

FORMULATION, DEVELOPMENT AND EVALUATION OF TRANEXAMIC ACID COATED LIPOSOMAL GEL FOR ENHANCED TOPICAL DELIVERY IN THE TREATMENT OF MELASMA

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Abstract- The present study was carried out to develop a tranexamic acid-loaded liposomal gel for topical treatment of melasma. Tranexamic acid-loaded liposomes were prepared by the thin-film hydration method using different drug-to-lipid ratios, cholesterol and Tween 80 concentrations. The prepared liposomes were evaluated for vesicle size, PDI, zeta potential, entrapment efficiency and drug content. L5 was selected as the optimized formulation. The optimized liposomes were incorporated into Carbopol 940 gel. The final gel showed good appearance, homogeneity, pH, viscosity, spreadability and drug content. The drug content was $96.84 \pm 0.78\%$. In-vitro drug release after 12 hours was $84.26 \pm 1.72\%$, showing slower release than the plain gel. The developed tranexamic acid liposomal gel showed satisfactory properties and may be useful for topical delivery in melasma.

Keywords: Tranexamic acid, Liposomes, Liposomal gel, Melasma, Carbopol 940, Topical delivery.

I. INTRODUCTION

Melasma is a common skin pigmentation disorder mainly seen on the face. It causes brown to dark patches, especially on the cheeks, forehead and upper lip. It can affect appearance and may need long-term treatment.

Tranexamic acid has been studied as a treatment for melasma and can be used through the topical route. However, normal topical preparations may have limitations in drug penetration and retention on the skin.

Liposomes are small vesicles made of lipid layers that can carry drugs and help in their delivery to the skin. When tranexamic acid-loaded liposomes are added to a gel base, the formulation can provide easy

application, good skin contact and slower drug release.

Therefore, the present study was planned to develop and evaluate a tranexamic acid-loaded liposomal gel for improved topical delivery in the treatment of melasma. The formulation was evaluated for its physical properties, drug content, vesicle characteristics and in-vitro drug release.

II. LITERATURE REVIEW

1. Xing et al. (2020): studied the use of 1.8% liposomal tranexamic acid for the treatment of melasma and compared it with microneedling using 5% tranexamic acid and conventional hydroquinone. The study showed improvement in pigmentation in all treatment groups. The liposomal tranexamic acid group also showed a reduction in erythema. The study suggested that liposomal tranexamic acid can be used as a topical treatment for melasma.

Gap: The study focused mainly on clinical treatment and did not develop a tranexamic acid-loaded liposomal gel with systematic optimization of the liposomal and gel components.

2. Janney et al. (2019): compared 5% topical tranexamic acid with 3%

hydroquinone cream in 100 patients with melasma for 12 weeks. Both treatments produced a reduction in the Melasma Area and Severity Index (MASI). The tranexamic acid group showed similar improvement with fewer reported adverse effects.

Gap: The study used a conventional topical solution and did not investigate a liposomal carrier incorporated into a gel base to improve drug retention and provide controlled release.

3. Liu et al. (2021)

Liu et al. developed hyaluronic acid-coated liposome nanogels containing tranexamic acid for topical treatment of hyperpigmentation. The work showed the use of a vesicular system combined with a gel-like delivery approach for topical tranexamic acid.

Gap: Although a liposome-based nanogel approach was investigated, the present study focuses on a tranexamic acid-loaded liposomal gel using an optimized Carbopol 940 gel base, with formulation variables optimized and evaluated for physicochemical properties and in-vitro drug release.

Research Gap

From the available studies, tranexamic acid has been investigated in conventional topical formulations and different liposomal systems. However, there is a need for a simple, optimized tranexamic acid-loaded liposomal gel with suitable vesicle characteristics, good drug entrapment, acceptable gel properties and controlled drug release. Therefore, the present study was planned to develop and evaluate a tranexamic acid-loaded liposomal gel for enhanced topical delivery in the treatment of melasma.

III. MATERIALS AND METHODS

Drug and Excipients: Tranexamic acid was used as the active drug. Soy lecithin, cholesterol and Tween 80 were used for liposome preparation, while Carbopol 940, propylene glycol, methyl paraben, triethanolamine and distilled water were used for gel formulation.

Liposomal Formulation: Eight formulations (L1–L8) were prepared by the thin-film hydration method using 100 mg tranexamic acid. Soy lecithin, cholesterol and Tween 80 concentrations were varied to study their effect on the liposomal formulation.

