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Fabrication of *Curcumin*-loaded Olaminosomes for Intracorneal Permeation Enhancement

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Abstract

Background: *Curcumin*, a polyphenolic compound obtained from *Curcuma longa*, demonstrates potent anti-inflammatory, antioxidant, and immunomodulatory properties, making it a promising candidate for treating ocular inflammatory conditions. However, it faces significant challenges, including low bioavailability, rapid metabolic degradation, poor aqueous solubility, and inadequate corneal penetration. **Aim:** To formulate and optimise drug-loaded olaminosomes encapsulating *Curcumin* for enhanced ocular delivery. **Methods:** Preformulation studies were conducted, including solubility analysis in various solvents and drug excipient compatibility studies using Fourier-Transform Infrared Spectroscopy (FTIR). Olaminosomes, a novel nanovesicular carrier, were prepared using the ethanol injection method, incorporating octadecyl amine, span 80, and oleic acid as lipid, nonionic surfactant, and edge activator to enhance drug entrapment and corneal penetration. **Results:** The formulation exhibited a vesicle size of 430 nm, a polydispersity index (PDI) of 0.41, an entrapment efficiency of 29.6%, and *ex vivo* corneal permeation of 40% *Curcumin* and 60% olaminosomes over 2 hours. **Conclusion:** These findings underscore the potential of olaminosomes as a promising nanovesicular platform for sustained and targeted ocular drug delivery.

Major Findings: *Curcumin*-loaded olaminosomes were successfully developed with a vesicle size of 430 nm, PDI of 0.41, and entrapment efficiency of 29.6%. The formulation significantly enhanced *ex vivo* corneal permeation (60%) compared to free *Curcumin* (40%).

Keywords: *Curcumin*, Octadecyl Amine, Ocular Delivery, Oleic Acid, Olaminosomes, Span 80

Abbreviations: ANOVA: Analysis of Variance, CCD: Central Composite Design; %EE: Per cent Entrapment Efficiency, FTIR: Fourier-Transform Infrared Spectroscopy, PDI: Polydispersity Index, PBS: Phosphate-Buffered Saline, PS: Particle Size, UV-Vis: Ultraviolet-Visible Spectrophotometry.

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1. Introduction

Olaminosomes are an emerging class of lipid-based nanovesicular drug delivery systems composed primarily of amphiphilic amine lipids that self-assemble into bilayered vesicular structures in aqueous environments. Compared with conventional liposomes, niosomes and other vesicular formations, olaminosomes possess a cationic surface and stronger membrane affinity, which improves drug loading, vesicle stability and also interaction with negatively charged biological membranes. Structurally, olaminosomes possess a spherical vesicle architecture like other lipid vesicles, consisting of one or multiple lipid bilayers surrounding an aqueous core. The presence of octadecyl amine imparts a cationic surface charge and amphiphilic character, facilitating strong interactions with negatively charged biological membranes and enhancing drug encapsulation efficiency for both hydrophilic and lipophilic therapeutics[1]. These vesicles exhibit several advantages, including improved drug stability, enhanced permeability and retention, controlled and sustained drug release, and increased cellular uptake due to electrostatic interactions with cell

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membranes. Additionally, olaminosomes can improve the bioavailability of poorly soluble drugs and protect labile compounds from enzymatic degradation.

The ocular surface and corneal epithelium are barriers that present unique challenges to effective drug delivery, such as limited tear turnover, rapid drug loss from the precorneal area, and low corneal permeability to most drugs. Olaminosomes are favoured for the intraocular delivery of drugs. The presence of a positive surface charge on the olaminosomes enables them to bind to the negatively charged mucin and corneal epithelium cells using an electrostatic attraction. As a result, the residence time of the olaminosomes in the precorneal area is increased, thus allowing for a greater chance of the olaminosomes being in proximity to the corneal surface. The lipid bilayer structure of the olaminosomes, combined with the amphiphilic nature of the octadecyl amine used to form their membranes, allows them to protect the encapsulated laboratory molecules from enzyme degradation in the tear fluid. Moreover, due to their relatively small size and the deformability of their membranes, olaminosomes can increase the effectiveness of paracellular and transcellular permeation through the corneal epithelium, leading to deeper penetration of drug molecules into the cornea and prolonged release of the drug from the olaminosomes and consequently help to overcome significant barriers in the delivery of therapeutic agents to the tissues within the eye.

Owing to these properties, olaminosomes have shown promising applications in various drug delivery strategies, including transdermal, topical, and ocular delivery, as well as targeted delivery of anticancer, antimicrobial, and anti-inflammatory agents, thereby representing a versatile and efficient platform for advanced pharmaceutical and nanomedicine applications.

Curcumin is obtained from *Curcuma longa*[2] and exhibited anti-inflammatory[3], antioxidant[4], and anticancer effects, including protection against cerebral ischemia[5]and inhibition of protein kinase D1 to halt tumour growth[6]. However, its poor solubility, poor bioavailability, and rapid degradation limited clinical use, despite its safety up to 12 g per day and faecal excretion after oral intake. However, it has some limitations, such as limited delivery to the intended target tissue due to permeability barriers. Encapsulating *Curcumin* into olaminsomes may be a viable option to increase *Curcumin*'s solubility, extend its retention time at the site of application, protect from degradation, and allow deeper penetration into tissues.

