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DEVELOPMENT AND EVALUATION OF IBUPROFEN LOADED CUBOSOMES FOR ENHANCED ORAL BIOAVAILABILITY

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Abstract:
The present study was undertaken to formulate and evaluate Ibuprofen-loaded cubosomes as a novel nanocarrier system for enhanced drug delivery and sustained drug release. Drug-excipient compatibility studies were carried out using FTIR spectroscopy, which confirmed the absence of any significant interaction between Ibuprofen and the selected excipients.The prepared cubosomal formulations were characterized for particle size, zeta potential, entrapment efficiency, and in vitro drug release. The particle size of the formulations ranged from 169 to 183 nm, while zeta potential values ranged from -25 to -30 mV, indicating good physical stability of the cubosomal dispersions. Entrapment efficiency was found to be in the range of 79.80% to 85.92%, demonstrating efficient incorporation of the drug within the cubosomal matrix.In vitro drug release studies revealed sustained release of Ibuprofen from all formulations over a period of 8 hours. Among the developed formulations, F4 exhibited the highest cumulative drug release (98.52%), maximum entrapment efficiency (85.92%), smallest particle size (169 nm), and highest zeta potential (-30 mV), indicating superior formulation characteristics. Stability studies conducted on the optimized formulation (F4) under accelerated storage conditions for three months showed no significant changes in drug release behavior, confirming the stability of the formulation.

Keywords: *Ibuprofen, Cubosomes, Controlled Drug Delivery, Glyceryl Monooleate, Poloxamer 407, Entrapment Efficiency, Sustained Release, Nanocarrier System.*

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INTRODUCTION:

CUBOSOMES

Cubosomes are nanostructured lipid-based drug delivery systems formed from bicontinuous cubic liquid crystalline phases. They are composed mainly of amphiphilic lipids such as glyceryl monooleate (GMO) or phytantriol, stabilized by surfactants like Poloxamer 407. When these lipids are dispersed in water under controlled conditions, they self-assemble into a three-dimensional cubic structure containing two continuous but non-intersecting aqueous channels separated by a lipid bilayer.

This unique internal structure provides cubosomes with a large internal surface area and the ability to encapsulate hydrophilic, lipophilic, and amphiphilic drugs simultaneously. Due to their nanoscale size and bioadhesive nature, cubosomes enhance drug solubilization, stability, and bioavailability. Cubosomes are considered promising carriers in Novel Drug Delivery Systems (NDDS) because they can provide controlled and sustained drug release. They have been widely investigated for oral, topical, transdermal, and parenteral drug delivery applications. Their structural similarity to biological membranes also contributes to improved drug absorption and reduced toxicity.

Controlled drug delivery systems are designed to release therapeutic agents at a predetermined rate for a specified period of time in order to maintain optimal drug concentration within the therapeutic window. Conventional dosage forms often produce fluctuations in plasma drug levels, leading to reduced efficacy and increased side effects. Therefore, there is a growing need for advanced delivery systems that can provide sustained and controlled release while improving bioavailability and patient compliance.

Cubosomes have emerged as a promising nanostructured lipid carrier for controlled drug delivery. They are discrete nanoparticles formed from the fragmentation of bulk cubic liquid crystalline phases composed of amphiphilic lipids such as glyceryl monooleate or phytantriol, stabilized by surfactants like Poloxamer 407. Cubosomes possess a unique bicontinuous cubic structure consisting of two non-intersecting aqueous channels separated by a lipid bilayer arranged in a three-dimensional periodic pattern. This internal structure provides a large surface area and enables encapsulation of hydrophilic, lipophilic, and amphiphilic drugs.

The structural architecture of cubosomes plays a critical role in achieving controlled drug release. The interconnected aqueous channels allow diffusion-controlled release of drug molecules, resulting in sustained therapeutic action over an extended period. Additionally, the lipid matrix provides protection to the encapsulated drug from enzymatic degradation and environmental instability. Due to their nanoscale size and bioadhesive properties, cubosomes enhance drug absorption and prolong residence time at the site of administration.

Cubosomes are versatile carriers suitable for various routes of administration, including oral, topical, ocular, and parenteral delivery. Their biocompatibility, biodegradability, and ability to improve solubility make them especially useful for poorly water-soluble drugs. Furthermore, the release rate can be modified by adjusting formulation variables such as lipid concentration, type of stabilizer, and particle size.

