 mg/mL) of Etoricoxib was prepared in methanol. Further dilutions were made using phosphate buffer (pH 7.4) to obtain concentrations ranging from 2–10 µg/mL. Absorbance was measured using a UV-visible spectrophotometer.

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### 1.4 Determination of λmax

The λmax of Etoricoxib was determined by scanning the drug solution (10 µg/mL) in the range of 200–400 nm using a UV-visible spectrophotometer. The maximum absorbance was observed at 231 nm, and a calibration curve was constructed.
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## 2. Experimental Design (DoE)
A Box–Behnken design was employed to optimize the formulation variables using Design Expert® software. The independent variables included glyceryl monooleate (GMO) concentration (X1), poloxamer 407 concentration (X2), and sonication time (X3).

**The responses evaluated were:**
- Entrapment efficiency (Y1) – to be maximized
- Particle size (Y2) – to be minimized

A total of 17 experimental runs were generated to analyze the effect of variables and optimize the formulation.

**Table 1: Box-Behnken Design for optimization of Etoricoxib loaded Cubosomes**

| Formulation variables | Levels | |
|---|---|---|
| | Low | High |
| GMO concentration w/w% (X1) | 1.125 | 3.18 |
| Pluronic F- 127 concentration w/w% (X2) | 0.2 | 1.58 |
| Sonication Time min (X3) | 8 | 10 |
| Response variables | Desirability | |
| Entrapment efficiency EE% (Y1) | Maximize | |
| Particle size (Y2) | Minimize | |

**Table 2: Formulation table of Cubosomes**

| | | Factor 1 | Factor 2 | Factor 3 |
|---|---|---|---|---|
| Std | Run | A:GMO | B:Plx 407 | C:Sonication time |
| | | gm | gm | min |
| 9 | 1 | 2.1525 | 0.2 | 8 |
| 2 | 2 | 3.18 | 0.2 | 9 |
| 12 | 3 | 2.1525 | 1.58 | 10 |
| 3 | 4 | 1.125 | 1.58 | 9 |
| 1 | 5 | 1.125 | 0.2 | 9 |
| 5 | 6 | 1.125 | 0.89 | 8 |
| 4 | 7 | 3.18 | 1.58 | 9 |
| 16 | 8 | 2.1525 | 0.89 | 9 |
| 6 | 9 | 3.18 | 0.89 | 8 |
| 7 | 10 | 1.125 | 0.89 | 10 |
| 14 | 11 | 2.1525 | 0.89 | 9 |
| 8 | 12 | 3.18 | 0.89 | 10 |
| 15 | 13 | 2.1525 | 0.89 | 9 |
| 10 | 14 | 2.1525 | 1.58 | 8 |
| 11 | 15 | 2.1525 | 0.2 | 10 |
| 13 | 16 | 2.1525 | 0.89 | 9 |
| 17 | 17 | 2.1525 | 0.89 | 9 |

## 3. Preparation of Etoricoxib Cubosomes
### 3.1 Top-Down Technique
Cubosomes were prepared by emulsification of a lipid phase consisting of glyceryl monooleate and poloxamer 407. The lipid components were melted at 60°C, and Etoricoxib was dissolved in the molten lipid phase. Preheated

distilled water was added dropwise under mechanical stirring (500 rpm) to form a dispersion.
The dispersion was further homogenized at 3000 rpm for 15 minutes and subsequently sonicated to obtain a uniform cubosomal dispersion.

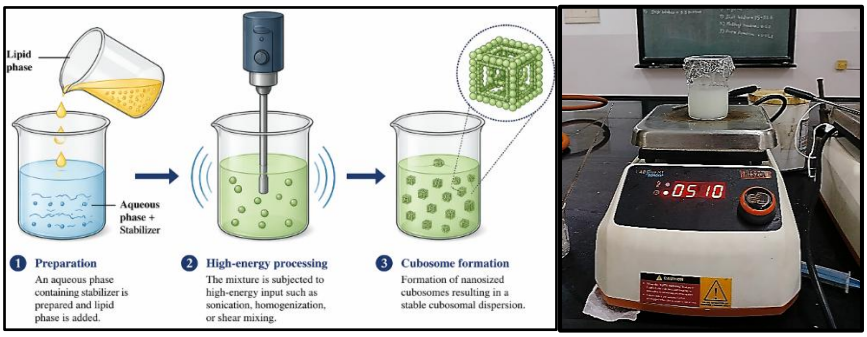


**Figure 2: Preparation method of Cubosomes by top down technique**

## 4. Preparation of Cubosomal Gel

The optimized cubosomal dispersion was incorporated into a Carbopol 934 gel base. The gel was prepared using distilled water and neutralized with triethanolamine. The cubosomal dispersion was then added with continuous stirring to obtain a homogeneous gel. Preservatives such as methyl paraben and propyl paraben were incorporated.