To the best of our knowledge, this is among the first attempts to develop *Curcumin*-loaded olaminosomes for improved intracorneal delivery, which highlights their potential as an advanced vesicular system for ocular drug delivery. The incorporation of oleylamine into the vesicular structure represents a novel approach that enhances vesicle deformability, drug loading capacity, and permeation characteristics. The

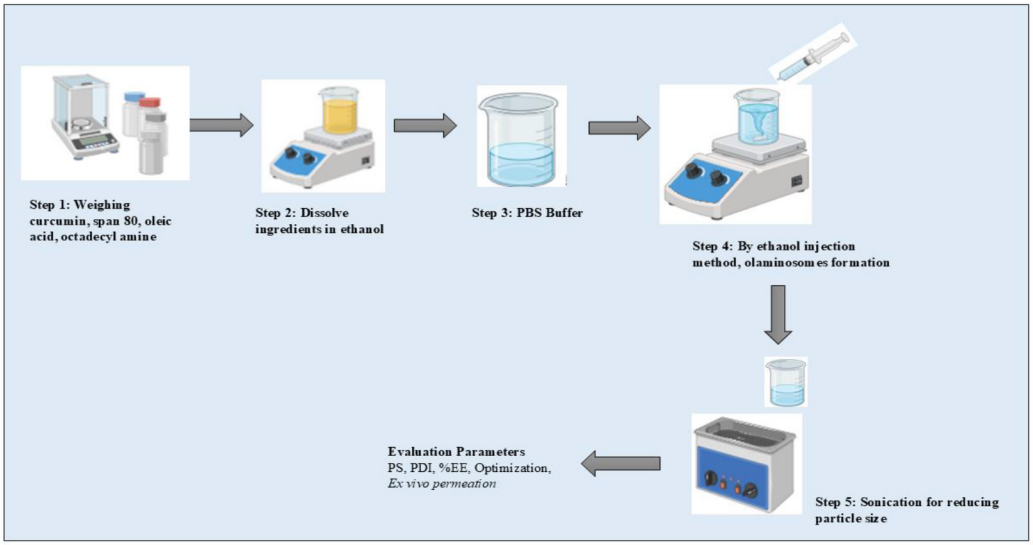


Figure 1. Schematic representation of olaminosomes preparation and evaluation.

developed olaminosomal formulation demonstrates significant potential as an alternative to existing nanocarriers for improving bioavailability and therapeutic performance. A Schematic representation of olaminosomes preparation and evaluation is depicted in (Figure 1).

2. Materials and Methods

2.1 Materials

Curcumin was purchased from Biotechnosis Scientific Solution, Noida, India. Span 80, Oleic acid, Octadecyl amine and ethanol were procured from Central Drug House (P) Ltd., Delhi. All other chemicals and reagents used were of analytical purity and used without further purification.

2.2 Methods

2.2.1 Preformulation Studies

Preformulation studies were carried out to evaluate the key physicochemical properties of the drug substance. These studies included solubility, melting point, excipient compatibility and calibration curve[7].

2.2.1.1 Solubility

The solubility of *Curcumin* and excipients like octadecyl amine, oleic acid and Span 80 was determined in various solvents like distilled water, PBS (pH 7.4), and ethanol by adding an excess amount of drug to 10 mL of solvent, shaking at 37°C for 48 h, filtering and quantifying the drug through UV spectroscopy at 430 nm[8].

2.2.1.2 Melting Point

Curcumin's melting point was measured using a digital melting point apparatus[9].

2.2.1.3 Drug Excipient Compatibility

A drug excipient compatibility study was conducted using FTIR. Spectra of *Curcumin*, octadecyl amine, oleic acid, span 80, spectra of the physical mixture of drug and excipients (1:1 ratio), and final olaminosomes formulation were obtained[10].

2.2.1.4 Calibration Curve

A linear calibration curve for *Curcumin* was plotted at different concentrations using UV-Vis at 430 nm[11].

2.2.2 Design of Experiments

A three-factor, three-level Central Composite Design (CCD) was employed to optimise *Curcumin*-loaded olaminosomes. The selected independent variables, Surfactant amount (X_1), lipid amount (X_2) and capping agent amount (X_3) were studied at three different levels coded as -1,0,1. Particle size (Y_1), polydispersity index (Y_2) and per cent entrapment efficiency (%EE) (Y_3) of the produced *Curcumin*-loaded olaminosomes were chosen as dependent variables. According to the CCD matrix generated by Design Expert Software (Stat Ease 360), a total of 20 runs were constructed as shown in Table 1. The effect of variables and their corresponding response was evaluated by using analysis of variance (ANOVA)[12].

2.2.3 Preparation of Curcumin-loaded Olaminosomes

Olaminosomes were prepared using the ethanol injection technique as delineated in Table 2. Exactly 10 mg of *Curcumin*, along with specified amounts of oleic acid, span 80 and octadecyl amine, were precisely weighed and dissolved in 10 mL of ethanol on a magnetic stirrer at 60°C. This ethanolic solution was then slowly injected into 4 times the volume (40 mL) of phosphate-buffered saline (PBS, pH 7.4), which was continuously stirred at 60°C until the ethanol completely evaporated, as indicated by the sudden appearance of turbidity, signalling the formation of olaminosomes. The resulting dispersion was sonicated at 15± 2°C to reduce particle size, then stored at 4°C for further assessments[13,14].

