

DEVELOPMENT, OPTIMIZATION AND EVALUATION OF ALLOPURINOL LOADED NANO CUBOSOMAL GEL FOR ENHANCED TOPICAL DRUG DELIVERY

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ABSTRACT

Background: Topical delivery of allopurinol may be limited by its physicochemical properties and challenges associated with effective drug penetration. Nano-cubosomal systems offer a lipid-based approach for improving drug incorporation and providing controlled release. The present study focused on developing an allopurinol-loaded nano-cubosomal gel for enhanced topical drug delivery. **Aim/Objectives:** To formulate, optimize and evaluate allopurinol-loaded nano-cubosomes and incorporate the optimized formulation into a suitable gel for controlled topical drug delivery. **Materials and Methods:** Nine formulations (F1–F9) containing varying concentrations of glyceryl monooleate (100–500 mg) and 50 mg poloxamer 407 were prepared using a top-down approach. Formulations were evaluated for particle size, PDI, zeta potential and entrapment efficiency. The optimized formulation was incorporated into a gel and assessed for pH, viscosity, gel strength, in vitro drug release and release kinetics. Stability was evaluated for 6 months at $25 \pm 2^\circ\text{C}/60 \pm 5\%$ RH and $40 \pm 2^\circ\text{C}/75 \pm 5\%$ RH. **Results:** F6 showed the most favourable characteristics, with particle size 168.42 ± 2.15 nm, PDI 0.198 ± 0.01 , zeta potential -34.62 ± 0.94 mV, and entrapment efficiency $86.0 \pm 0.9\%$. Its pH was 6.8, viscosity 6840 cP, and gel strength 52 s. Drug release reached $84.695 \pm 0.8\%$ at 12 h. The Korsmeyer–Peppas model showed the best fit ($R^2 = 0.9973$; $n = 0.7145$). **Conclusion:** The optimized F6 nano-cubosomal gel demonstrated favourable physicochemical properties, sustained drug release and satisfactory stability, indicating its potential as a promising topical allopurinol delivery system. **Keywords:** Allopurinol; Nano-cubosomes; Topical drug delivery; Glyceryl monooleate; Controlled release; Cubosomal gel **How to cite this article:** Prasath Sivakumar^{*1} Dr R Manivannan². Development, Optimization And Evaluation Of Allopurinol Loaded Nano Cubosomal Gel For Enhanced Topical Drug Delivery. Int J Drug Deliv Technol. 2026;16(84s):1975-1977. DOI: 10.25258/ijddt.16.84s.199

INTRODUCTION

Topical drug delivery has become an important area of pharmaceutical research because it can provide localized drug exposure, improve patient convenience and potentially reduce some limitations associated with conventional systemic administration. However, the stratum corneum presents a major barrier to drug penetration, particularly for compounds with poor aqueous solubility. Nanostructured lipid-based carriers have therefore attracted

increasing interest because they can improve drug incorporation, protect the active molecule and provide controlled release at the site of application [1,2].

Allopurinol is a xanthine oxidase inhibitor widely used in the management of hyperuricemia and gout. Its low aqueous solubility and high melting point present challenges for effective formulation and topical delivery. Varrica et al. demonstrated that incorporation of allopurinol into

nanostructured lipid carriers could produce nanosized particles with effective drug association and measurable drug retention within epidermal and dermal layers, supporting the potential of lipid-based nanocarriers for topical allopurinol delivery [3].

Cubosomes are nanostructured lipid carriers characterized by a bicontinuous cubic liquid-crystalline architecture. They are generally prepared using amphiphilic lipids such as glyceryl monooleate (GMO) together with stabilizers such as poloxamers. Their internal structure provides a large interfacial area and enables incorporation of hydrophilic, lipophilic and amphiphilic drugs, while also offering opportunities for sustained drug release [4,5]. Both top-down and bottom-up approaches have been described for cubosome preparation, with the top-down method involving disruption of bulk cubic phases to produce nanoscale dispersions [4].

MATERIALS AND METHODS

Study design: A laboratory-based experimental formulation study.

Study population: Allopurinol and pharmaceutical-grade excipients used for developing the nano-cubosomal gel.

Sample size: Nine formulations (F1–F9) were prepared using varying concentrations of glyceryl monooleate.