## 5. Characterization of Cubosomes

### 5.1 Compatibility Studies (FT-IR)

Drug-excipient compatibility was evaluated using FT-IR spectroscopy over a range of 4000–400 $cm^{-1}$.

### 5.2 Particle Size and Zeta Potential

Particle size, polydispersity index (PDI), and zeta potential were measured using a Zetasizer based on dynamic light scattering.

### 5.3 Entrapment Efficiency

Entrapment efficiency was determined using the dialysis bag method. The percentage entrapment efficiency was calculated using:

$$EE\% = \frac{(Total\ Drug - Free\ Drug)}{Total\ Drug} \times 100$$

### 5.4 Morphological Analysis

The morphology of cubosomes was examined using transmission electron microscopy (TEM).
5.5 Differential Scanning Calorimetry (DSC)
Thermal behavior of the drug was analyzed using DSC over a temperature range of 25–200°C under nitrogen atmosphere.

## 6. Evaluation of Cubosomal Gel

### 6.1 Visual Inspection and Homogeneity

The prepared gel was evaluated for color, appearance, homogeneity, and absence of lumps.

### 6.2 Grittiness

The formulation was examined microscopically for the presence of particulate matter.

### 6.3 Spreadability

Spreadability was determined using the formula:

$$Spreadability(g \times cm/sec) = Weight(g) \times Length(cm)/Time\ (\text{sec.})$$

### 6.4 pH Determination

The pH of the gel was measured using a digital pH meter.

### 6.5 Drug Content

Drug content was determined by dissolving the gel in methanol followed by UV spectrophotometric analysis at

231 nm.

**6.6 Viscosity**
Viscosity was measured using a Brookfield viscometer.

**6.7 Texture Analysis**
Texture properties were evaluated using a texture analyzer to determine firmness and consistency.

**7. Stability Studies**
Stability studies were conducted at 25°C ± 2°C and 40°C ± 2°C/75% RH for one month. Parameters such as pH and drug content were evaluated.

**8. In-vitro Drug Release Study**
Drug release was studied using a vertical diffusion cell with phosphate buffer (pH 7.4) as the medium. Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically.

**9. Ex-vivo Skin Permeation Study**
Ex-vivo permeation studies were performed using Franz diffusion cells with pig skin. The receptor compartment contained phosphate buffer (pH 7.4), and samples were analyzed at regular intervals to determine drug permeation.

## RESULTS AND DISCUSSION:

1. Drug Characterization
1.1 Organoleptic Properties
Etoricoxib was found to be a white, odorless powder, confirming its purity and suitability for formulation.
1.2 Melting Point
The observed melting point of Etoricoxib (133–135°C) was in close agreement with the reported value (134–136°C), indicating the drug's purity.
1.3 Standard Calibration Curve and λmax
The calibration curve of Etoricoxib in methanol: phosphate buffer (pH 7.4) showed good linearity in the concentration range of 2–14 µg/mL. The λmax was observed at 231 nm, which was used for further analysis.

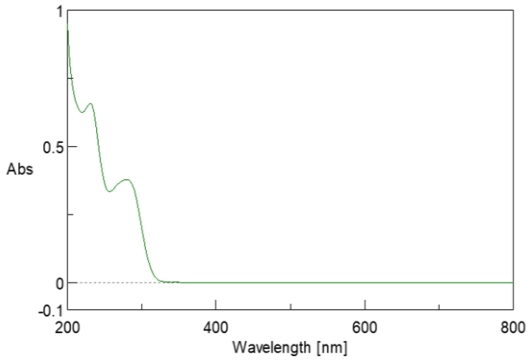


**Figure 3: $\lambda_{max}$ of Etoricoxib in (10 ppm) Methanol : pH 7.4 Phosphate Buffer at 231nm**

**1.4 FT-IR Analysis**
FT-IR spectra confirmed the presence of characteristic functional groups of Etoricoxib. No significant shifts or disappearance of peaks were observed in the drug-excipient mixture, indicating compatibility between Etoricoxib, glyceryl monooleate (GMO), and poloxamer 407.

