

Formulation and Evaluation of Triamcinolone Acetonide Loaded Mucoadhesive Nanoemulgel for Oral Mucosal Delivery in Recurrent Aphthous Stomatitis

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Abstract—Recurrent aphthous stomatitis (RAS) is a common inflammatory disorder of the oral mucosa characterized by recurrent, painful ulcerations that can interfere with eating, swallowing, speaking, and overall quality of life. Triamcinolone Acetonide is an effective topical corticosteroid used for the management of RAS; however, conventional oral formulations are often associated with inadequate mucosal retention and rapid removal from the application site due to salivary flow and oral movements. The present study aimed to develop a mucoadhesive nanoemulgel of Triamcinolone Acetonide to enhance local drug delivery, prolong mucosal residence, and provide sustained drug release at the site of ulceration. The nanoemulsion was formulated using oleic acid as the oil phase, Tween 80 as the surfactant, and propylene glycol as the co-surfactant, followed by incorporation into a Carbopol 934 gel matrix to impart mucoadhesive properties. The developed formulations were evaluated for various physicochemical characteristics, including appearance, pH, viscosity, drug content, particle size, zeta potential, mucoadhesive strength, Fourier-transform infrared spectroscopy (FTIR) compatibility, and in vitro drug release. The nanoemulgel approach was expected to provide nanosized droplets for improved drug dispersion and a mucoadhesive gel matrix for prolonged retention on the oral mucosa. The formulation demonstrating satisfactory physicochemical characteristics and drug-release behaviour was considered for optimization. Overall, the developed Triamcinolone Acetonide mucoadhesive nanoemulgel represents a potential approach for improving the local delivery and residence time of the drug in the management of recurrent aphthous stomatitis.

Index Terms—Recurrent aphthous stomatitis, Triamcinolone Acetonide, Nanoemulgel, Mucoadhesion, Carbopol 934, Topical drug delivery, Oral mucosa.

I. INTRODUCTION

Recurrent aphthous stomatitis (RAS) is one of the most common inflammatory disorders affecting the oral mucosa and is characterised by recurrent, painful, shallow ulcers surrounded by an erythematous halo. The disease affects approximately 5–25% of the global population and significantly impairs eating, swallowing, speaking, and overall quality of life. Although the exact aetiology remains unclear, RAS is considered a multifactorial disorder associated with genetic predisposition, immune dysregulation, nutritional deficiencies, hormonal imbalance, psychological stress, local trauma, microbial infections, and systemic diseases.(1)

Topical corticosteroids remain the first-line therapeutic option for the management of recurrent aphthous ulcers because they effectively suppress inflammation and accelerate ulcer healing.(2) Among these agents, Triamcinolone Acetonide is widely used owing to its potent anti-inflammatory and immunosuppressive properties. The drug inhibits phospholipase A₂ activity, thereby reducing the synthesis of inflammatory mediators such as prostaglandins and leukotrienes.(3) Despite its therapeutic efficacy, conventional dosage forms including oral pastes, gels, mouth rinses, and ointments exhibit several limitations(4). Continuous salivary secretion, tongue movement, swallowing,

and poor adhesion to the oral mucosa result in rapid drug removal from the application site, thereby reducing drug residence time and therapeutic effectiveness.(5)

Nanotechnology-based drug delivery systems have emerged as promising alternatives to overcome the limitations associated with conventional topical formulations. Nanoemulsions are isotropic colloidal dispersions consisting of oil, water, surfactant, and co-surfactant with droplet sizes generally ranging between 20 and 200 nm (5). The small droplet size provides a larger interfacial surface area, leading to enhanced drug solubilization, improved permeation through biological membranes, greater physical stability, and increased local bioavailability.(6)

However, nanoemulsions possess relatively low viscosity, making them unsuitable for prolonged retention on the oral mucosal surface. Incorporation of nanoemulsions into a mucoadhesive gel matrix offers an effective strategy to enhance mucosal residence time. (7)

Mucoadhesive polymers such as Carbopol 934 interact with mucin through hydrogen bonding and other intermolecular forces, thereby increasing adhesion to the oral mucosa and minimizing salivary washout. This approach promotes sustained drug release, prolonged therapeutic action, reduced dosing frequency, and improved patient compliance.(8)