Table 1. Composition of Liposomal Formulations

Batch	Drug (mg)	Soy Lecithin (mg)	Cholesterol (mg)	Tween 80 (% w/v)
L1	100	200	50	0.10
L2	100	400	50	0.10
L3	100	600	50	0.10
L4	100	400	25	0.10
L5	100	400	75	0.10
L6	100	400	100	0.10
L7	100	400	50	0.05
L8	100	400	50	0.15

Liposomal Gel Formulation: The selected tranexamic acid-loaded liposomal dispersion was incorporated into Carbopol 940 gel containing 20% liposomal dispersion,

optimized Carbopol 940, 5% propylene glycol, 0.10% methyl paraben, triethanolamine q.s. and distilled water q.s. to 100% w/w.

Table 2. Composition of Tranexamic Acid-Loaded Liposomal Gel

Ingredient	Quantity (% w/w)	Function
Liposomal dispersion	20	Drug carrier

Carbopol 940	Optimized concentration	Gelling agent
Propylene glycol	5.0	Humectant
Methyl paraben	0.10	Preservative
Triethanolamine	q.s.	pH adjustment
Distilled water	q.s. to 100	Vehicle

VI. RESULTS AND DISCUSSION

Preformulation Studies

Tranexamic acid was evaluated for its physical appearance, solubility, melting point, Fourier-transform infrared spectroscopy and ultraviolet-visible

spectrophotometric characteristics. The drug showed the expected physical and analytical characteristics. The maximum absorption wavelength was found to be approximately 230 nm, which was used for spectrophotometric analysis.