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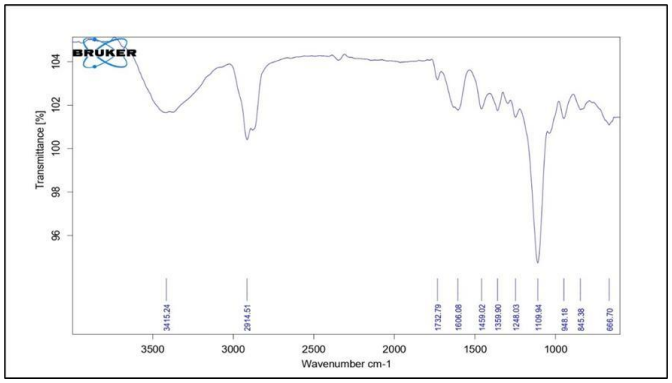


**Figure 4: FTIR of drug and excipients**

## 2. Optimization Using DoE

A Box–Behnken design was applied to evaluate the influence of formulation variables on entrapment efficiency (EE%) and particle size (PS).

**Table 3: DOE formulation of cubosomes with responses**

| | | Factor 1 | Factor 2 | Factor 3 | Response 1 | Response 2 |
|---|---|---|---|---|---|---|
| Std | Run | A:GMO | B:Plx 407 | C:Sonication time | EE | Particle size |
| | | gm | gm | min | % | nm |
| 9 | 1 | 2.1525 | 0.2 | 8 | 82.63 | 295.2 |
| 2 | 2 | 3.18 | 0.2 | 9 | 74.42 | 252.72 |
| 12 | 3 | 2.1525 | 1.58 | 10 | 81.12 | 284.13 |
| 3 | 4 | 1.125 | 1.58 | 9 | 72.42 | 245.7 |
| 1 | 5 | 1.125 | 0.2 | 9 | 70.32 | 234.02 |
| 5 | 6 | 1.125 | 0.89 | 8 | 76.62 | 264.24 |
| 4 | 7 | 3.18 | 1.58 | 9 | 90.8 | 379.26 |
| 16 | 8 | 2.1525 | 0.89 | 9 | 86.65 | 347.53 |
| 6 | 9 | 3.18 | 0.89 | 8 | 85.52 | 344.16 |
| 7 | 10 | 1.125 | 0.89 | 10 | 65.52 | 194.04 |
| 14 | 11 | 2.1525 | 0.89 | 9 | 86.83 | 347.75 |
| 8 | 12 | 3.18 | 0.89 | 10 | 77.22 | 272.07 |
| 15 | 13 | 2.1525 | 0.89 | 9 | 87.12 | 348.48 |
| 10 | 14 | 2.1525 | 1.58 | 8 | 89.12 | 361.67 |
| 11 | 15 | 2.1525 | 0.2 | 10 | 67.62 | 216.54 |
| 13 | 16 | 2.1525 | 0.89 | 9 | 86.34 | 346.37 |
| 17 | 17 | 2.1525 | 0.89 | 9 | 86.14 | 345.18 |

### 2.1 Entrapment Efficiency (EE%)

EE% ranged from 65.52% to 90.8%. Statistical analysis indicated that GMO and poloxamer 407 concentrations significantly increased EE%, whereas increased sonication time reduced EE%. The quadratic model showed good fit ($R^2 = 0.9971$), confirming model validity.