A mucoadhesive nanoemulgel combines the advantages of nanotechnology with the prolonged retention characteristics of bio adhesive polymers. Such systems provide enhanced drug penetration, controlled drug release, improved physicochemical stability, and localized delivery with minimal systemic exposure. Therefore, the development of a mucoadhesive nanoemulgel containing Triamcinolone Acetonide represents a promising approach for improving the management of recurrent aphthous stomatitis.(9)

The present study was undertaken to formulate and evaluate a mucoadhesive nanoemulgel containing Triamcinolone Acetonide using oleic acid as the oil phase, Tween 80 as the surfactant, propylene glycol as the co-surfactant, and Carbopol 934 as the

mucoadhesive polymer. The prepared formulations were evaluated for their physicochemical characteristics, particle size, zeta potential, viscosity, drug content, pH, mucoadhesive strength, FTIR compatibility, and in vitro drug release to identify an optimized formulation for effective topical oral drug delivery. (10)

The purpose of the present study was to develop a mucoadhesive nanoemulgel of Triamcinolone Acetonide to overcome the limitations associated with conventional topical treatment of recurrent aphthous stomatitis. Conventional oral formulations are rapidly removed from the ulcerated mucosal surface due to salivary flow, swallowing, and movement of the tongue, resulting in short drug residence time and repeated application. The proposed nanoemulgel was designed to improve the solubilization and local delivery of Triamcinolone Acetonide through nanosized droplets while Carbopol 934 was incorporated to provide mucoadhesion and prolong the residence of the formulation at the site of ulceration. Thus, the study aimed to achieve enhanced mucosal retention, sustained drug release, improved local therapeutic availability, and potentially better treatment effectiveness with reduced drug loss from the application site. The developed formulation was subsequently evaluated for its physicochemical properties and in vitro drug-release characteristics to identify a suitable formulation for topical management of recurrent aphthous stomatitis.(11)

II. MATERIALS AND METHODOLOGY

Materials

Triamcinolone Acetonide was obtained as a gift sample from Avik Pharmaceutical Pvt. Ltd., India. Oleic acid was used as the oil phase, Tween 80 as the surfactant, and Propylene Glycol as the co-surfactant. Carbopol 934 was employed as the mucoadhesive gelling polymer, while Triethanolamine was used as the neutralizing agent. Methyl Paraben was incorporated as the preservative. Methanol was used as the analytical solvent for UV spectrophotometric estimation, and distilled water was used as the aqueous phase for nanoemulsion preparation and formulation development. All chemicals and reagents

used in the study were of analytical reagent grade and used without further purification.

Methodology

Identification of Pure Drug by FTIR

The identity and purity of Triamcinolone Acetonide were confirmed by Fourier Transform Infrared (FTIR) spectroscopy. The drug was mixed with IR-grade potassium bromide (KBr) in a ratio of 1:10 and compressed using a hydraulic press to obtain a transparent pellet. The pellet was scanned over the spectral range of 4000–400 cm^{-1} . The obtained spectrum was compared with the standard reference spectrum to identify the characteristic functional groups.(12)

FTIR Spectroscopic Analysis of the Final Nanoemulgel

The final Triamcinolone Acetonide-loaded nanoemulgel was subjected to Fourier Transform Infrared (FTIR) spectroscopy to evaluate the compatibility of the drug with the formulation components and to identify any major changes in the characteristic functional groups after formulation. The formulation sample was analyzed over the spectral range of 4000–400 cm^{-1} . The obtained FTIR spectrum was examined for the characteristic absorption bands of Triamcinolone Acetonide and compared with the reported spectral characteristics of the pure drug. The retention of characteristic drug peaks in the final formulation was used to assess the absence of any major detectable drug–excipient interactions.(13)

Solubility Study

The solubility of Triamcinolone Acetonide was determined in different oils, surfactants, and co-surfactants to identify suitable formulation components. An excess amount of the drug was added separately to 2 mL of each vehicle in stoppered glass vials. The mixtures were vortexed and shaken

for 48 hours at room temperature to attain equilibrium. The samples were centrifuged, and the supernatant was filtered and suitably diluted with methanol. Drug concentration was determined using a UV–Visible spectrophotometer at the predetermined wavelength. The excipients showing maximum solubility were selected for nanoemulsion development.(14)

Analytical method development by uv-visible spectrophotometer

Approximately 10 mg of Triamcinolone Acetonide was dissolved in methanol, and the solution was suitably diluted. The prepared solution was scanned between 200 and 400 nm using a UV–Visible spectrophotometer against methanol as the blank. The maximum absorbance (λ_{max}) was observed at 232 nm, which was selected for subsequent quantitative estimation.