Table 1. Independent and dependent variables used in the central composite design for the formulation of *Curcumin*-loaded olaminosomes

Independent variables	**Levels**		
	-1	**0**	**1**
X_1: Span 80 (ml)	1	2	3
X_2: Oleic acid (ml)	1	5	6
X_3: Octadecyl amine (mg)	5.5	7.5	8
Dependent Variables	**Target**		
Y_1: Particle size	Minimum		
Y_2: Polydispersity index	Minimize		
Y_3: Entrapment efficiency	Maximize		

Table 2. Composition of the various formulated *Curcumin*-loaded olaminosomes with their measured response of CCD

Samples	Factor 1: A Span 80 (ml)	Factor 2 B: Oleic acid (ml)	Factor 3C: Octadecyl amine (mg)	Response 1 Particle size (nm)	Response 2: Polydispersity index	Response 3 EE%
T1	0	0	0	300±0.55	0.27±0.01	86±0.24
T2	-1	1	-1	470±0.13	0.46±0.02	74±0.16
T3	0	0	0	305±2.50	0.28±0.00	85±1.10
T4	-1.68179	0	0	360±7.39	0.34±0.04	82±0.03
T5	1	-1	-1	260±0.20	0.24±0.03	88±1.65
T6	-1	-1	-1	390±0.22	0.36±0.00	80±1.05
T7	0	0	0	295±0.32	0.26±0.01	87±0.04
T8	0	0	-1.68179	330±0.42	0.31±0.02	83±0.05
T9	0	0	0	300±2.03	0.27±0.02	86±1.15
T10	0	0	1.68179	285±1.45	0.25±0.03	89±0.06
T11	-1	1	1	480±0.12	0.47±0.01	73±1.56
T12	1.68179	0	0	220±2.13	0.21±0.00	92±1.05
T13	0	0	0	305±2.24	0.28±0.01	85±1.20
T14	0	1.68179	0	490±0.02	0.48±0.03	72±1.05
T15	-1	-1	1	350±0.05	0.32±0.02	82±0.06
T16	0	0	0	290±1.03	0.26±0.01	87±1.07
T17	1	-1	1	240±2.03	0.22±0.05	90±1.05
T18	1	1	1	430±1.06	0.41±0.03	77±1.65
T19	1	1	-1	450±0.05	0.43±0.01	76±1.60
T20	0	-1.68179	0	270±0.07	0.25±0.04	88±0.45

Values are represented as mean± SD

2.2.4 Characterisation of the Prepared Curcumin-loaded Olaminosomes

The characterisation of *Curcumin*-loaded olaminosome includes particle size determination, polydispersity index, per cent entrapment efficiency, and *ex vivo* permeation[15].

2.2.4.1 Particle size (PS) and Polydispersity Index (PDI)

PS and PDI of *Curcumin*-loaded olaminosomes were determined by Anton par particle size analyser after appropriate dilution with deionised water. Measurements were performed in triplicate to ensure the reproducibility and reliability of the polydispersity index values, which indicate the uniformity of the nanoparticles' size distribution[16].

2.2.4.2 Per cent Entrapment Efficiency (EE%)

Entrapment efficiency was calculated by ultracentrifugation (6000 rpm for 1 hr) followed by quantifying free *Curcumin* in supernatant through UV spectrophotometry at 430 nm. Spectrophotometer (Shimadzu, model UV-1700, Kyoto, Japan) was utilised to detect the concentrations of *Curcumin* in the supernatant at the predetermined ƛmax 430 nm employing the calibration curve[17].

The EE% was estimated using the formula:

$$\%\,Entrapment\ efficiency = \frac{Total\ drug - Free\ drug}{Total\ drug} \times 100$$

2.2 4.3 Ex Vivo Permeation

Ex vivo permeation studies were conducted using a Franz diffusion cell apparatus. The study involves mounting freshly excised goat cornea between the donor compartment and receptor compartment (filled with PBS pH 7.4, maintained at 32°C under magnetic stirring). Samples (0.5-1 mL) were withdrawn at fixed time points, such as 15, 30, 60, 90, and 120 min (i.e., 2 h), analysed for *Curcumin* content by UV-Vis spectrophotometry at