The increase in EE% with higher GMO concentration may be attributed to increased viscosity and improved drug entrapment, while poloxamer enhanced drug solubilization

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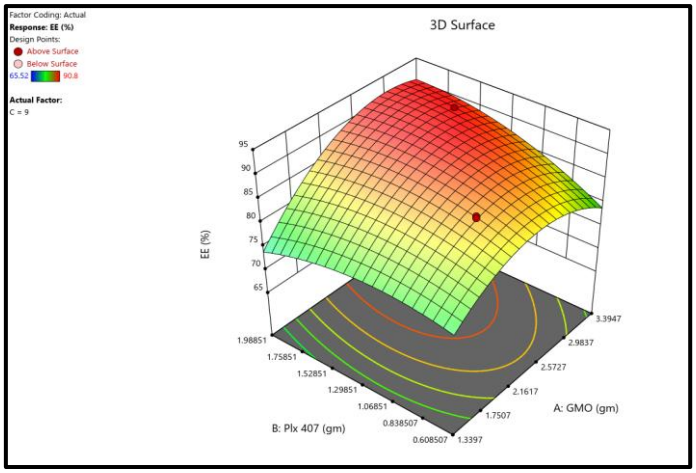


**Figure 5: Effect of GMO and PLX 407 on Entrapment efficiency (3D Graph)**

## 2.2 Particle Size (PS)

Particle size ranged from 194 nm to 379 nm. Results indicated that increasing GMO and poloxamer concentration increased particle size, whereas increasing sonication time reduced it. The model was significant ($p < 0.0001$) with excellent fit ($R^2 = 0.9993$).

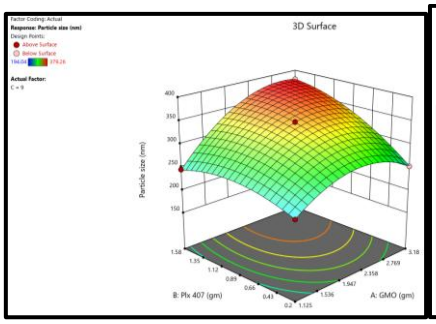


**Figure 6: Effect of GMO and PLX 407 on Particle Size (3D Graph )**

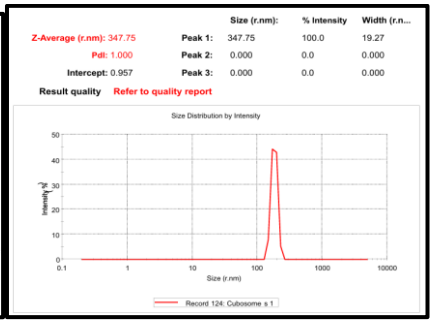


**Figure 7: Particle Size of Optimized Cubosome formulation**

## 2.3 Polydispersity Index (PDI)

PDI values ranged from 0.127 to 1.0, indicating acceptable size distribution of cubosomes.

## 2.4 Optimized Formulation

The optimized formulation consisted of GMO (2.75%), poloxamer 407 (1.57%), and sonication time (9.5 min), showing:

- Particle size: ~347 nm
- Entrapment efficiency: ~86.83%

The desirability value close to 1 confirmed successful optimization.

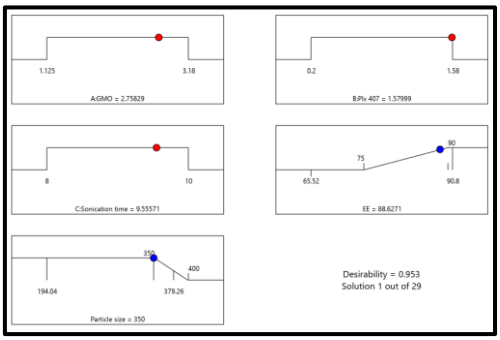


**Figure 8: Target Set using DoE**

### 3. Zeta Potential

Zeta potential values ranged from –19.6 to –29.5 mV, indicating good stability due to sufficient electrostatic repulsion between particles.

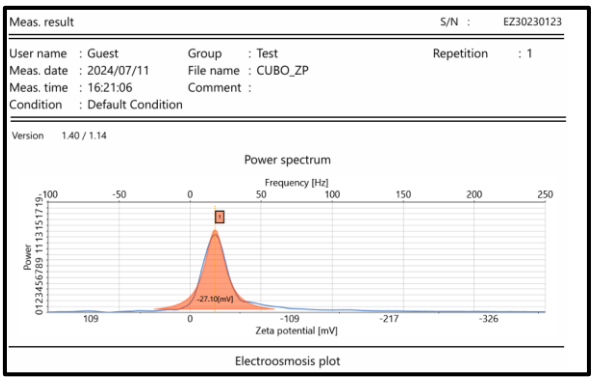


**Figure 9: Zeta potential of optimized formulation**

### 4. Morphological Analysis (TEM)

TEM analysis revealed cubosomes with predominantly cubic structures and nanoscale size, confirming successful formation of cubosomal nanoparticles.