A stock solution of Triamcinolone Acetonide was prepared by dissolving an accurately weighed quantity of drug in methanol. Appropriate dilutions were prepared to obtain concentrations of 2, 4, 6, 8, and 10 $\mu\text{g/mL}$. The absorbance of each solution was measured at 232 nm using methanol as the blank. A calibration curve was plotted by taking concentration on the X-axis and absorbance on the Y-axis. The calibration curve showed good linearity with a correlation coefficient (R^2) of 0.9998.

Formulation Method

The nanoemulsion was prepared by the spontaneous emulsification (aqueous titration) method. In this method, the oil phase and surfactant–co-surfactant mixture were combined, followed by gradual addition of the aqueous phase under continuous stirring. The optimized nanoemulsion was subsequently incorporated into a Carbopol 934 gel base to form the mucoadhesive nanoemulgel.(15)

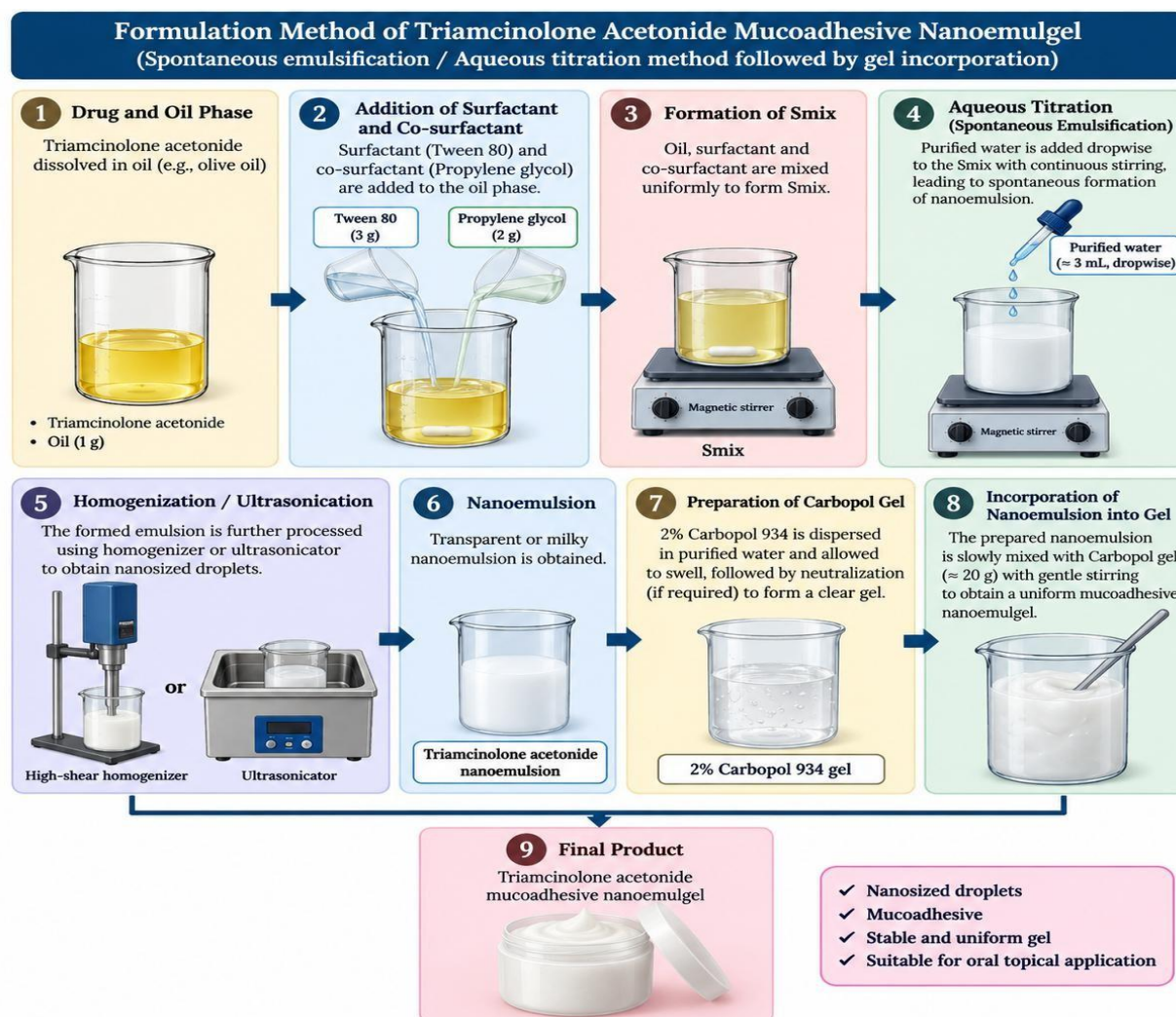


Figure No.01: Formulation method of Triamcinolone Acetonide Mucoadhesive Nanoemulgel(16)

III. FORMULATION TABLE

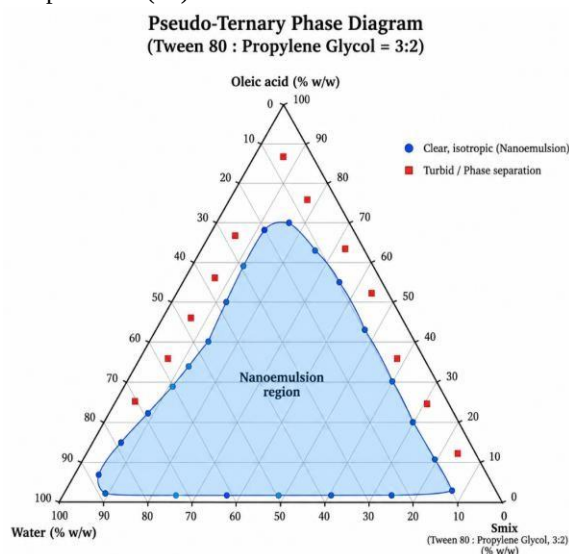
Sl.no	Oleic acid(ml)	Tween 80(ml)	Propylene glycol(ml)	Ratio	Water (ml)
F1	1	2	1	1:2:1	2.5
F2	1	3	1	1:3:1	2.3
F3	1	4	1	1:4:1	2.4
F4	1	2	2	1:2:2	2.8
F5	1	3	2	1:3:2	3.1
F6	1	4	2	1:4:2	3.5