Study duration: The study was conducted over the formulation and evaluation period, with stability testing carried out for 6 months.

Study setting/location: The study was conducted in a pharmaceutical formulation and analytical laboratory.

Inclusion criteria:

- Suitable allopurinol drug substance.
- Pharmaceutical-grade excipients.
- Stable nano-cubosomal formulations suitable for evaluation.

The incorporation of optimized cubosomes into a gel base can further improve topical application by increasing formulation residence time, providing suitable rheological properties and facilitating controlled drug release. Recent literature has particularly emphasized the potential of cubosomes for topical and transdermal applications because of their bioadhesion, drug-loading capacity and sustained-release characteristics [6]. The study aims to develop and evaluate an allopurinol-loaded nano-cubosomal gel designed to improve topical drug delivery and provide controlled drug release. The objectives include optimizing the cubosomal formulation, assessing its physicochemical properties, drug entrapment, morphology, and release behaviour, incorporating the optimized formulation into a suitable gel base, and evaluating its stability under long-term and accelerated storage conditions.

Exclusion criteria:

- Physically unstable formulations.
- Formulations with unsuitable physicochemical properties.
- Formulations unsuitable for further optimization.

Statistical Analysis

All experimental results were expressed as mean $\pm$ standard deviation (SD) based on replicate measurements. Descriptive statistics were used to summarize the physicochemical characteristics of the formulations, including particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, pH, viscosity, gel strength, drug content, and cumulative drug release. The nine formulations (F1–F9) were compared to identify the formulation providing the most favourable overall characteristics. In vitro drug-release data were analysed using zero-order, first-order, Higuchi, and Korsmeyer–Peppas models,

and the coefficient of determination (R^2) was used to determine the model providing the best fit. The release exponent (n) was interpreted to characterize the mechanism of drug release. For stability assessment, changes in formulation characteristics during long-term and accelerated storage were

evaluated descriptively by comparing values at baseline and subsequent time points. Statistical analyses were performed using appropriate pharmaceutical statistical software, with a p-value <0.05 considered statistically significant, where inferential comparisons were applicable.

RESULT

Table 1. Physicochemical Characterization of Allopurinol-Loaded Nano-Cubosomal Formulations (F1–F9)

Formulation n	GM O (mg)	Poloxamer 407 (mg)	Particle Size (nm)	PDI	Zeta Potential (mV)	pH	Viscosity (cP)	Gel Strength (s)	EE (%)
F1	100	50	286.53 ± 3.41	0.356 ± 0.02	-18.74 ± 1.12	6.3	4120	28	72.0 ± 1.4
F2	150	50	251.84 ± 2.96	0.318 ± 0.01	-22.68 ± 0.95	6.4	4680	34	75.0 ± 1.2
F3	200	50	229.67 ± 2.34	0.287 ± 0.02	-25.91 ± 1.08	6.6	5330	41	78.0 ± 1.5
F4	250	50	205.31 ± 2.11	0.254 ± 0.01	-28.36 ± 1.17	6.5	5890	47	83.0 ± 1.1
F5	300	50	182.94 ± 1.86	0.221 ± 0.01	-31.48 ± 0.89	6.7	6210	45	74.0 ± 1.6
F6	350	50	168.42 ± 2.15	0.198 ± 0.01	-34.62 ± 0.94	6.8	6840	52	86.0 ± 0.9
F7	400	50	214.30 ± 2.45	0.267 ± 0.02	-29.85 ± 1.05	6.6	7250	58	81.2 ± 1.3
F8	450	50	268.12 ± 3.10	0.332 ± 0.01	-25.10 ± 1.20	6.7	7890	63	77.8 ± 1.7
F9	500	50	312.45 ± 3.65	0.384 ± 0.02	-21.34 ± 0.88	6.8	8450	69	73.5 ± 1.5

Table 2. In Vitro Cumulative Drug Release (%) of Allopurinol-Loaded Nano-Cubosomal Formulations