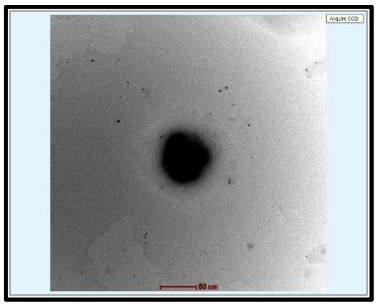

**Figure 10: TEM of optimized Cubosomes formulation**

### 5. Differential Scanning Calorimetry (DSC)

DSC analysis showed a shift in the melting peak of Etoricoxib from 134.88°C to 89.2°C, indicating conversion of the drug into an amorphous form within the cubosomal system.

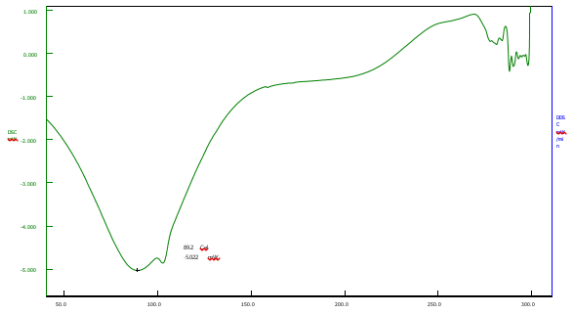

**Figure 11: DSC of Cubosomal dispersion**

### 6. Evaluation of Cubosomal Gel

- Homogeneity & Appearance: Smooth, homogeneous gel with no grittiness
- pH: 6.75 (compatible with skin)
- Spreadability: 7.23 g·cm/sec (good applicability)
- Drug Content: 97.93% (uniform distribution)
- Viscosity: Exhibited pseudoplastic behavior, suitable for topical application
- Texture Analysis: Adequate firmness and consistency

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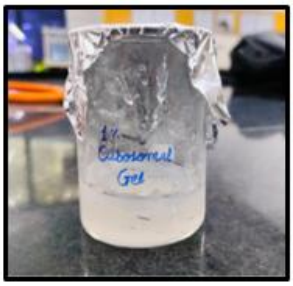


**Figure 12: Formulation of 1% cubosomal gel**

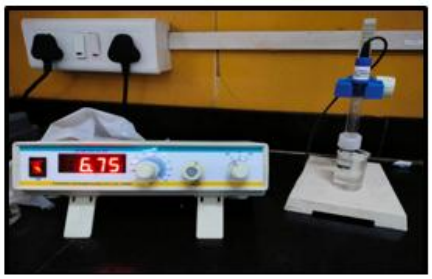


**Figure 13: pH of cubosomal gel**

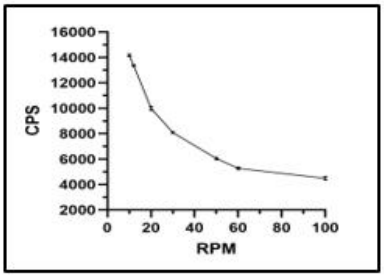


**Figure 14: Viscosity of cubosomal gel**

After one month, the formulation showed minimal changes:

- Drug content: 93.23% (25°C), 88.52% (40°C)
- pH remained within acceptable range

This indicates good stability of the formulation.

8. In-vitro Drug Release Study

The optimized cubosomal gel showed sustained drug release over 6 hours. The cumulative drug release reached ~1058.99 µg/cm², compared to marketed gel (~1152.05 µg/cm²).

Drug release followed the Higuchi model ($R^2 = 0.9644$), indicating diffusion-controlled release.