MATERIALS:

Ibuprofenv was procured from Synpharma Research Labs, Pluronic acid F-127, Glyceryl monostearate and Ethanol were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY:

Formulation development

Top-Down Method

Table-1: Composition of Ibuprofen-Loaded Cubosomal Formulations

Ingredients	F1(1:1)	F2(1:2)	F3(1:3)	F4(1:4)
Ibuprofen	100	100	100	100
Glyceryl monostearate	100	200	300	400
Pluronic F-127	100	100	100	100
Ethanol	10	10	10	10
Water	q. s	q. s	q.s	q. s

Method of Preparation:

Top-Down Method

Preparation of Lipid Phase

Accurately weighed quantity of glyceryl monostearate (as per formulation F1–F4) was taken in a clean beaker and melted at 60–70°C (above its melting point). Ibuprofen (10 mg) was added to the molten lipid and mixed thoroughly to obtain a uniform drug–lipid mixture.

Addition of Organic Solvent

Ethanol (10 mL) was added to the molten lipid mixture to facilitate proper dissolution and uniform distribution of the drug in the lipid phase. The

mixture was stirred continuously until a clear solution was obtained.

Preparation of Aqueous Phase
Pluronic F-127 (100 mg) was dissolved in a required quantity of distilled water under continuous stirring to form a clear aqueous solution. The aqueous phase was maintained at the same temperature as the lipid phase.

Formation of Bulk Cubic Phase
The molten lipid phase containing the drug was slowly added to the aqueous phase with continuous stirring at 800–1000 rpm. The mixture was allowed to hydrate, forming a viscous bulk cubic gel.

Homogenization (Size Reduction)
The formed bulk cubic phase was subjected to high-speed homogenization (10,000–15,000 rpm) for 5–10 minutes to reduce particle size and obtain a uniform cubosomal dispersion.

Sonication
The dispersion was further sonicated using a probe sonicator for 3–5 minutes to reduce particle size and improve uniformity.

Cooling and Storage
The final cubosomal dispersion was allowed to cool to room temperature and stored in airtight containers at refrigerated conditions until further evaluation.

Evaluation of Cubosomes:
Particle size
The particle size of Ibuprofen cubosomes were determined using Dynamic Light Scattering (DLS) technique.A small quantity of cubosomal dispersion was diluted appropriately with distilled water to avoid multiple scattering effects. The diluted sample was transferred into a clean cuvette and placed in a particle size analyzer. Measurements were performed at 25°C, and the average particle size were recorded. All measurements were carried out in triplicate, and the mean values were reported.

SEM analysis:
Surface morphology of the cubosomes was examined using SEM. A drop of cubosomal dispersion was placed on a clean glass slide or aluminum stub and allowed to dry at room temperature. The dried sample was coated with a thin layer of gold using a sputter coater to make it electrically conductive. The sample was then placed in the SEM chamber and observed at suitable magnifications. The shape, surface characteristics, and structural integrity of the cubosomes were recorded.

Zeta potential:
Zeta potential was measured to determine the surface charge and stability of the cubosomal dispersion. The cubosomal formulation was diluted suitably with distilled water and filled into a zeta potential cell. The sample was analyzed using a zeta potential analyzer based on electrophoretic mobility. The measurements were performed at 25°C, and the average zeta potential value was recorded. The analysis was conducted in triplicate.

Entrapment efficiency:
Entrapment efficiency was determined by separating free drug from entrapped drug using centrifugation. A known volume of cubosomal dispersion was placed in centrifuge tubes and centrifuged at 15,000 rpm for 30–45 minutes. The supernatant containing free (unentrapped) Ivabradine was carefully collected and analyzed using a UV–Visible spectrophotometer at 286 nm after suitable dilution.

$$EP = [(C_t - C_r)/ C_t] * 100$$

where,
Ct, concentration of total Ivabradine,
Cr, concentration of free Ivabradine.

In vitro drug Release Study:
The in vitro drug release of Ibuprofen from cubosomal formulations was carried out using the dialysis bag diffusion method. A dialysis membrane (molecular weight cut-off 12,000–14,000 Da) was soaked in distilled water for 12 hours prior to use to ensure proper hydration. An accurately measured quantity of cubosomal dispersion equivalent to a known amount of Ivabradine was placed inside the pre-soaked dialysis bag, and both ends were securely tied to prevent leakage. The dialysis bag was immersed in 100 mL of dissolution medium maintained at 37 ± 0.5°C. The medium was stirred continuously at 50–100 rpm using a magnetic stirrer to maintain uniform conditions and sink conditions throughout the experiment. At predetermined time intervals 5 mL of sample was withdrawn from the dissolution medium and immediately replaced with an equal volume of fresh pre-warmed medium to maintain constant volume and sink conditions. The withdrawn samples were filtered if necessary, suitably diluted, and analyzed using a UV–Visible spectrophotometer at the λmax of Ivabradine. The cumulative percentage drug release was calculated and plotted against time to evaluate the release profile of the cubosomal formulation.