Time (h)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	7.225	6.778	6.897	5.498	5.296	8.787	6.12	5.01	4.11
1	14.774	11.176	10.437	10.426	9.587	16.451	12.45	9.88	8.21
2	19.536	18.512	16.984	17.779	12.943	24.677	19.34	15.67	13.45
3	25.988	23.834	24.112	21.968	16.286	33.264	26.11	21.45	18.9
4	33.276	31.521	30.486	26.364	20.575	38.543	32.78	27.89	23.56
5	39.751	36.314	36.791	30.184	27.439	47.387	38.9	33.12	29.34
6	44.594	41.633	40.613	35.911	31.772	54.789	45.34	38.76	34.12
7	49.689	48.124	46.861	39.887	38.496	61.155	51.67	44.34	39.8
8	57.629	54.788	51.655	45.732	42.949	67.391	57.89	50.12	45.23
9	61.368	60.467	57.933	51.396	49.562	75.463	63.45	56.78	50.67
10	67.797	67.956	64.115	58.859	54.275	79.617	69.12	62.45	56.12
11	71.466	73.681	69.589	63.241	58.194	83.141	74.56	67.89	61.34
12	74.536	77.347	73.298	69.579	64.696	84.695	78.45	71.23	65.18

Table 3. Release Kinetic Analysis of Optimized Formulation (F6)

Formulation	Zero-Order R^2	First-Order R^2	Higuchi R^2	Korsmeyer–Peppas R^2	Release Exponent (n)
F6 (Allopurinol)	0.9604	0.9718	0.9794	0.9973	0.7145

Table 4. Long-Term Stability of Optimized Nano-Cubosomal Gel (F6) at $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{ RH}$

Parameter	Initial	1 Month	2 Months	3 Months	6 Months
Visual appearance	Opalescent, smooth, homogeneous	Opalescent, homogeneous	Opalescent, homogeneous	Opalescent, homogeneous	Opalescent, homogeneous
pH	6.80 ± 0.03	6.79 ± 0.02	6.78 ± 0.04	6.76 ± 0.03	6.74 ± 0.02
Viscosity (cP)	6840 ± 45	6820 ± 50	6795 ± 40	6760 ± 60	6710 ± 55
Particle size (nm)	168.42 ± 2.15	169.10 ± 1.95	169.95 ± 2.20	170.80 ± 2.10	172.18 ± 2.40
PDI	0.198 ± 0.01	0.201 ± 0.01	0.203 ± 0.02	0.205 ± 0.01	0.208 ± 0.01
Zeta potential (mV)	-34.62 ± 0.94	-34.10 ± 0.88	-33.45 ± 1.05	-32.70 ± 0.92	-31.45 ± 1.10
Entrapment efficiency (%)	86.0 ± 0.9	85.7 ± 0.8	85.3 ± 1.0	84.9 ± 0.9	84.3 ± 1.1
Drug content (%)	99.42 ± 0.5	99.15 ± 0.6	98.80 ± 0.4	98.45 ± 0.7	97.90 ± 0.5
12-h in vitro release (%)	84.695 ± 0.8	84.520 ± 0.7	84.310 ± 0.9	84.150 ± 0.8	83.850 ± 1.0

Table 5. Accelerated Stability of Optimized Nano-Cubosomal Gel (F6) at $40 \pm 2^\circ\text{C}/75 \pm 5\% \text{ RH}$

Parameter	Initial	1 Month	2 Months	3 Months	6 Months
Visual appearance	Opalescent, smooth, homogeneous	Opalescent, homogeneous	Opalescent, homogeneous	Opalescent, homogeneous	Opalescent, homogeneous
pH	6.80 ± 0.03	6.77 ± 0.03	6.74 ± 0.02	6.71 ± 0.04	6.68 ± 0.03
Viscosity (cP)	6840 ± 45	6780 ± 40	6715 ± 50	6630 ± 55	6540 ± 65
Particle size (nm)	168.42 ± 2.15	170.45 ± 2.30	172.80 ± 2.65	175.20 ± 2.45	178.65 ± 2.85
PDI	0.198 ± 0.01	0.204 ± 0.01	0.209 ± 0.02	0.216 ± 0.01	0.224 ± 0.01
Zeta potential (mV)	-34.62 ± 0.94	-33.25 ± 0.95	-32.10 ± 1.12	-30.75 ± 1.02	-29.18 ± 1.15
Entrapment efficiency (%)	86.0 ± 0.9	85.2 ± 0.8	84.5 ± 1.1	83.6 ± 0.9	82.4 ± 1.3
Drug content (%)	99.42 ± 0.5	98.85 ± 0.6	98.20 ± 0.7	97.55 ± 0.5	96.82 ± 0.6
12-h in vitro release (%)	84.695 ± 0.8	84.220 ± 0.7	83.750 ± 0.9	83.100 ± 0.8	82.100 ± 1.1