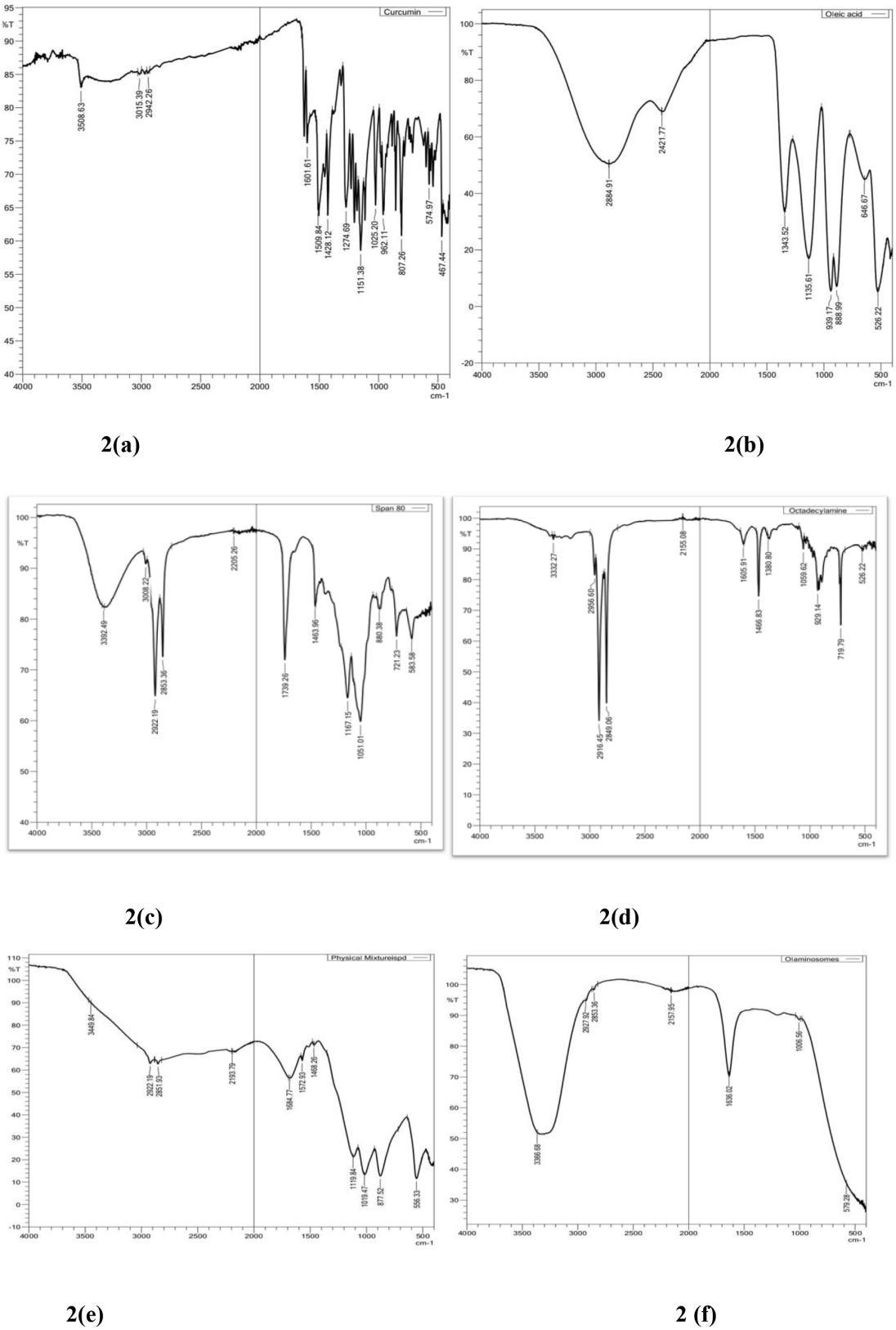


Figure 2. **(a).** FTIR of *Curcumin*; **(b).** FTIR of oleic acid; **(c).** FTIR of span 80; **(d).** FTIR of octadecyl amine; **(e).** FTIR of physical mixture (*Curcumin*, oleic acid, span 80, octadecyl amine); **(f).** FTIR of formulation (*Curcumin*-loaded olaminosomes.

430 nm, and immediately replaced with an equal volume of fresh receptor medium to maintain sink conditions[18].

3. Results and Discussion

3.1 Solubility

Curcumin exhibits high solubility in ethanol, moderate solubility in octadecyl amine and oleic acid, but limited solubility in Span 80[19].

3.2 Melting Point

The melting point of *Curcumin*[20] was found to be 178°C.

3.3 Excipient Compatibility

FTIR analysis of *Curcumin*[21] with other excipients like Span80, oleic acid, and octadecyl amine in a physical mixture shows no new peaks, confirming compatibility for olaminosomes formulation (Figures 2a, 2b, 2c, 2d, 2e, and 2f).

3.4 Calibration Curve

The calibration curve[22] for the analyte exhibited excellent linearity over 0.5-2.5 µg/mL, i.e., $R^2 = 0.9894$, $y = 7.3484x - 1.2889$ (Figure 3).

3.5 Optimisation of *Curcumin*-loaded Olaminosomes

A total of 20 formulations (T1-T20) were prepared and characterised for particle size, PDI and % entrapment efficiency. The particle size of the formulation (*Curcumin*-loaded olaminosomes) varied significantly, ranging from approximately 220 nm to 490 nm, indicating that the composition strongly influences vesicle size. Lower particle sizes were generally observed at higher levels of span 80 and optimised levels of oleic acid, while higher oleic acid concentrations tended to increase particle size. The polydispersity index values ranged from 0.21 to 0.48, suggesting moderate uniformity, with lower PDI values indicating better homogeneity of vesicles. %EE ranged from 72% to 92%, showing that most formulations exhibited good drug encapsulation. A higher per cent entrapment efficiency was observed in *Curcumin*-loaded olaminosomes with balanced concentrations of Span 80 and oleic acid, while extreme levels of variables resulted in reduced entrapment. Hence, the data indicate the formulation variables significantly affect all three responses (PS, PDI and %EE) and an optimised combination is required to achieve a smaller particle size, low polydispersity index and high entrapment efficiency[23].