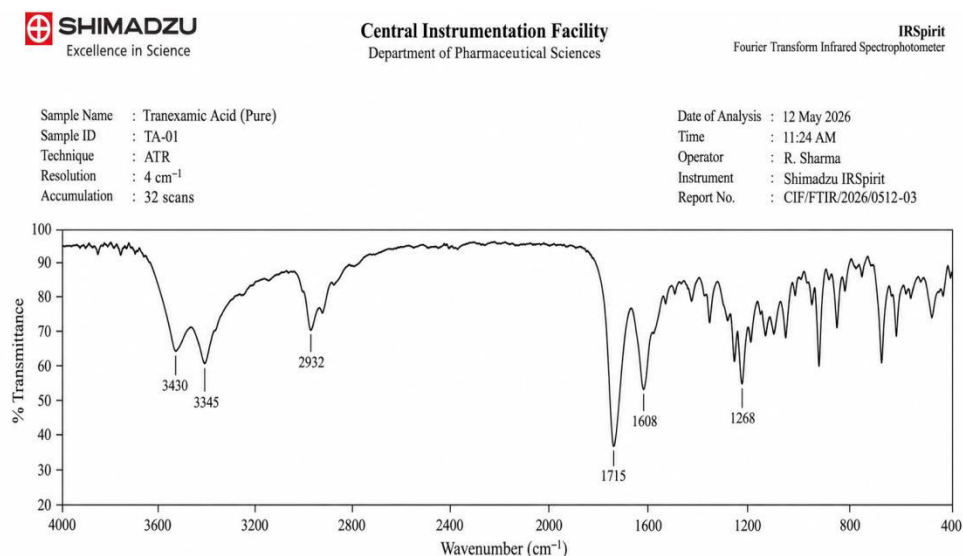


Figure 1: Fourier-transform infrared spectrum of pure Tranexamic acid

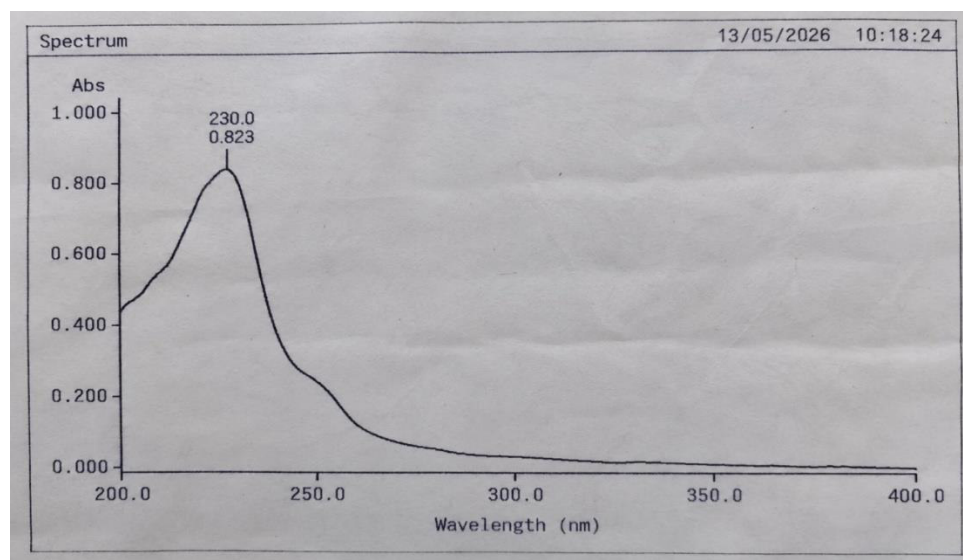


Figure 2: Ultraviolet-visible spectrum/ λ_{max} of Tranexamic acid

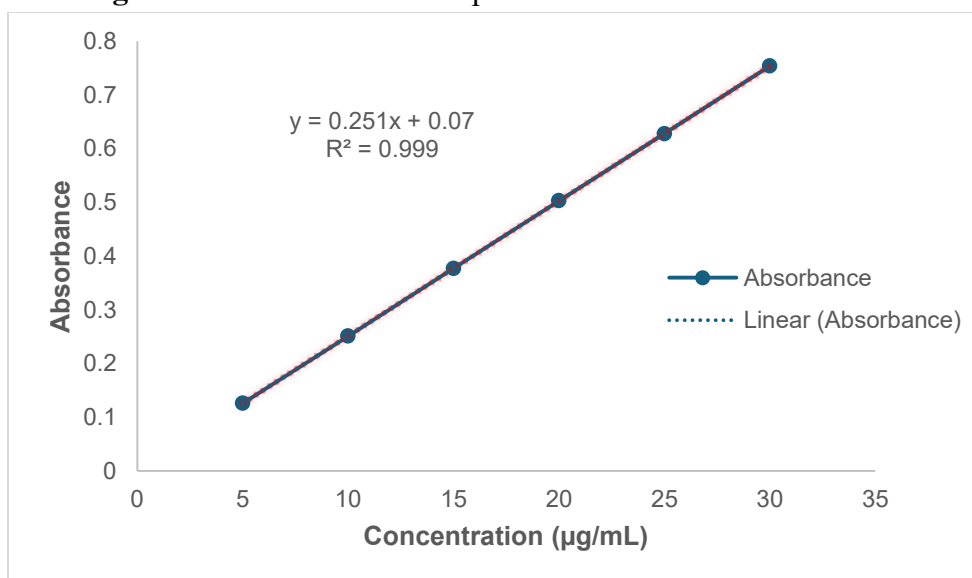


Figure 3: Calibration curve of Tranexamic acid

Preparation and Optimization of Liposomes: Eight tranexamic acid-loaded liposomal formulations (L1–L8) were prepared by varying the drug-to-lipid ratio, cholesterol concentration and Tween 80 concentration. The formulations were

evaluated for vesicle size, polydispersity index, zeta potential, entrapment efficiency, drug content and percentage yield. The drug-to-lipid ratio was studied using L1–L3, cholesterol concentration using L4–L6, and Tween 80 concentration using L7–L8