F7	1	2	3	1:2:3	2.6
F8	1	3	3	1:3:3	2.2
F9	1	4	3	1:4:3	2.5

Preparation of Triamcinolone Acetonide Nanoemulsion

Nine formulations (F1–F9) were prepared by varying the proportions of oleic acid, Tween 80, and Propylene Glycol according to the formulation design. Triamcinolone Acetonide was dissolved in the oil phase containing oleic acid. Tween 80 and Propylene Glycol were mixed separately to prepare the surfactant mixture (Smix), which was gradually added to the oil phase under continuous stirring. Distilled water was added dropwise with constant stirring to obtain a coarse emulsion. The resulting emulsion was homogenized at 10,000 rpm for 15 minutes, followed by probe ultrasonication for 15 minutes to obtain a stable nanoemulsion with nanometric droplet size. (17)

Construction of Pseudo-Ternary Phase Diagram

A pseudo-ternary phase diagram was constructed using oleic acid as the oil phase, Tween 80 and propylene glycol as the surfactant-co-surfactant mixture (Smix) at a 3:2 ratio, and distilled water as the aqueous phase. Different oil-to-Smix ratios were prepared and titrated gradually with water under continuous stirring. The clear and isotropic regions were identified as the nanoemulsion region and used for selection of suitable formulation compositions.(18)