Figure 1. Particle Size and Entrapment Efficiency

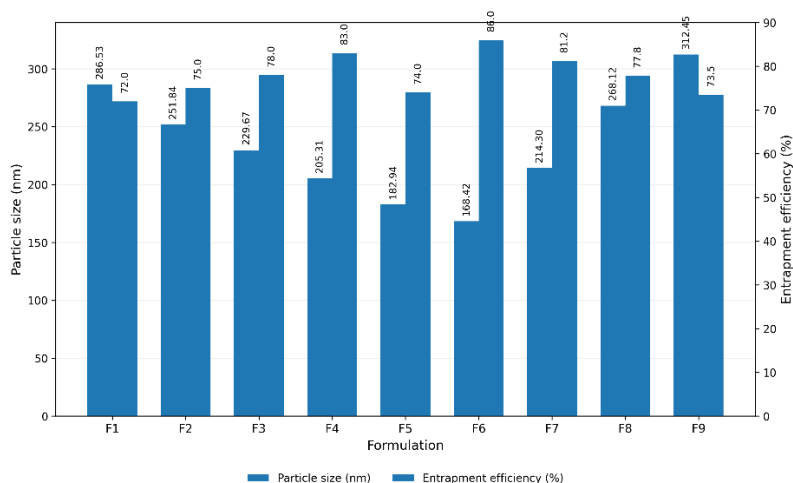
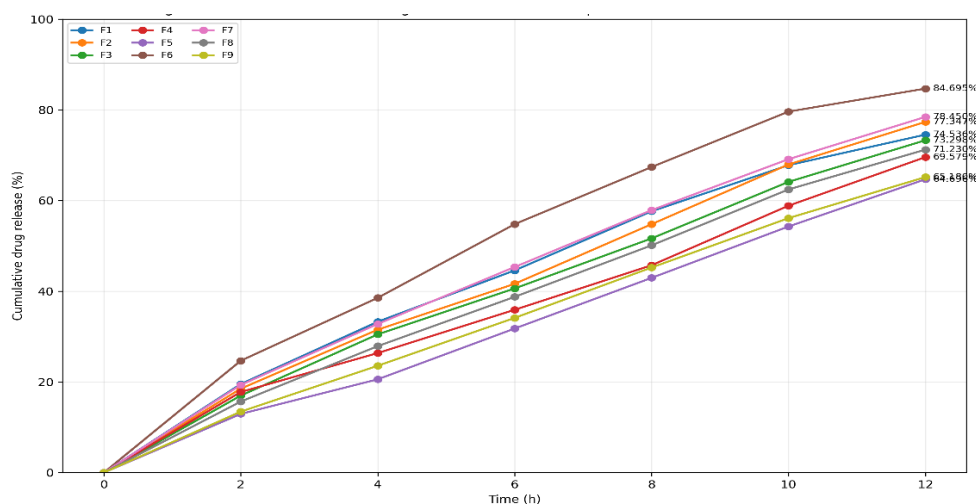


Figure 2. Cumulative Drug Release Profile

Development, Optimization And Evaluation Of Allopurinol Loaded Nano Cubosomal Gel For Enhanced Topical Drug Delivery



The physicochemical characteristics of the nine allopurinol-loaded nano-cubosomal formulations (F1–F9) are presented in Table 1. Increasing the concentration of glyceryl monooleate (GMO) from 100 to 500 mg initially reduced particle size, with the lowest value observed for F6 (168.42 ± 2.15 nm), followed by a gradual increase in F7–F9. A similar pattern was observed for PDI, which decreased from 0.356 ± 0.02 in F1 to 0.198 ± 0.01 in F6, indicating a relatively narrow particle-size distribution, and then increased to 0.384 ± 0.02 in F9. Zeta potential became progressively more negative from -18.74 ± 1.12 mV in F1 to -34.62 ± 0.94 mV in F6, suggesting improved colloidal stability, followed by a reduction in magnitude at higher GMO concentrations. The pH values ranged from 6.3 to 6.8, indicating acceptable values for topical application. Viscosity increased progressively from 4120 cP in F1 to 8450 cP in F9. Gel strength also increased from 28 s to 69 s across the formulations, although F5 showed a slight reduction to 45 s compared with F4. Entrapment efficiency varied between $72.0 \pm 1.4\%$ and $86.0 \pm 0.9\%$, with F6 showing the highest value. Overall, F6 demonstrated a favourable combination of small particle size, low PDI, relatively high negative zeta potential and maximum drug entrapment efficiency.