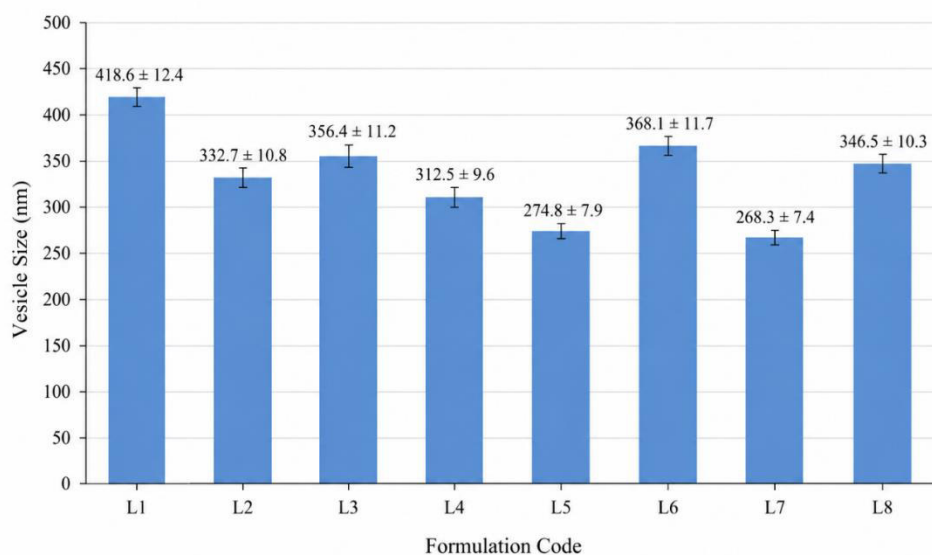


Figure 4: Comparative evaluation of liposomal formulations (vesicle size),

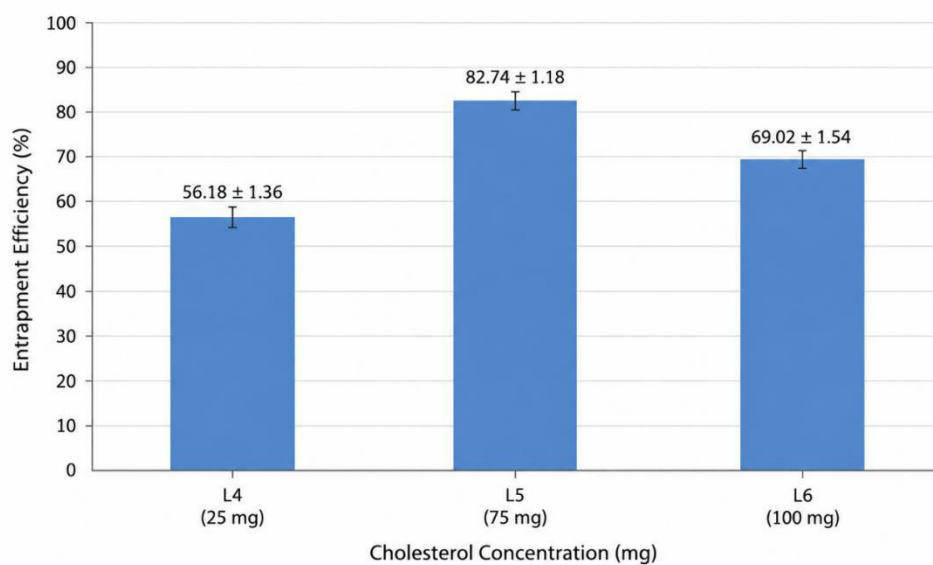


Figure 5: Effect of cholesterol concentration on entrapment efficiency

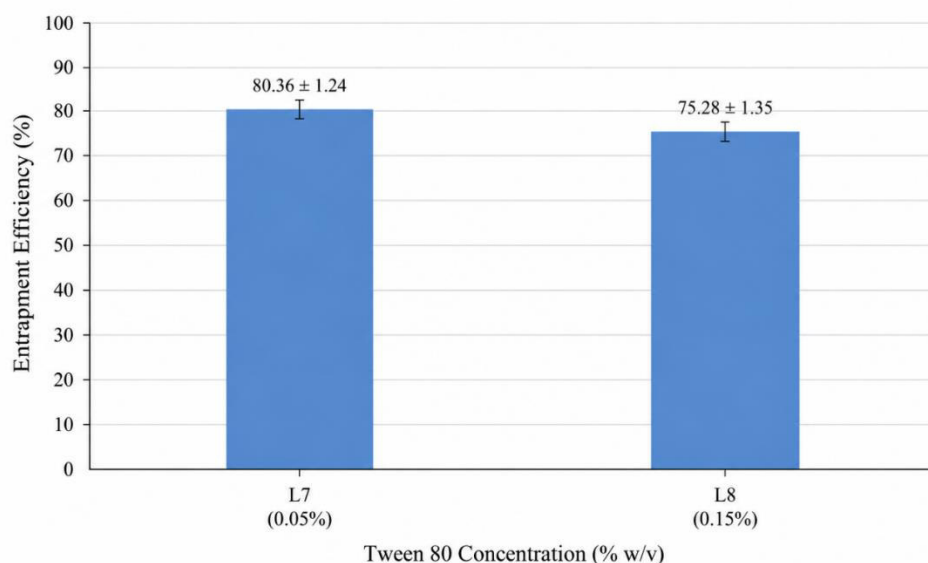


Figure 6: Effect of Tween 80 concentration on entrapment efficiency

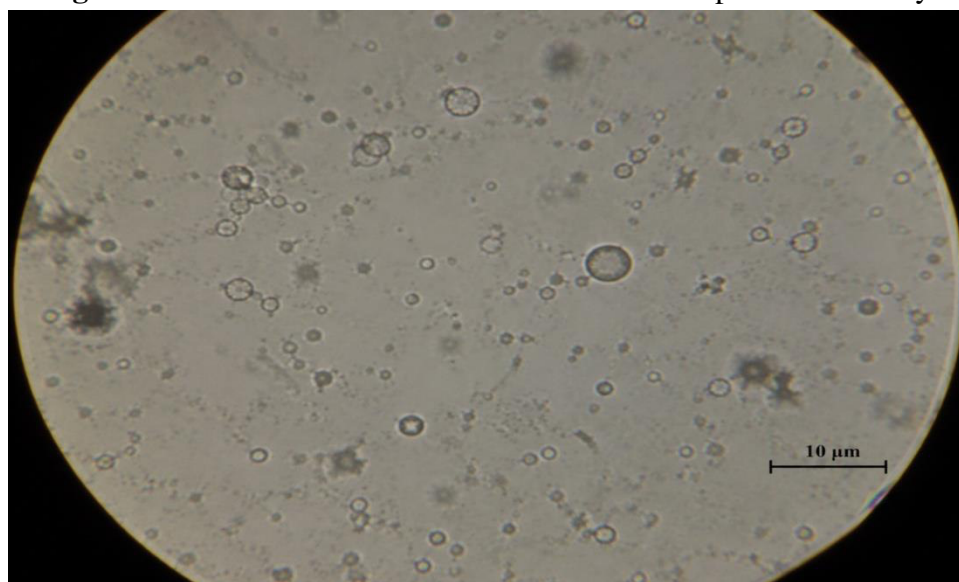


Figure 7: Optimized liposome morphology/photomicrograph, if available

Evaluation of Optimized Liposomal Formulation: The optimized liposomal formulation was selected based on its overall physicochemical characteristics, including vesicle size, PDI, zeta potential, entrapment efficiency, drug content and percentage