Analysis of the response for particle size has been presented in Table 3. ANOVA analysis for particle size reveals a highly significant model, i.e., F=8.61, p=0.0003, confirming that the quadratic model effectively explains variations in particle size influenced by *Curcumin*-loaded olaminosomes variables. Linear effects of span 80, i.e., F=69.27, p=0.0001 and oleic acid (F=14.99, p=0.0026) are statistically significant, as is

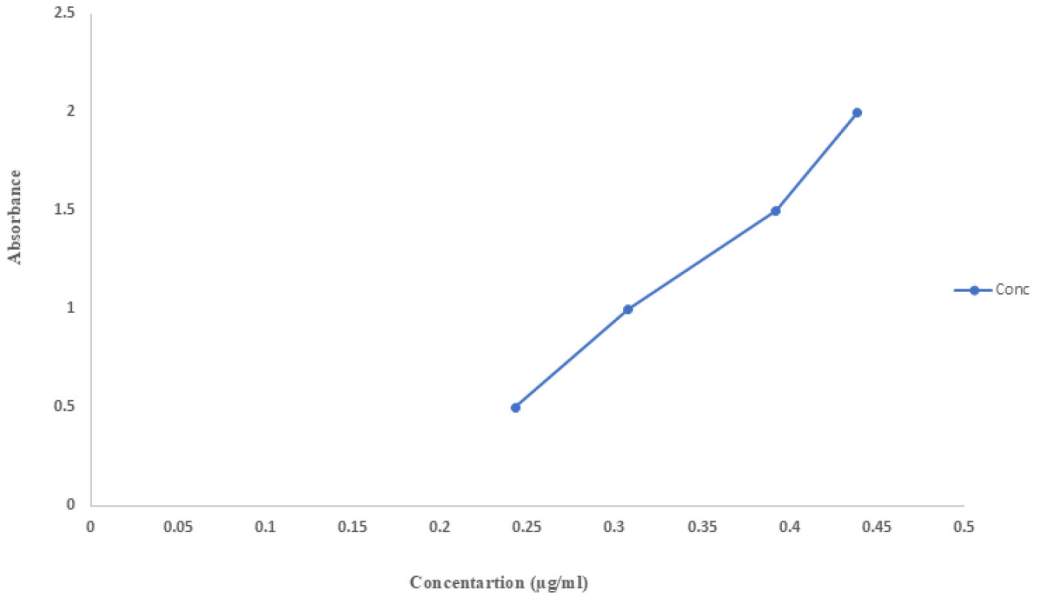


Figure 3. Linear calibration curve of absorbance vs concentration for *Curcumin*.

Table 3. Fit summary of the developed statistical models showing regression and ANOVA parameters for response 1 (mean particle size)

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	1.202E+05	9	13360.54	12.22	0.0003	significant
A- Span 80	21785.16	1	21785.16	19.92	0.0012	
B-Oleic acid	67481.81	1	67481.81	61.71	<0.0001	
C-Octadecyl amine	1554.01	1	1554.01	1.42	0.2607	
AB	3612.50	1	3612.50	3.30	0.0992	
AC	12.50	1	12.50	0.0114	0.9170	
A^2	1075.69	1	1075.69	0.9837	0.3447	
B^2	23590.70	1	23590.75	21.57	0.0009	
C^2	3168.06	1	3168.06	2.90	0.1196	
Residual	10935.15	10	1093.52			
Lack of Fit	10764.32	5	2152.86	63.01	0.0002	significant
Pure Error	170.83	5	34.17			
Cor Total	1.312E+05	19				

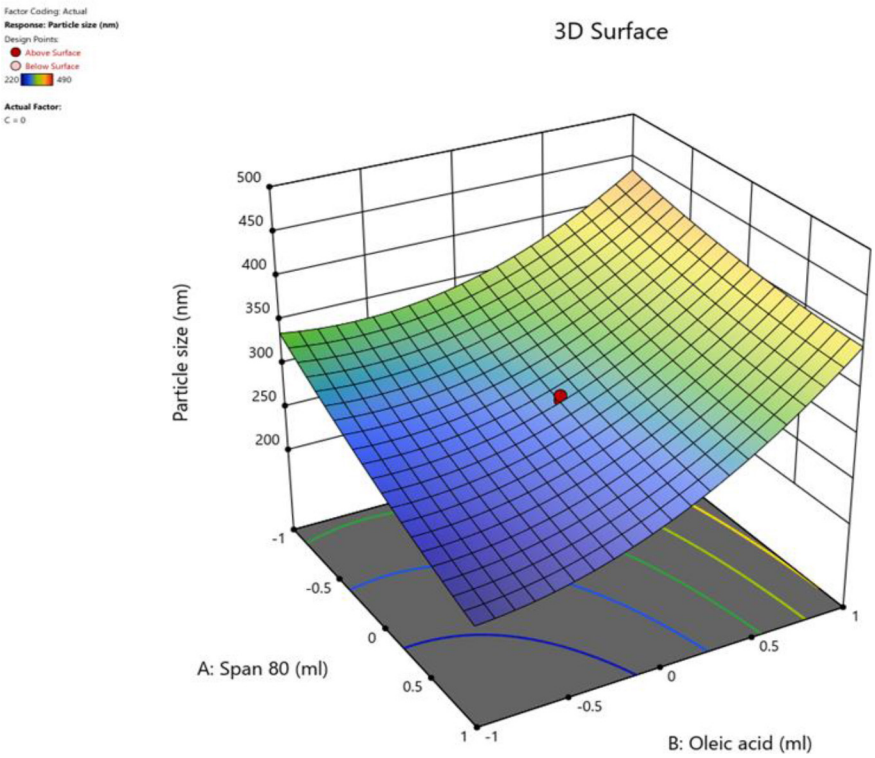


Figure 4. 3D response surface plot showing the combined effect of oleic acid concentration and Span 80 concentrations on particle size.

the interaction term AB, i.e., F= 34.86, p=0.0001, and quadratic term $A^{2,}$ i.e., F=29.87, p=0.0002, indicating non-linear curvature and synergistic interaction between factors A and B on particle size. The lack-of-fit test is non-significant, i.e., p=0.8279, validating the model's adequacy without the need for higher order