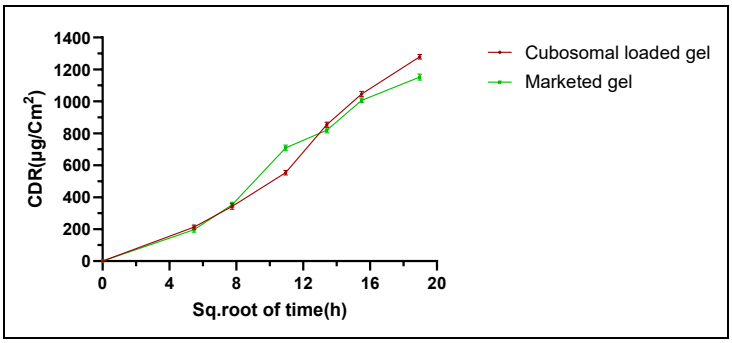


**Figure 15: Cumulative Drug Release of Cubosomal Gel and 1% Etoricoxib Marketed Gel**

**9. Ex-vivo Skin Permeation Study**

The cubosomal gel exhibited higher permeation (3424.9 µg/cm²) compared to marketed gel (2582.72 µg/cm²) after 6 hours.

This enhanced permeation may be due to the presence of GMO and poloxamer 407, which improve drug solubility and penetration through the skin.

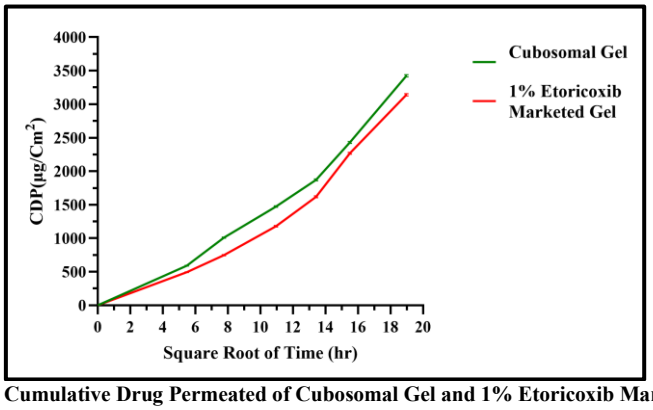


**Figure 16: Cumulative Drug Permeated of Cubosomal Gel and 1% Etoricoxib Marketed Gel**

## SUMMARY AND CONCLUSION:

The present study successfully focused on the formulation and development of an Etoricoxib-loaded cubosomal gel for topical delivery. Cubosomes were effectively prepared using the top-down technique with glyceryl monooleate and poloxamer 407, resulting in a stable nanostructured system with high entrapment efficiency and desirable physicochemical properties.

Optimization using a Design of Experiments (DoE) approach identified an optimal formulation that exhibited suitable particle size, high entrapment efficiency, and good stability. The incorporation of cubosomes into a Carbopol-based gel resulted in a formulation with acceptable pH, viscosity, spreadability, and homogeneity, making it suitable for topical application.

In-vitro drug release studies demonstrated a controlled and sustained release pattern following the Higuchi diffusion model. Ex-vivo permeation studies revealed enhanced skin penetration of Etoricoxib from the cubosomal gel compared to conventional marketed formulations. This improved permeation can be attributed to the unique cubic structure and penetration-enhancing properties of the formulation components.

Overall, the developed cubosomal gel system showed improved drug delivery, enhanced bioavailability, and reduced potential for systemic side effects. The optimized formulation demonstrated promising potential as an effective topical therapeutic system for the management of rheumatoid arthritis.

Thus, Etoricoxib-loaded cubosomal gel represents a novel and efficient drug delivery approach, offering improved therapeutic efficacy, better patient compliance, and a promising alternative to conventional formulations.