The cumulative in vitro drug-release profiles of formulations F1–F9 are shown in Table 2.

All formulations exhibited a gradual increase in drug release with increasing time, indicating sustained release of allopurinol from the nano-cubosomal systems. At 12 h, cumulative drug release ranged from 64.696% for F5 to 84.695% for F6. Formulation F6 showed the highest release throughout most of the study period, reaching 24.677% at 2 h, 47.387% at 5 h, 67.391% at 8 h, 79.617% at 10 h, and 84.695% at 12 h. In comparison, F1 and F2 released 74.536% and 77.347%, respectively, at 12 h, while F3, F4, F7, F8 and F9 showed 73.298%, 69.579%, 78.45%, 71.23% and 65.18% release, respectively. The relatively slower release observed with some formulations may be related to differences in lipid content and the internal structure of the cubosomal system. Based on the overall release profile together with the physicochemical characteristics and entrapment efficiency, F6 was selected as the optimized formulation.

The release kinetics of the optimized formulation F6 were evaluated using zero-order, first-order, Higuchi and Korsmeyer–Peppas mathematical models (Table 3). The coefficient of determination (R^2) values were 0.9604 for the zero-order model, 0.9718 for the first-order model, and 0.9794 for the Higuchi model. The Korsmeyer–Peppas model showed the highest R^2 value of 0.9973, indicating the best fit among the tested models. The release exponent (n) was

0.7145. This value suggests a non-Fickian or anomalous release mechanism, in which drug diffusion and relaxation/erosion-related processes may contribute to drug release from the cubosomal matrix. Thus, the release behaviour of F6 was predominantly described by the Korsmeyer–Peppas model.

The long-term stability results of the optimized F6 nano-cubosomal gel stored at $25 \pm 2^\circ\text{C}/60 \pm 5\%$ RH are presented in Table 4. The formulation retained its opalescent, smooth and homogeneous appearance throughout the 6-month storage period, with no visible evidence of instability. The pH showed only a small decline from 6.80 ± 0.03 initially to 6.74 ± 0.02 at 6 months. Viscosity decreased gradually from 6840 ± 45 to 6710 ± 55 cP, while particle size increased slightly from 168.42 ± 2.15 to 172.18 ± 2.40 nm. PDI increased from 0.198 ± 0.01 to 0.208 ± 0.01 , indicating only a minor change in particle-size distribution. Zeta potential changed from -34.62 ± 0.94 to -31.45 ± 1.10 mV. Entrapment efficiency decreased modestly from $86.0 \pm 0.9\%$ to $84.3 \pm 1.1\%$, while drug content declined from $99.42 \pm 0.5\%$ to $97.90 \pm 0.5\%$. The 12-h drug release showed a small reduction from $84.695 \pm 0.8\%$ to $83.850 \pm 1.0\%$.

DISCUSSION

The present investigation demonstrated that variation in glyceryl monooleate concentration produced clear changes in the physicochemical characteristics of the allopurinol-loaded nano-cubosomal formulations. Among F1–F9, formulation F6 provided the most favourable overall combination of particle size, PDI, zeta potential and entrapment efficiency. This observation is consistent with the established influence of lipid concentration and stabilizer–lipid interactions on cubosome formation and colloidal characteristics. Reviews by Nasr et al. and other recent investigators have emphasized that the composition of the lipid phase and stabilizer concentration can substantially

influence particle size, surface charge, dispersity and drug loading of cubosomal systems [7,8].