Preparation of Mucoadhesive Nanoemulgel

Carbopol 934 (2% w/w) was dispersed in distilled water and allowed to hydrate completely. The optimized nanoemulsion (F9) was gradually incorporated into the hydrated gel base under continuous stirring. Methyl Paraben was added as the preservative, and the pH of the formulation was adjusted using Triethanolamine added dropwise until a homogeneous, smooth, and transparent gel was obtained. The prepared nanoemulgel was kept undisturbed for 24 hours to remove entrapped air before evaluation.(19)

Evaluation of Nanoemulsion

The prepared nanoemulsions were evaluated for:

- Particle size
- Polydispersity Index (PDI)
- Zeta potential
- In vitro drug release (Bag method)

Particle size, PDI, and zeta potential were determined using a Malvern Zetasizer based on dynamic light

scattering after suitable dilution with distilled water. Measurements were performed in triplicate and the average values were recorded.(20)

Evaluation of Mucoadhesive Nanoemulgel

The optimized nanoemulgel formulation was evaluated for the following parameters:

Physical Appearance

The prepared formulation was visually examined for colour, homogeneity, consistency, transparency, grittiness, and phase separation.

pH

The pH of the formulated triamcinolone acetonide mucoadhesive nanoemulgel was determined using a calibrated digital pH meter. Approximately 1 g of the nanoemulgel was dispersed in 30 mL of distilled water, and the pH was measured by immersing the electrode into the sample after allowing sufficient time for equilibration.

Viscosity

The viscosity of the formulated triamcinolone acetonide mucoadhesive nanoemulgel was measured using a Brookfield viscometer equipped with a CPE-63 spindle at an optimum rotational speed of 10 rpm.

Spreadability

The spreadability of the formulated triamcinolone acetonide mucoadhesive nanoemulgel was determined by the parallel-plate method. Approximately 1 g of the nanoemulgel formulation, prepared 48 hours prior to the test, was placed uniformly between two clean glass plates. A 100 g weight was carefully placed over the upper glass plate and allowed to remain for 1 minute to facilitate uniform spreading of the formulation. After removal of the weight, the diameter of the spread formulation was measured at different points and the mean diameter was calculated.

The spreading area of the nanoemulgel was calculated using the following equation:

$$Si = d^2 \times (\pi/4)$$

Where:

- Si = Spreading area of the nanoemulgel (mm²)
- d = Mean diameter of the spread formulation (mm)

A higher spreading area indicates better spreadability of the triamcinolone acetonide mucoadhesive nanoemulgel, which is desirable for uniform

application over the affected oral mucosal surface.(21)

Drug Content

The drug content of the formulated triamcinolone acetonide mucoadhesive nanoemulgel was determined by accurately weighing 1 g of the formulation and dissolving it in 10 mL of a suitable solvent. The resulting solution was mixed thoroughly to ensure complete extraction of triamcinolone acetonide and then filtered through Whatman No. 41 filter paper. An aliquot of 1 mL of the filtrate was suitably diluted to 10 mL with phosphate buffer pH 6.8. The absorbance of the resulting solution was measured using a UV–Visible spectrophotometer at the predetermined λ_{max} of triamcinolone acetonide. The drug content was calculated from the previously prepared calibration curve. The analysis was carried out in triplicate ($n = 3$).

In vitro drug diffusion and kinetics study

The in vitro drug diffusion study of the formulated triamcinolone acetonide mucoadhesive nanoemulgel was performed using a Franz diffusion cell fitted with a suitable dialysis membrane. The dialysis membrane was adequately treated and pre-soaked in phosphate buffer pH 6.8 prior to the study. The membrane was positioned between the donor and receptor compartments of the Franz diffusion cell, with phosphate buffer pH 6.8 used as the receptor medium. A measured quantity of the triamcinolone acetonide mucoadhesive nanoemulgel was uniformly applied over the membrane in the donor compartment.(22)

The diffusion assembly was maintained at 37 ± 0.5 °C and continuously stirred using a magnetic stirrer to maintain uniform distribution of the drug in the receptor medium. At predetermined time intervals, samples were withdrawn from the receptor compartment through the sampling port and immediately replaced with an equal volume of fresh phosphate buffer pH 6.8 to maintain a constant volume.