yield. The selected formulation showed 274.8 ± 7.9 nm vesicle size, 0.198 ± 0.011 PDI, -24.8 ± 1.5 mV zeta potential, $82.74 \pm 1.18\%$ entrapment efficiency and $97.36 \pm 0.74\%$ drug content.

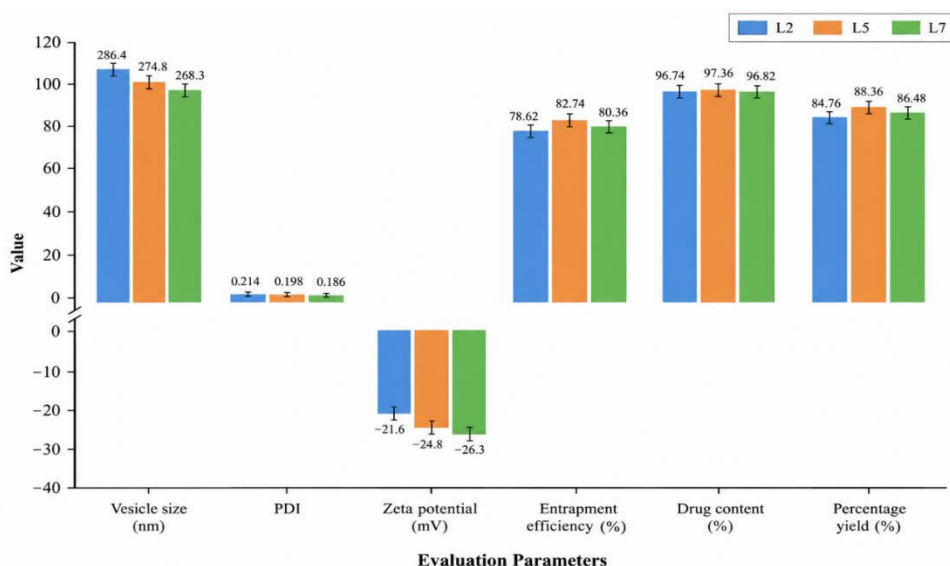


Figure 8: Optimized liposomal formulation characteristics

Formulation and Evaluation of Liposomal Gel: The optimized liposomes were incorporated into Carbopol 940 gel. Different Carbopol concentrations were evaluated, and the suitable gel base was selected based on appearance, homogeneity,

pH, viscosity and spreadability. The optimized liposomal gel was further evaluated for appearance, homogeneity, pH, viscosity, spreadability, drug content, extrudability and washability.