These relatively small changes indicate that F6 maintained its physical and formulation characteristics under long-term storage. The accelerated stability findings for F6 at $40 \pm 2^\circ\text{C}/75 \pm 5\%$ RH are summarized in Table 5. The formulation maintained its opalescent, smooth and homogeneous appearance throughout the 6-month period. However, slightly greater changes were observed compared with long-term storage. The pH decreased from 6.80 ± 0.03 to 6.68 ± 0.03 , while viscosity declined from 6840 ± 45 to 6540 ± 65 cP. Particle size increased from 168.42 ± 2.15 to 178.65 ± 2.85 nm, accompanied by an increase in PDI from 0.198 ± 0.01 to 0.224 ± 0.01 . The zeta potential became less negative, changing from -34.62 ± 0.94 to -29.18 ± 1.15 mV. Entrapment efficiency decreased from $86.0 \pm 0.9\%$ to $82.4 \pm 1.3\%$, and drug content decreased from $99.42 \pm 0.5\%$ to $96.82 \pm 0.6\%$. Similarly, 12-h drug release decreased from $84.695 \pm 0.8\%$ initially to $82.100 \pm 1.1\%$ after 6 months. Despite these changes, the formulation remained physically homogeneous and retained relatively high drug content and entrapment efficiency, indicating reasonable stability under accelerated storage conditions.

influence particle size, surface charge, dispersity and drug loading of cubosomal systems [7,8].

In the present study, particle size decreased from 286.53 ± 3.41 nm in F1 to 168.42 ± 2.15 nm in F6, followed by an increase in F7–F9. PDI similarly decreased from 0.356 ± 0.02 to 0.198 ± 0.01 in F6 and subsequently increased to 0.384 ± 0.02 in F9. This pattern indicates that an intermediate GMO concentration produced the most favourable nanoscale organization, whereas further lipid addition may have promoted particle enlargement and increased heterogeneity. A comparable relationship between formulation composition and cubosome size has been reported in topical cubosomal studies, where changes in GMO

and poloxamer concentrations produced significant differences in particle characteristics [8,9].

The zeta potential of F6 was -34.62 ± 0.94 mV, compared with -18.74 ± 1.12 mV in F1. The more negative surface charge observed in F6 suggests improved electrostatic contribution to colloidal stability. This is consistent with the general observation that surface charge and steric stabilization provided by poloxamer can influence the physical stability of cubosomal dispersions [7]. The entrapment efficiency also increased from $72.0 \pm 1.4\%$ in F1 to $86.0 \pm 0.9\%$ in F6, before declining at higher GMO concentrations. This suggests that the lipid content in F6 provided a favourable environment for allopurinol incorporation without excessive lipid accumulation. Importantly, previous research on allopurinol-loaded lipid nanoparticles also demonstrated successful drug incorporation and topical suitability, supporting the broader applicability of lipid-based nanocarriers for this poorly soluble drug [3].

The pH values of the formulations ranged from 6.3 to 6.8, with F6 showing a pH of 6.8, indicating compatibility with the mildly acidic-to-neutral environment generally desirable for topical formulations. Viscosity increased progressively from 4120 cP in F1 to 8450 cP in F9, while gel strength increased from 28 to 69 s. The progressive increase in viscosity with higher GMO content indicates greater structural organization of the formulation. Similar changes in rheological properties have been described following incorporation of cubosomal dispersions into topical gel systems [9,10]. However, excessive viscosity may potentially influence spreadability and drug diffusion, making the intermediate characteristics of F6 advantageous for balancing structural integrity with drug release.

The in vitro release study showed a gradual increase in cumulative allopurinol release

over 12 hours. Formulation F6 demonstrated the highest release, reaching 24.677% at 2 h, 47.387% at 5 h, 67.391% at 8 h, 79.617% at 10 h and 84.695% at 12 h. The gradual release pattern suggests that the cubosomal structure was able to retard rapid drug liberation while maintaining substantial drug release over the study period. Similar sustained-release behaviour has been reported for other cubosomal formulations intended for topical delivery. Sanjana et al. developed dexamethasone-loaded cubosomes using GMO and poloxamer 407 and reported 88.12% release at 12 h; after incorporation into a Carbopol 940 gel, release remained sustained at approximately 83.58% at 12 h [11]. The 84.695% release obtained with F6 is therefore comparable with previously reported topical cubosomal systems.