Stability Studies:
Stability studies were performed according to ICH guidelines to evaluate the physical and chemical stability of the optimized cubosomal formulation.

The optimized formulation was filled in airtight glass containers and stored under the following conditions:

- **Long-term condition:** 25 ± 2°C / 60 ± 5% RH
- **Accelerated condition:** 40 ± 2°C / 75 ± 5% RH

RESULT & DISCUSSION:

Determination of Vesicle morphology and Size

The morphological characteristics of formulated Cubosomes were carried by using Scanning electron microscopy (SEM). A small drop of Cubosomes was placed between two rivets fixed on a gold-plated copper sample holder. The whole system was slushed under vacuum in liquid nitrogen. The sample was heated to -85 ^{0}C for 30 min to sublime the surface moisture. Finally the sample was coated with gold and allowed the SEM to capture the images at a temperature of – 120 ^{0}c and voltage of 5kV.Scanning electron microscopy are the direct method to measure cubosomes, physical characterization of cubosomes with the former method being used for morphological examination.

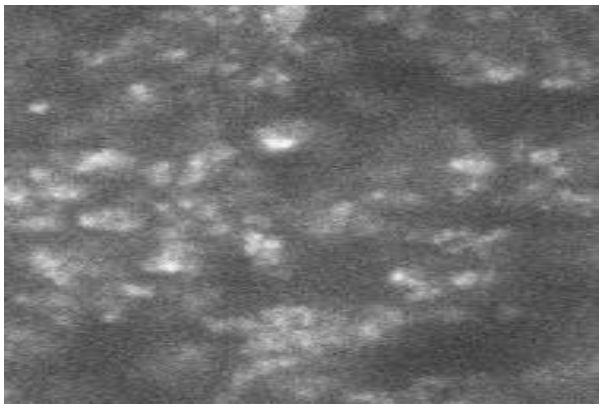


Fig-1: SEM Analysis of optimized formulation

Zeta potential:

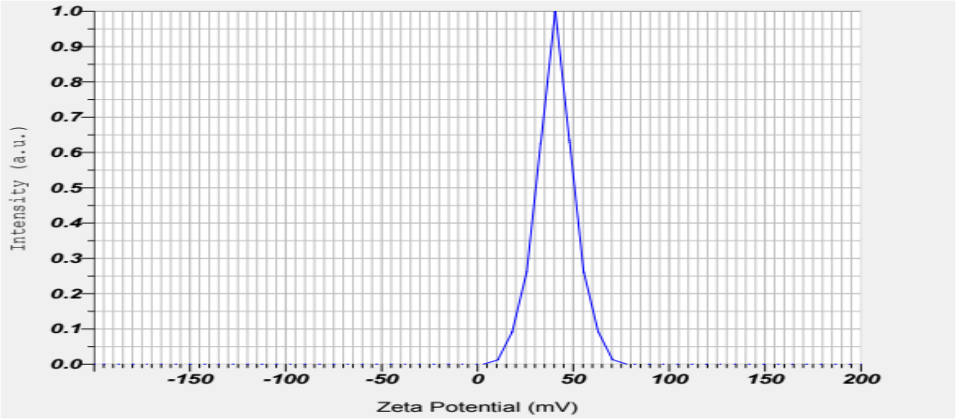


Fig-2: Zeta potential of optimized formulation

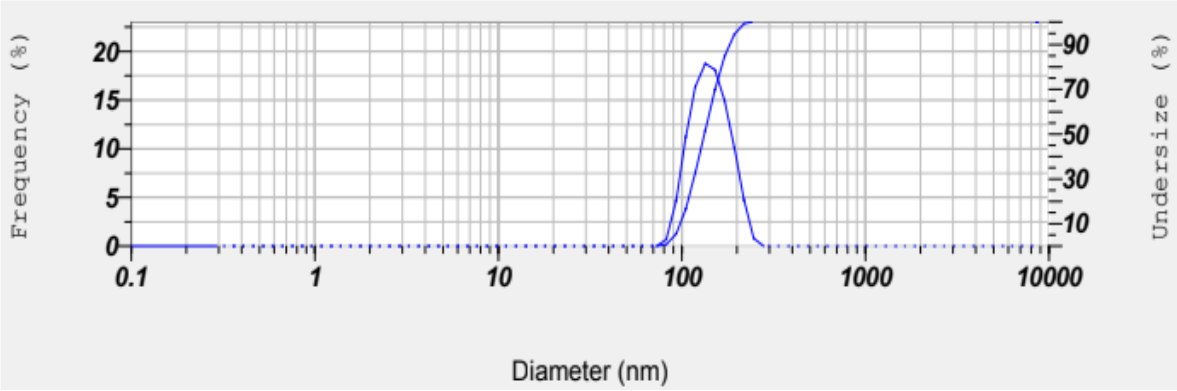


Fig-3: Particle size of optimized formulation

Table-2: Evaluation Studies of particle size and Zeta potential Cubosomes

F. No	Particle size (nm)	Zeta potential (mV)
F1	175	-25
F2	178	-29
F3	183	-26
F4	169	-30

Entrapment Efficiency:

Entrapment efficiency was determined by separating free drug from entrapped drug using centrifugation. A known volume of cubosomal dispersion was placed in centrifuge tubes and centrifuged at 15,000 rpm for 30–45 minutes. The supernatant containing free (unentrapped) Ibuprofen was carefully collected and analyzed using a UV–Visible spectrophotometer at 222 nm after suitable dilution.

$$EP = [(C_t - C_r)/ C_t] * 100$$

Table-3: Drug entrapment efficiency of all formulation

F.no	Drug entrapment efficiency
F1	82.39
F2	81.54
F3	79.80
F4	85.92

In vitro drug release studies:

Table-4: Results of Ibuprofen cubosomes of all formulations

Time(hr.)	F1	F2	F3	F4
0	0	0	0	0
1	17.12	18.15	19.25	19.62
2	24.69	31.98	36.88	37.55
3	39.86	45.86	47.55	44.78
4	47.96	52.68	58.75	50.27
5	59.45	67.85	69.38	65.28
6	70.25	71.25	75.86	72.85
7	81.26	80.45	84.40	84.64
8	93.68	94.50	95.28	98.52

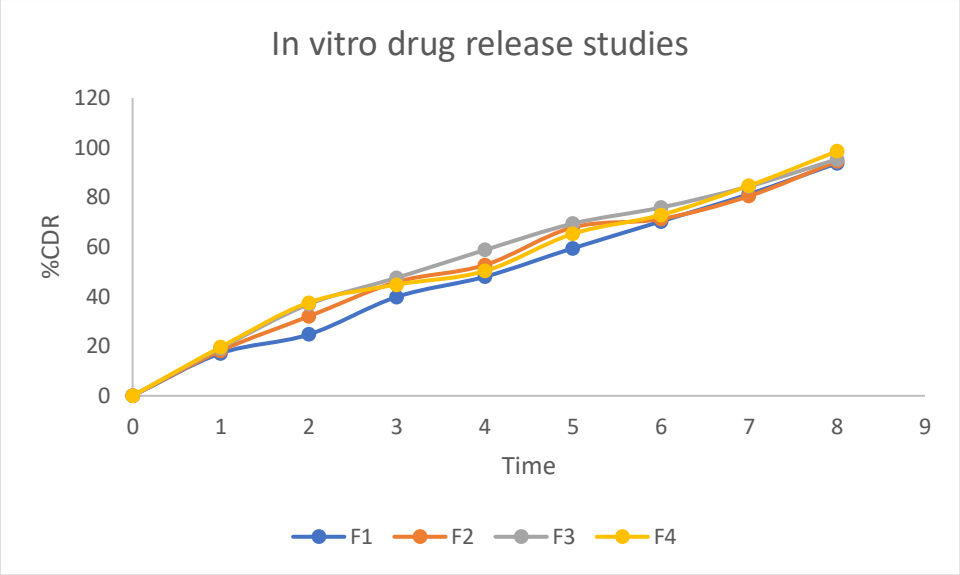


Fig-4: Drug release studies of (F1-F4) formulations

Most formulations reach >90% release, showing that the formulations are capable of complete drug release over the 8-hour period.F4 reaches the highest release at 8 hr (98.52%), which may indicate a formulation optimized for maximum drug release.

Stability studies

Optimized formulations F4 was selected for accelerated stability studies as per ICH guidelines.