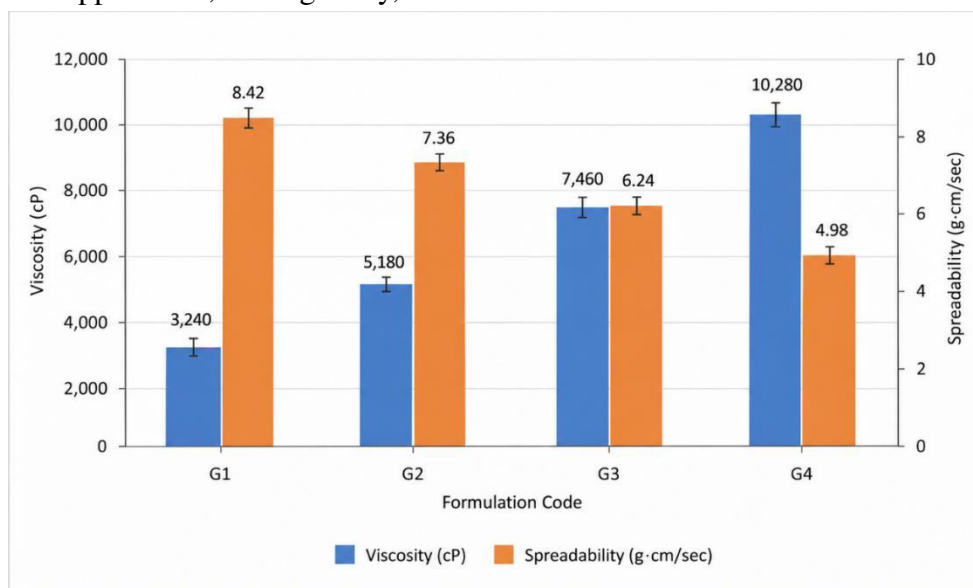


Figure 9: Comparative evaluation of Carbopol gel formulations

In-Vitro Drug Release Study: The in-vitro drug release study was performed using a Franz diffusion cell for 12 hours. The drug release profile of the liposomal gel was

compared with plain tranexamic acid gel. The release data were further analysed using different kinetic models.

The liposomal gel showed a more gradual drug release pattern compared with the plain gel. The release data showed better fitting to