The collected samples were suitably diluted and analyzed for triamcinolone acetonide content using a UV–Visible spectrophotometer at the predetermined analytical wavelength. The study was performed in triplicate ($n = 3$). The cumulative percentage of drug released was calculated and plotted against time.(23)

The obtained drug release data were fitted to various mathematical kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. The regression coefficient (R^2) values obtained from each model were compared to determine the best-fit kinetic model and to understand the drug-release kinetics and possible mechanism of drug release from the triamcinolone acetonide mucoadhesive nanoemulgel.(24)

Ex Vivo Drug Permeation Study

The ex vivo drug permeation study of the formulated triamcinolone acetonide mucoadhesive nanoemulgel was performed using a Franz diffusion cell apparatus with suitable modifications. Fresh goat buccal mucosa was obtained and carefully separated from the underlying tissues. The mucosal membrane was washed thoroughly with suitable medium to remove adhering tissue and blood and was used for the permeation study.

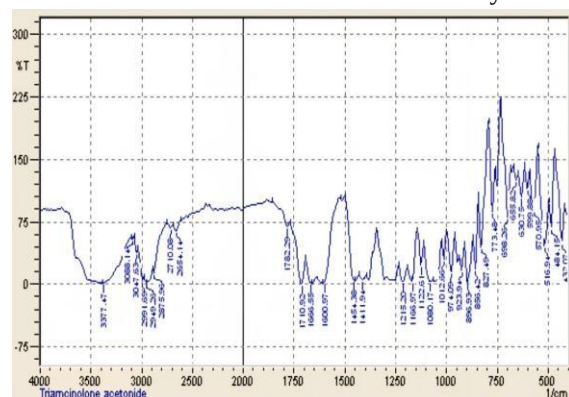
The goat buccal mucosa was mounted between the donor and receptor compartments of the Franz diffusion cell, with the mucosal surface facing the donor compartment. Care was taken to ensure intimate contact between the mucosa and receptor medium without formation of air bubbles. A measured quantity of the triamcinolone acetonide mucoadhesive nanoemulgel was uniformly applied onto the mucosal surface in the donor compartment. The receptor compartment was filled with phosphate buffer pH 6.8 and maintained at 37 ± 0.5 °C with continuous stirring to ensure uniform distribution of the drug in the receptor medium. At predetermined time intervals, aliquots of the receptor medium were withdrawn and immediately replaced with an equal volume of fresh phosphate buffer pH 6.8 to maintain a constant volume and sink conditions.

The withdrawn samples were suitably diluted and analysed spectrophotometrically for triamcinolone acetonide content at the predetermined analytical wavelength. The cumulative amount of drug permeated through the goat buccal mucosa was calculated and expressed as the amount of drug permeated per unit area. The cumulative drug permeation, steady-state flux, and permeability coefficient were determined from the obtained permeation data.(25)

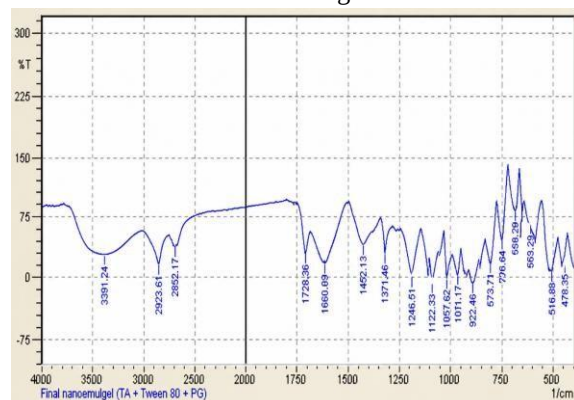
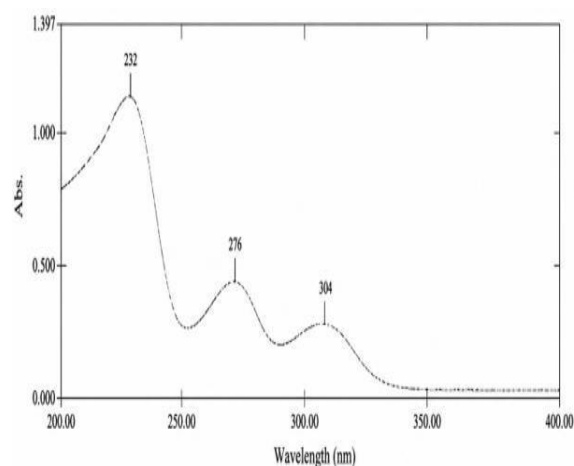
IV. RESULTS AND DISCUSSION