Further support comes from studies using GMO and poloxamer 407 for other topical drugs. An erythromycin-loaded cubosomal formulation demonstrated nanoscale particle formation, high entrapment efficiency and prolonged release after incorporation into a Carbopol gel [12]. Similarly, a lidocaine hydrochloride cubosomal system prepared using GMO and poloxamer 407 showed a particle size of approximately 228 nm, an entrapment efficiency of 89.85%, and prolonged drug release over 12 hours [13]. These studies, although involving different active pharmaceutical ingredients, support the suitability of GMO-based cubosomes for topical sustained drug delivery.

The release kinetic analysis of F6 further clarified the mechanism of drug liberation. The formulation showed R^2 values of 0.9604, 0.9718 and 0.9794 for the zero-order, first-order and Higuchi models, respectively, whereas the Korsmeyer–Peppas model demonstrated the highest R^2 value of 0.9973. The release exponent was 0.7145, suggesting anomalous or non-Fickian release. This indicates that drug transport was likely influenced by more than simple diffusion and may have involved a combination of diffusion and relaxation or

restructuring of the lipid-based matrix. Such behaviour is compatible with the complex internal architecture of cubosomes, which contains interconnected aqueous channels within a lipid bilayer structure [7,8].

The long-term stability study demonstrated that F6 remained physically acceptable for the entire 6-month period at $25 \pm 2^\circ\text{C}/60 \pm 5\%$ RH. The formulation remained opalescent, smooth and homogeneous. Particle size increased only slightly from 168.42 ± 2.15 to 172.18 ± 2.40 nm, while PDI changed from 0.198 ± 0.01 to 0.208 ± 0.01 . Entrapment efficiency decreased from $86.0 \pm 0.9\%$ to $84.3 \pm 1.1\%$, and drug content remained high at $97.90 \pm 0.5\%$. The relatively small changes suggest good physical stability under long-term storage. The role of poloxamers in providing steric stabilization and maintaining the colloidal integrity of cubosomal systems has been discussed extensively in the literature [4,7].

Under accelerated conditions of $40 \pm 2^\circ\text{C}/75 \pm 5\%$ RH, greater but still moderate changes were observed. After 6 months, particle size increased to 178.65 ± 2.85 nm, PDI to 0.224 ± 0.01 , and the zeta potential changed from

-34.62 ± 0.94 to -29.18 ± 1.15 mV. Entrapment efficiency decreased to $82.4 \pm 1.3\%$, while drug content remained $96.82 \pm 0.6\%$. The 12-h drug release decreased from $84.695 \pm 0.8\%$ to $82.100 \pm 1.1\%$. The greater changes under accelerated conditions are consistent with the possibility of increased molecular mobility and gradual alterations in lipid organization at elevated temperature. Nevertheless, the formulation retained its homogeneous appearance and remained within a relatively narrow nanoscale range, suggesting acceptable stability during the tested period.

Overall, F6 containing 350 mg GMO and 50 mg poloxamer 407 demonstrated the most balanced formulation characteristics. Its particle size of 168.42 ± 2.15 nm, PDI of 0.198 ± 0.01 , zeta potential of -34.62 ± 0.94 mV, entrapment efficiency of $86.0 \pm 0.9\%$, and 12-h release of $84.695 \pm 0.8\%$ indicate a well-characterized nano-cubosomal system with sustained drug-release behaviour. The findings are broadly consistent with previous cubosomal research involving topical drugs and with evidence supporting lipid nanocarriers for topical allopurinol delivery [3,11-13].

CONCLUSION

The present study successfully developed and evaluated an allopurinol-loaded nano-cubosomal gel for enhanced topical drug delivery. Among the nine formulations, F6, containing 350 mg glyceryl monooleate and 50 mg poloxamer 407, demonstrated the most favourable characteristics, with a particle size of 168.42 ± 2.15 nm, PDI of 0.198 ± 0.01 , zeta potential of -34.62 ± 0.94 mV, and entrapment efficiency of $86.0 \pm 0.9\%$. It achieved $84.695 \pm 0.8\%$ drug

release at 12 hours and best fitted the Korsmeyer–Peppas model ($R^2 = 0.9973$; $n = 0.7145$), indicating anomalous release behaviour. The optimized gel maintained acceptable appearance, pH, viscosity, and drug content during long-term and accelerated stability studies. Overall, these findings indicate that the developed nano-cubosomal gel provides a promising platform for controlled and sustained topical delivery of allopurinol.

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