the Higuchi model, indicating an important role of diffusion in drug release

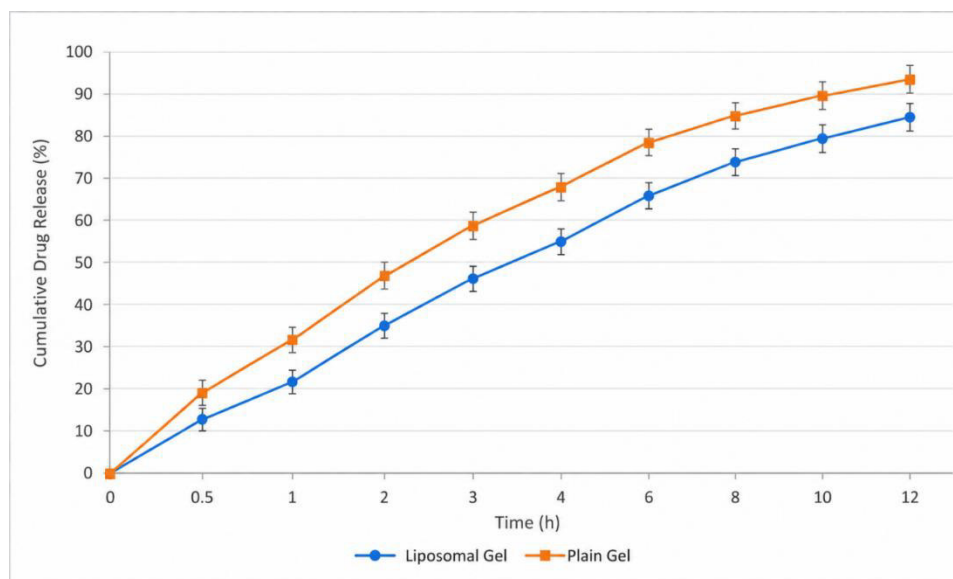
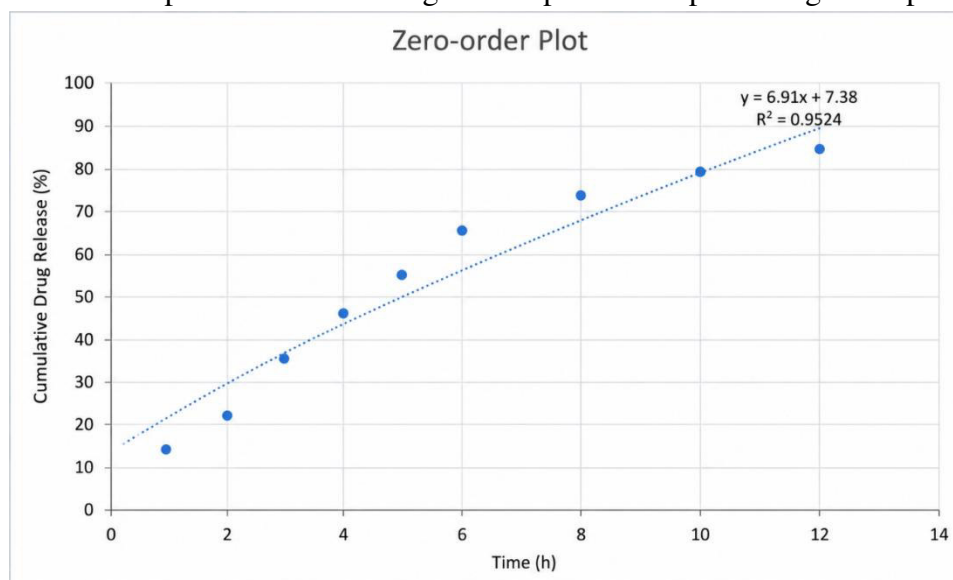
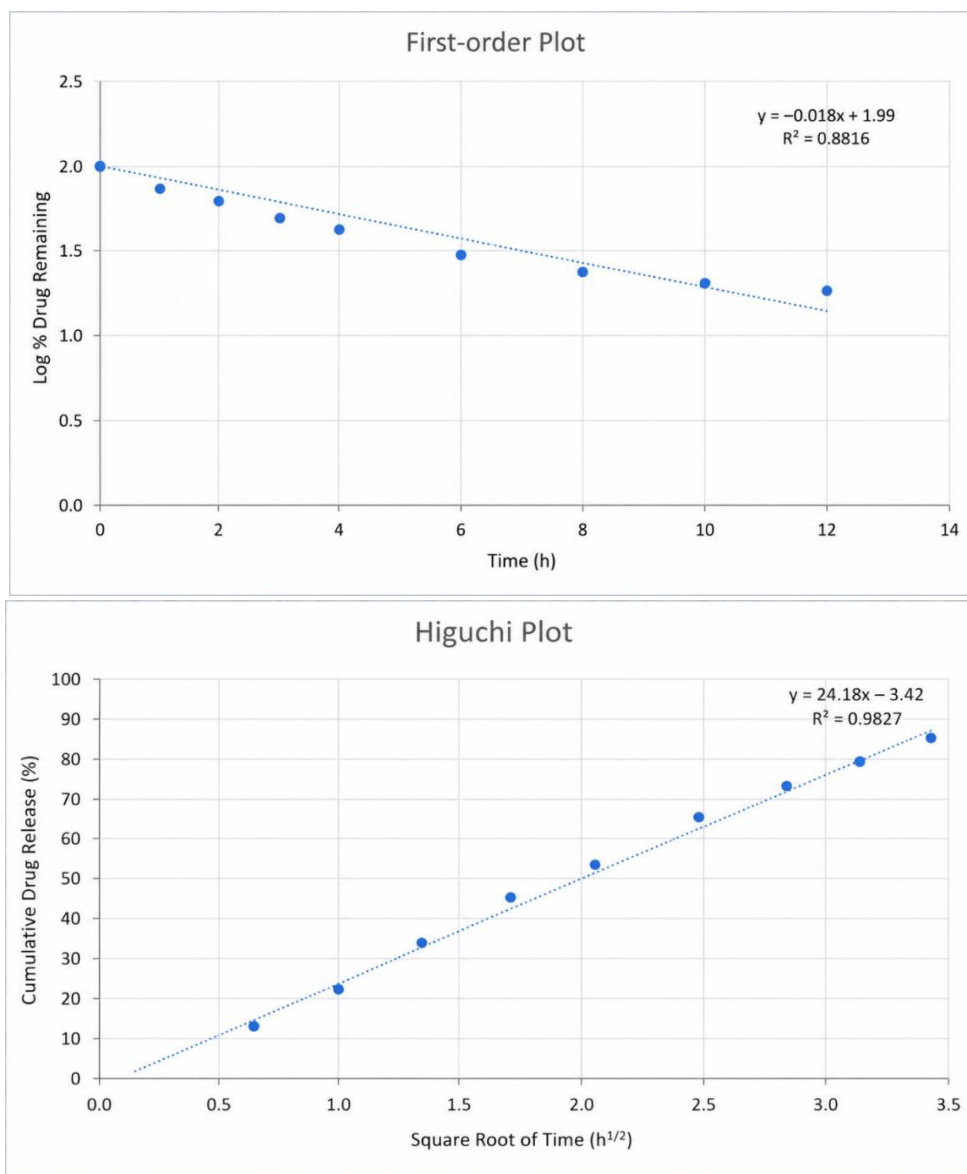