Table 4. Fit summary of the developed statistical models showing regression and ANOVA parameters for response 2 (polydispersity index)

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	0.1327	9	0.0147	13.46	0.0002	significant
A-Span 80	0.0205	1	0.0205	18.68	0.0015	
B-Oleic acid	0.0757	1	0.0757	69.11	<0.0001	
C-Octadecyl amine	0.0021	1	0.0021	1.95	0.1925	
AB	0.0021	1	0.0021	1.93	0.1951	
AC	0.0000	1	0.0000	0.0114	0.9170	
BC	0.0003	1	0.0003	0.2853	0.6049	
A^2	0.0026	1	0.0026	2.34	0.1569	
B^2	0.0294	1	0.0294	26.84	0.0004	
C^2	0.0033	1	0.0033	3.00	0.1137	
Residual	0.0110	10	0.0011			
Lack of Fit	0.0106	5	0.0021	26.39	0.0013	significant
Pure Error	0.0004	5	0.0001			
Cor Total	0.1437	19				

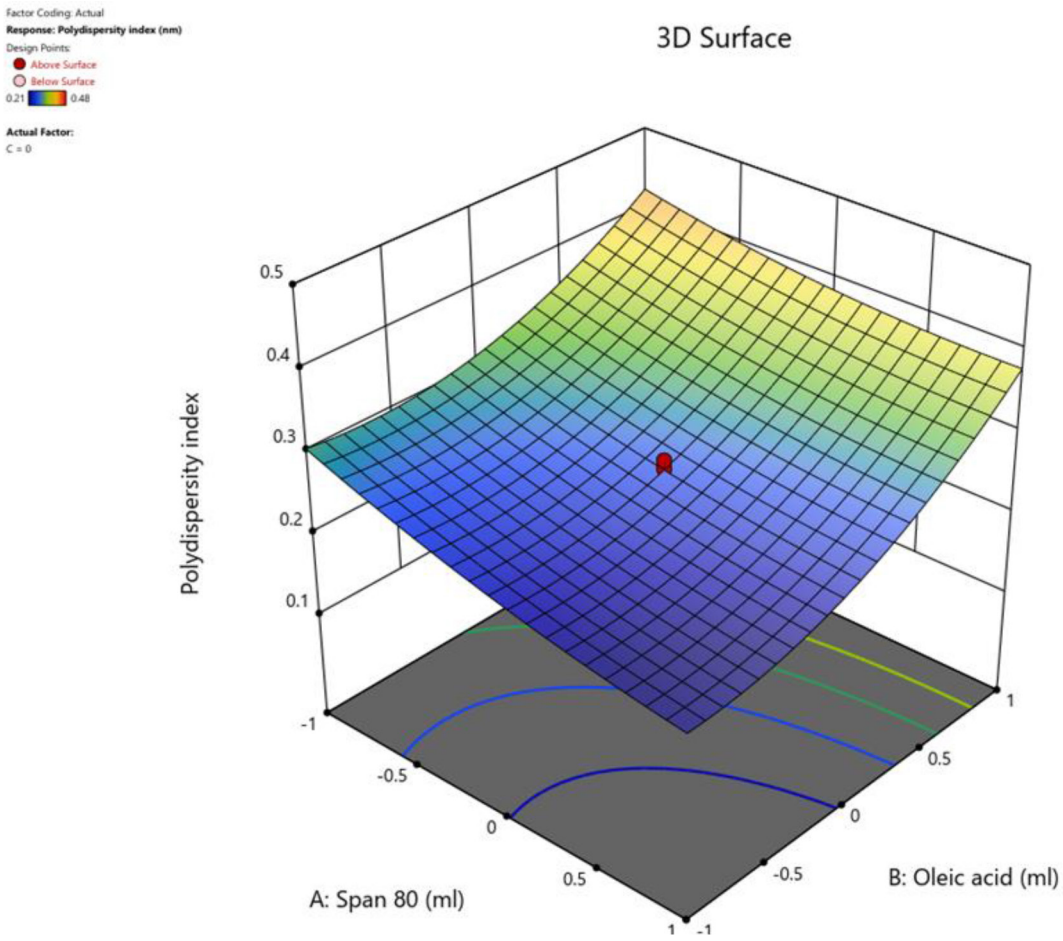


Figure 4. 3D response surface plot showing the combined effect of oleic acid concentration and Span 80 concentrations on polydispersity index.

terms. The low residual variability supports reliable predictions for olaminosomes optimisation in ocular delivery systems (Figure 4).

The analysis of variance for the polydispersity index has been presented in Table 4. The ANOVA results for PDI indicate a significant quadratic model, i.e., F=11.46, p=0.002, effectively accounting for polydispersity index variability in *Curcumin*-loaded olaminosomes with a sum of squares = 0.1137 (df=9). Oleic acid concentration exerts the strongest linear influence, i.e., SS=O.0307, F=18.68. p=0.0015, while the quadratic term B^2 shows pronounced curvature, i.e., SS=0.0324, F=26.84, p=0.001 alongside moderate contributions from AB interaction, i.e., F=1.93, p=0.195 and other terms like A^2, i.e., F=2.34, p=0.157. Although lack-of-fit is significant, i.e., F=2.34, p=0.0013, signalling possible model outliers, the analysis underscores oleic acid's important role in modulating polydispersity index for uniform nano vesicular size distribution suitable for ocular drug delivery (Figure 4).