Table-5: Stability studies of optimized formulations at 40 ± 2 ^{0}C and 75 ± 5% RH for 3 months

Formulation Code	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-4	98.52	97.86	96.75	95.72	Not less than 85 %
F-4	98.52	97.52	96.25	95.36	Not less than 85 %
F-4	98.52	97.43	96.42	95.20	Not less than 85 %

SUMMARY AND CONCLUSION:

Summary

The present study was carried out to formulate and evaluate Ibuprofen-loaded cubosomes for enhanced drug delivery. FTIR studies confirmed the compatibility of Ibuprofen with the selected excipients, as no significant changes in the characteristic peaks were observed.The prepared cubosomal formulations were characterized for particle size, zeta potential, and entrapment efficiency. The particle size ranged from 169–183 nm, while zeta potential values ranged from -25 to -30 mV, indicating good stability of the formulations. Entrapment efficiency was found to be between 79.80% and 85.92%.In vitro drug release studies demonstrated sustained drug release from all formulations over 8 hours. Among the prepared formulations, F4 exhibited the highest cumulative drug release (98.52%), smallest particle size (169 nm), highest zeta potential (-30 mV), and maximum entrapment efficiency (85.92%), indicating superior formulation performance.Accelerated stability studies conducted on the optimized formulation F4 showed no significant changes in drug release characteristics over a period of three months, confirming the stability of the formulation.

CONCLUSION:

Among all formulations, F4 was identified as the optimized formulation based on its highest drug release (98.52%), highest entrapment efficiency (85.92%), smallest particle size (169 nm), and favorable zeta potential (-30 mV). Stability studies further demonstrated that the optimized formulation remained stable under accelerated storage conditions without significant changes in its performance.Therefore, it can be concluded that Ibuprofen-loaded cubosomes represent a promising nano-drug delivery system capable of enhancing drug encapsulation, improving formulation stability,

and providing sustained drug release for improved therapeutic effectiveness.

REFERENCES:

1. Thakur, K.T., E. Albanese, P. Giannakopoulos Neurological Disorders, in Mental, Neurological, and Substance Use Disorders: Disease Control Priorities, Third Edition (Volume 4), V. Patel, et al., Editors. 2016, The International Bank for Reconstruction and Development / The World Bank Washington (DC).
2. Hebert, L.E., P.A. Scherr, J.L. Bienias, D.A. Bennett, and D.A. Evans, Alzheimer disease in the us population: Prevalence estimates using the 2000 census. Archives of Neurology, 2003. **60**(8): p. 1119-1122.
3. Dorsey, E.R., R. Constantinescu, J.P. Thompson, et al., Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. Neurology, 2007. **68**(5): p. 384-386.
4. Albert, S.M., Projecting neurologic disease burden: Difficult but critical. Neurology, 2007. **68**(5): p. 322-323.
5. Hirtz, D., D.J. Thurman, K. Gwinn-Hardy, et al., How common are the "common" neurologic disorders? Neurology, 2007. **68**(5): p. 326-337.
6. Gabathuler, R., Approaches to transport therapeutic drugs across the blood-brain barrier to treat brain diseases. Neurobiology of Disease, 2010. **37**(1): p. 48-57.
7. Begley, D.J., ABC Transporters and the Blood-Brain Barrier. Current Pharmaceutical Design, 2004. **10**(12): p. 1295-1312.
8. Muller, R.H. and C.M. Keck, Challenges and solutions for the delivery of biotech drugs – a review of drug nanocrystal technology and lipid nanoparticles. Journal of Biotechnology, 2004. **113**(1): p. 151-170.
9. P.T. Spicer, K.L. Hayden, M.L. Lynch, A. Ofori-Boateng, J.L. Burns, Novel process for producing cubic liquid crystalline nanoparticles (cubosomes), Langmuir. 17 (2001) 5748–5756.
10. J. Barauskas, T. Landh, Phase Behavior of the Phytantriol / Water System, Langmuir. 19 (2003) 9562–9565.
11. J. Gustafsson, H. Ljusberg-Wahren, M. Almgren, K. Larsson, Cubic Lipid-Water
12. Phase Disperesed into Submicron Particles, Langmuir. 12 (1996) 1994–1996.
13. J. Gustafsson, H. Ljusberg-Wahren, M. Almgren, K. Larsson, Submicron Particles of Reversed Lipid Phases in Water Stabilized by a Nonionic Amphiphilic Polymer, Langmuir. 13 (1997) 6964–6971.
14. C.M. Chang, R. Bodmeier, Swelling of and drug release from monoglyceride based drug delivery systems, J. Pharm. Sci. 86 (1997) 747–752.
15. G. Garg, S. Saraf, S. Saraf, Cubosomes : An Overview, Biol. Pharm. Bull. 30(2007) 350–353.
16. P.T. Spicer, Cubosomes: Bicontinuous Cubic Liquid Crystalline Nanostructured Particles, Encycl. Nanosci. Nanotechnol. (2004) 1–11.