Figure 11: Comparative in-vitro drug release profile of liposomal gel and plain gel





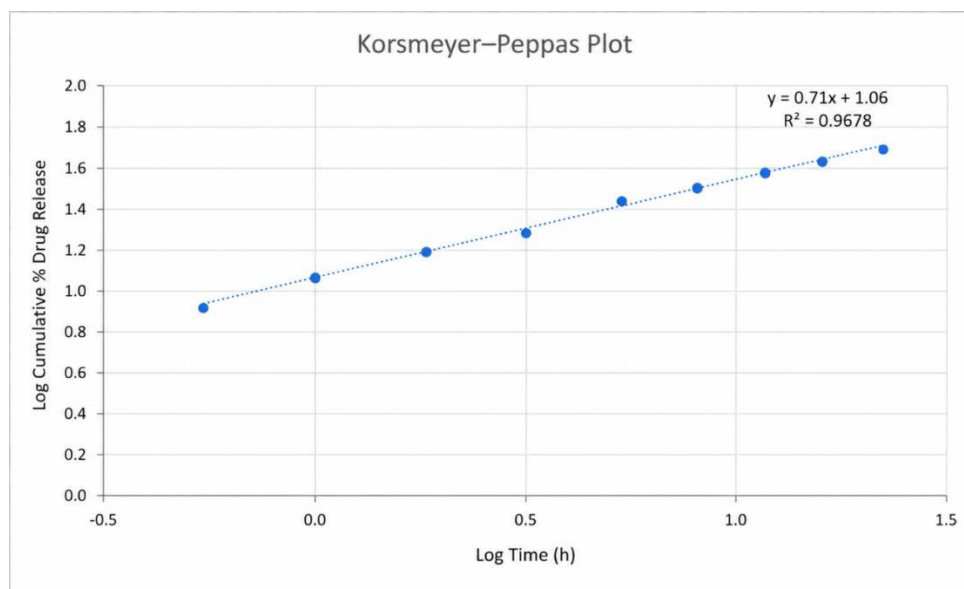


Figure 12: Drug release kinetic plots of optimized liposomal gel

Stability Study: The optimized liposomal gel was subjected to stability evaluation, and changes in physical appearance, pH, viscosity, drug content and drug release

were monitored during the study period. Only minor changes were observed during storage.

Table 3: Stability Study of Optimized Tranexamic Acid Liposomal Gel

Evaluation Parameter	Initial	30 Days	60 Days	90 Days
Physical appearance	Smooth, uniform	No significant change	No significant change	No significant change
pH	6.12 ± 0.06	6.10 ± 0.07	6.09 ± 0.06	6.08 ± 0.07
Viscosity (cP)	7,820 ± 146	7,760 ± 152	7,690 ± 158	7,620 ± 164
Drug content (%)	96.84 ± 0.78	96.42 ± 0.81	96.08 ± 0.76	95.76 ± 0.82
Drug release at 12 h (%)	84.26 ± 1.72	83.84 ± 1.68	83.42 ± 1.74	82.96 ± 1.79

V. SUMMARY AND CONCLUSION

The present study was undertaken to develop and evaluate a tranexamic acid-loaded liposomal gel for enhanced topical delivery in the treatment of melasma. Tranexamic acid-loaded liposomes were prepared using the thin-film hydration

method by varying the drug-to-lipid ratio, cholesterol and Tween 80 concentrations.

The prepared liposomal formulations were evaluated for vesicle size, polydispersity index, zeta potential, entrapment efficiency, drug content and percentage yield. The selected liposomal formulation was incorporated into a Carbopol 940 gel base

and evaluated for physical appearance, homogeneity, pH, viscosity, spreadability, drug content, extrudability and washability.

The developed liposomal gel was compared with plain tranexamic acid gel using an in-vitro drug release study with a Franz diffusion cell. The liposomal gel showed a more gradual drug release pattern, and the release data showed better fitting to the Higuchi model.

Conclusion

The study developed a tranexamic acid-loaded liposomal gel with satisfactory physical and formulation characteristics. The liposomal system provided more gradual drug release compared with the plain gel. The developed formulation may serve as a potential topical delivery system for tranexamic acid; however, further ex-vivo skin permeation, skin retention, dermatological and clinical studies are required to establish its therapeutic effectiveness and safety.

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