The analysis of variance is presented in Table 5. The ANOVA for %EE confirms a robust quadratic model, i.e., F=15.8, p=0.0013, effectively explaining percent entrapment efficiency variance in *Curcumin*-loaded olaminosomes, driven primarily by the linear effect of span 80, i.e., SS-106.34, F=19.34, p=0.0006, which dominates drug loading capacity. Oleic acid contributes significantly as a secondary linear factor, i.e., SS=37.80, F=12.51, p=0.00070, while interactions such as AB, I.E., SS=10.50, F-1.85, p=0.201 and AC, i.e., SS=4.20, F=0.72, show weaker influences with low residuals, i.e., SS=13.59, df=11, supporting predictive accuracy. Despite a significant lack of fit, i.e., F=15.8, p=0.0043 hinting at possible unmodeled outliers, these results highlight span 80 critical role in enhancing percent entrapment efficiency for stable ocular nanocarrier delivery of anti-inflammatory bioactive (Figure 5).

The coefficients table of responses is presented in Table 6. This coefficient table shows that different ingredients affect PS, PDI and %EE in *Curcumin*-loaded olaminosomes. Span 80 strongly increases PS and %EE, but lowers PDI, acting as the main driver for better size control and drug loading. Oleic acid reduces PS and %EE, significantly affecting PDI, while interactions such as AB slightly improve polydispersity index uniformity. Hence, these patterns confirm that the model works well to fine-tune formulations for stable ocular delivery. The particle size, PDI and entrapment efficiency of optimised olaminosomes were found to be 430 nm, 0.41, and 77%, respectively (Figure 6).

Table 5. Fit summary of the developed statistical models showing regression and ANOVA parameters for response 3 (%EE)

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	604.27	9	67.14	9.94	0.0006	significant
A-Span 80	110.34	1	110.34	16.34	0.0024	
B-Oleic acid	327.80	1	327.80	48.54	<0.0001	
C-Octadecyl amine	14.54	1	14.54	2.15	0.1730	
AB	12.50	1	12.50	1.85	0.2035	
AC	0.5000	1	0.5000	0.0740	0.7911	
BC	2.00	1	2.00	0.2962	0.5982	
A^2	4.20	1	4.20	0.6213	0.4489	
B^2	130.95	1	130.95	19.39	0.0013	
C^2	11.49	11.49	1.70	0.2212		
Residual	67.53	10	6.75			
Lack of Fit	63.53	5	12.71	15.88	0.0043	significant
Pure Error	4.00	5	0.8000			
Cor Total	671.80	19				

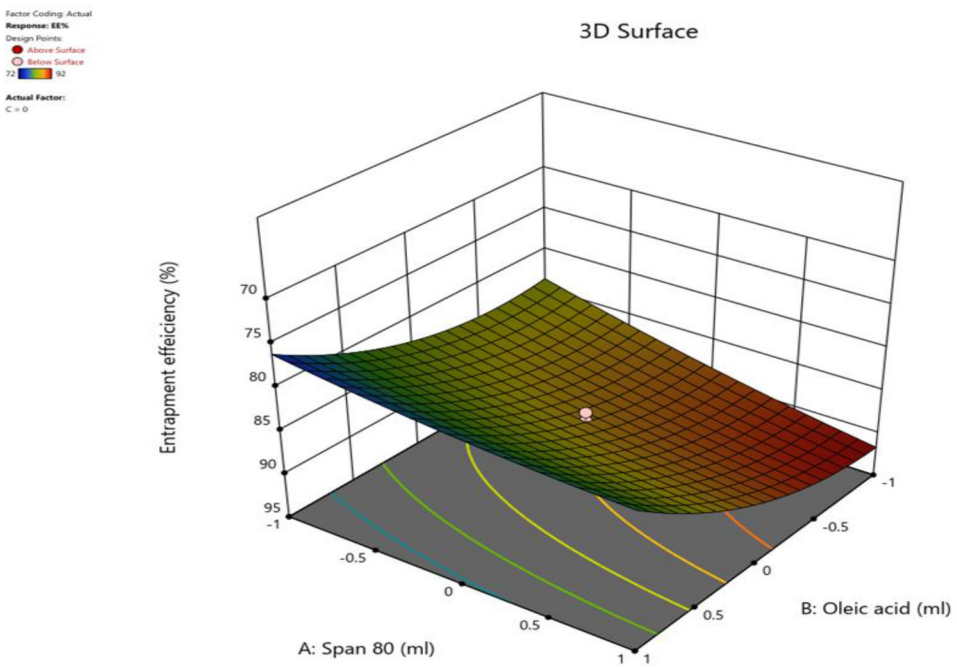


Figure 5. 3D response surface plot showing the combined effect of oleic acid concentration and Span 80 concentrations on EE%.