## REFERENCES:

1. Hu, J., Huang, W., Huang, S., ZhuGe, Q., Jin, K., Zhao, Y., 2016. Magnetically active Fe 3 O 4 nanorods loaded with tissue plasminogen activator for enhanced thrombolysis. Nano Res. 9, 2652–2661.
2. Jin, C., Wang, K., Oppong-Gyebi, A., Hu, J., 2020. Application of nanotechnology in cancer diagnosis and therapy-a mini-review. Int. J. Med. Sci. 17, 2964.
3. Hu, J., Huang, S., Zhu, L., Huang, W., Zhao, Y., Jin, K., ZhuGe, Q., 2018. Tissue plasminogen activator-porous magnetic microrods for targeted thrombolytic therapy after ischemic stroke. ACS Appl. Mater. Interfaces 10, 32988–32997.
4. Chaturvedi, V.K., Singh, A., Singh, V.K., Singh, M.P., 2019. Cancer nanotechnology: a new revolution for cancer diagnosis and therapy. Curr. Drug Metab. 20, 416–429.
5. Ali S, Shabbir M, Shahid N. The structure of skin and transdermal drug delivery system-a review. Research journal of pharmacy and technology. 2015;8(2):103-9.
6. Patel V, Sharma OP, Mehta T. Nanocrystal: a novel approach to overcome skin barriers for improved topical drug delivery. Expert opinion on drug delivery. 2018, 3;15(4):351-68.
7. Ameen M. Epidemiology of superficial fungal infections. Clinics in Dermatology (2010) 28, 197–201.
8. Mehveen S, Hussain L, Maqsood S , begum A , Nayak S. The Pharmacology and Efficacy of Antifungals: A Literature Review. International journal of pharmacy and pharmaceutical research.2020;19(3): 96-114.
9. Rao SV, Sravya BN, Padmalatha K. A review on cubosome: The novel drug delivery system. GSC Biological and Pharmaceutical Sciences. 2018;5(1).
10. Kumar I, Thakur B. Liquid Crystal Nanoparticles (Cubosomes): A Novel Nanoparticulate Drug Delivery System. International journal of pharmacy and pharmaceutical research. 2020;19 (3): 177-194.
11. Bansal S, Kashyap CP, Aggarwal G, Harikumar SL. A comparative review on vesicular drug delivery system and stability issues. Int J Res Pharm Chem. 2012;2(3):704-13.
12. Hundekar YR, Saboji JK, Patil SM, Nanjwade BK. Preparation and evaluation of diclofenac sodium cubosomes for percutaneous administration. World J Pharm Pharm Sci. 2014 Mar 5;3(5):523-39
13. Shahana S, Sabu A , Mathew P. formulation and evaluation of cubosomal gel for topical application. International journal of pharmaceutical sciences and research. 2024; 15(2): 518-525.
14. Karthika VT, Sheri PS, Kuriachan MA. Fabrication & Evaluation of Ketoprofen Loaded Cubogel for Topical Sustained Delivery. Int. J. Res. Rev. 2018;5:149-59.
15. Tadwee. I. K., Gore. S., Giradkar. P. Advances in Topical Drug Delivery System. International Journal of Pharmaceutical Research & Allied Science. 2012;1(1):14-23.
16. Gaballa. S. A., Omar H. Garhy. E., Abdelkader. H. Cubosomes: composition, preparation, and drug delivery applications. Journal of Advanced Biomedical and Pharmaceutical Sciences. 2020;1-9.
17. Sakpal. G. G., Vaidya V., Kumar. P. formulation and evaluation of terbinafine hydrochloride as a cubosomal topical gel to treat dermatological infections. Journal of Global Trends in Pharmaceutical Sciences.2020;11 (3):8028 – 8039.
18. Anand B, Thomas I, Abraham E. Formulation and Evaluation of Cubosomal Gel of an Anti-Inflammatory Agent. Internationale Pharmaceutica Sciencia. 2020;10(1):103 120.
19. Varghese. J., Sufairath and S. Mahendran . Formulation And Evaluations Of Cubosome Loaded Emulgel Of Oxiconazole Nitrate. European Journal of Biomedical And Pharmaceutical sciences,2022; 9( 5):188-196.
20. Chettupalli. A. K., Ananthula M., Amarachinta P.R., Vasudha Bakshi., Vinod Kumar Yata. Design, Formulation, In Vitro and Ex Vivo Evaluation of Atazanavir Loaded Cubosomal Gel. Biointerface Research in Applied Chemistry. 2021;11(4):12037 – 12054.
21. Omar, S. M., Ismail, A., Hassanin, K. D., Dawoud. S. H. Formulation and Evaluation of Cubosomes as Skin Retentive System for