Table 6. Coefficients table of responses (PS, PDI, %EE)

	Intercept	A	B	C	AB	AC	BC	A^2	B^2	C^2
R1: PS	297.349	-39.9397	70.294	-10.6672	21.25	-1.25	6.25	8.63955	40.4594	14.8267
p-values		0.0012	<0.0001	0.2607	0.0992	0.9170	0.6046	0.3447	0.0009	0.1196
R2: PDI	0.268229	-0.0387083	0.0744544	-0.0125144	0.01625	-0.00125	0.00625	0.0133444	0.0451642	0.0151121
p-values		0.0015	<0.0001	0.1925	0.1951	0.9170	0.6049	0.1569	0.0004	0.1137
R3: %EE	86.1367	2.84238	-4.89928	1.03177	-1.25	0.25	-0.5	-0.53955	-3.01442	-0.893103
p-values		0.0024	<0.0001	0.1730	0.2035	0.7911	0.5982	0.4489	0.0013	0.2212

p-value shading $p < 0.05$ $0.05 \leq p \leq 0.1$ $p \geq 0.1$

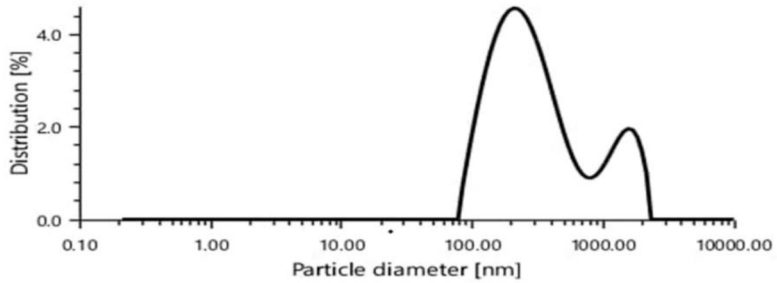


Figure 6. Particle size of *Curcumin*-loaded olaminosomes.

3.6 *Ex Vivo* Permeation

The optimised olaminosomes were evaluated for *ex vivo* permeation using a Franz diffusion cell[24]. The study was conducted for 2 h, demonstrating 40% *Curcumin* and olaminosomes exhibited a cumulative release of 60% permeation, as presented in Table 7. The improved permeation may be attributed to the vesicular structure of olaminosomes, which enhances drug solubilization

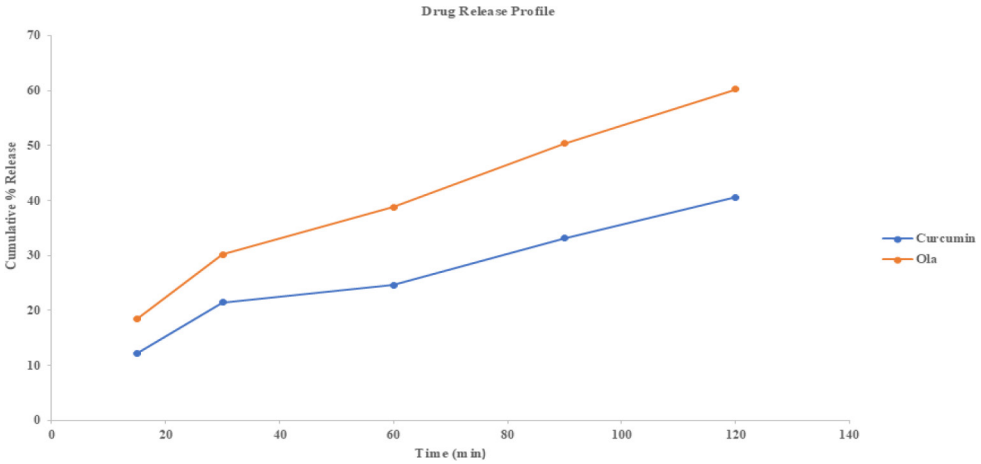


Figure 7. *In vitro* drug release profile of the *Curcumin*-loaded olaminosomes.

Table 7. Percentage drug permeation of the *Curcumin* and *Curcumin*-loaded olaminosomes

Time (min)	% *Curcumin* Released (Mean ± SD)	% Olaminosomes Released (Mean ± SD)
15	12.24 ± 0.8	18.50 ± 0.22
30	21.50 ± 0.12	30.20 ± 0.15
60	24.63 ± 0.31	38.75 ± 1.82
90	33.15 ± 0.51	50.40 ± 0.21
120	40.55 ± 0.74	60.25 ± 0.32

Values are represented as mean± SD

and facilitates better diffusion across the membrane. Additionally, the steady increase in release over time indicated a controlled and sustained drug delivery behaviour (Figure 7).

4. Conclusion

Curcumin-loaded olaminosomes were successfully formulated using the ethanol injection method and optimised through a three-factor, three-level Central Composite Design (CCD). Preformulation studies confirmed *Curcumin* compatibility with excipients such as oleic acid, span 80, and octadecyl amine through FTIR and solubility assessments (high in ethanol, moderate in lipid components, limited in span 80. The optimised formulation exhibits a particle size of 430±1.06 nm, a polydispersity index of 0.41±0.03, and an entrapment efficiency of 77±1.65, as confirmed by Anton Paar particle size analysis and ultracentrifugation, while *ex vivo* Franz diffusion cell studies with goat cornea demonstrated 40.55±0.74 *Curcumin* and 60.25±0.32 olaminosomes permeation over 2h in PBS pH 7.4. ANOVA analysis confirmed the model's significance, i.e., $p<0.05$ with span 80 and oleic acid as key influencers of vesicle size, % EE, and PDI. These results revealed olaminosomes as a promising nanovesicular platform to enhance *Curcumin*'s poor solubility, bioavailability, and corneal penetration for targeted ocular anti-inflammatory therapy.

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Author Contribution

The authors confirm contribution to the paper as follows: Study conception and design: MR, RM; Data collection: AR, RKM; Draft manuscript: MR; Analysis and interpretation of results: RM, AR. All authors have read and agreed to the published version of the manuscript.