Topical Delivery of Clotrimazole. Journal of Advanced Pharmacy Reasearch. 2019;3(2):68-82.
22. Anju K P., Shripathy D., Shabaraya A R. Antifungal topical nanoemulgel containing miconazole nitrate. International Journal of Health Sciences and Research 2021; 11(11):208-229.
23. Maha KA Khalifa. Miconazole Nitrate based cubosome hydrogels for topical application. International Journal of Drug Delivery.2015;7(1):01-12
24. Salwa Salah et al; Etodolac transdermal cubosomes for the treatment of rheumatoid arthritis: ex vivo permeation and in vivo pharmacokinetic studies; Taylor and Francis Group, May 2017; 846-885
25. Borkar A, Bhopale S, Deshmukh N, Rathod H, Musale S. an overview on preformulation studies, World Journal of Pharmacy and Pharmaceutical Sciences 11, (11), 2022.
26. Thadanki M: Overview of cubosomes: a nanoparticle, Int. J Res Pharm and Chem 2011; 1: 535-41.
27. Zaki, R.M., Alfadhel, M.M., Alossaimi, M.A., Elsawaf, L.A., Devanathadesikan Seshadri, V., Almurshedi, A.S., Said, M., 2022a. Central composite optimization of glycerosomes for the enhanced oral bioavailability and brain delivery of quetiapine fumarate. Pharmaceuticals 15, 940.
28. Said, M., Aboelwafa, A.A., Elshafeey, A.H., Elsayed, I., 2021. Central composite optimization of ocular mucoadhesive cubosomes for enhanced bioavailability and controlled delivery of voriconazole. J. Drug Deliv. Sci. Technol. 61, 102075.
29. Eldeeb, A.E., Salah, S., Ghorab, M., 2019. Formulation and evaluation of cubosomes drug delivery system for treatment of glaucoma: Ex-vivo permeation and in-vivo pharmacodynamic study. J. Drug Deliv. Sci. Technol. 52, 236–247.
30. Spicer PT: Cubosomes Bicontinuous Cubic Liquid Crystalline. Trans I Chem E, Part A, 2005; 83(11): 1283 86
31. Barreiro Iglesias R, Alvarez-Lorenzo and Concheiro C: Poly (acrylic acid) microgels carbopol 934)/surfactant interactions in aqueous media Part I: nonionic surfactants, Int J Pharm 2003; 258(2): 165-77
32. Gulsu A, Ayhan F and Ayhan H: Preparation and characterization of Ketoprofen loaded albumin microspheres. Turk J Biochem 2012; 37(2): 120–28.
33. Urvi S, Dhiren D, Bhavin P, Patel U and Shah R: Overview of Cubosomes: A Nano Particle. International Journal of Pharmacy and Integrated Life Sciences 2013; 1(5): 36 47.
34. Saly S, Ehab RB and Sabry B: The design and evaluation of novel encapsulation technique for topical application of alpha lipoic acid. Journal of Advanced Pharmaceutical Research 2013; 4(1): 13-22
35. Leung SSW and Leal C: The stabilization of primitive bicontinuous cubic phases with tunable swelling over a wide composition range. Soft Matter 2019; 15: 1269-77.
36. Sastri KT, Radha GV, Pidikiti S and P Vajjhala: Solid lipid nanoparticles: preparation techniques, their characterization, and an update on recent studies. J Appl Pharmaceut Sci 2020; 10: 126-41.
37. Alam MM, Ushiyama K and Aramaki K: Phase formation, and rheology of cubic phase and related gel emulsion in tween 80/water/oil system. J Oleo Sci 2009; 58: 361 367.
38. Souto EB, Baldim I, Oliveira WP, Rao R, Yadav N and Gama FM: SLN and NLC for topical, dermal, and transdermal drug delivery Expet Opin Drug Deliv 2020; 17: 357-77.
39. Vinod KR, Sravya K, Sandhya S, Banji D, Anbazhagan S and Prameela RA: Tailoring active compounds across biological membranes by cubosomal technology: an updated review. J Chine Pharm Sci 2013; 22: 303-11.
40. Lakshmi N, Yalavarthi P, Vadlamudi H, Thanniru J, Yaga G, K H. Cubosomes as Targeted Drug Delivery Systems - A Biopharmaceutical Approach. Curr Drug Discov Technol. 2014;11(3):181–188.
41. Duttagupta AS, Chaudhary HM, Jadhav KR, Kadam VJ. Cubosomes: Innovative Nanostructures for Drug Delivery. Curr Drug Deliv. 2016;13(4):482–493.