RESULTS:

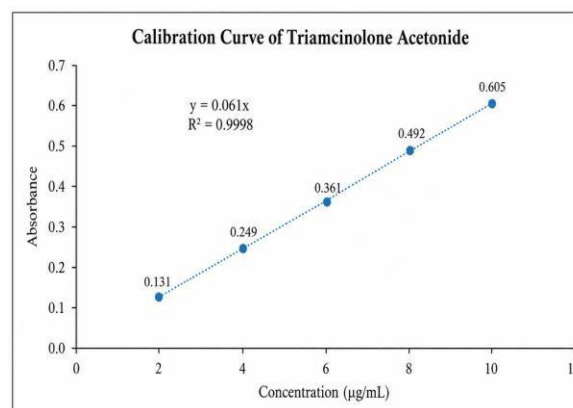
Identification of Triamcinolone Acetonide by FTIR



FTIR Spectroscopic Analysis of the Final Nanoemulgel

Determination of λ_{max} of Triamcinolone AcetonideFig 5.1: λ_{max} of Triamcinolone Acetonide

Standard Calibration Curve of Triamcinolone Acetonide

Fig. 2. Calibration curve of triamcinolone acetonide in phosphate buffer pH 6.8 (λ_{max} = 232 nm).

Evaluation of Triamcinolone Acetonide Nanoemulsion Formulations

Formulation	Particle size (nm)	PDI	Zeta potential (mV)	Drug content (%)	Entrapment efficiency (%)
F1	142.6	0.342	-18.4	96.2	88.4
F2	128.3	0.318	-21.7	96.8	89.7
F3	118.9	0.291	-24.3	97.1	90.5
F4	108.4	0.264	-26.8	97.3	91.2
F5	98.7	0.238	-28.9	97.6	92.0
F6	91.2	0.214	-30.5	97.8	92.8
F7	85.6	0.192	-32.1	98.0	93.4
F8	79.4	0.171	-33.6	98.2	94.0
F9	73.2	0.153	-35.0	98.0	94.5

V. EVALUATION OF MUCOADHESIVE NANOEMUGEL

Physical Appearance

The optimized F9 nanoemulgel appeared as a smooth, homogeneous, white-to-off-white gel with uniform consistency. No grittiness or phase separation was observed.

pH

The pH of the optimized F9 formulation was found to be 6.8, indicating suitability for application to the

oral mucosal surface. The near-neutral pH suggests good formulation compatibility.

Viscosity

The viscosity of F9 was found to be 12,550 cP at 10 rpm. The relatively high viscosity provided adequate consistency and may contribute to prolonged retention at the application site.

Spreadability

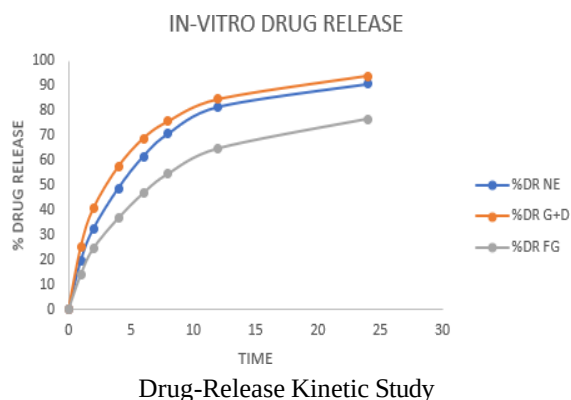
The F9 formulation showed a mean spreading diameter of 58.6 ± 1.1 mm, corresponding to a spreading area of 2697 ± 101 mm². This indicated satisfactory spreading and uniform application over the mucosal surface.

Drug Content

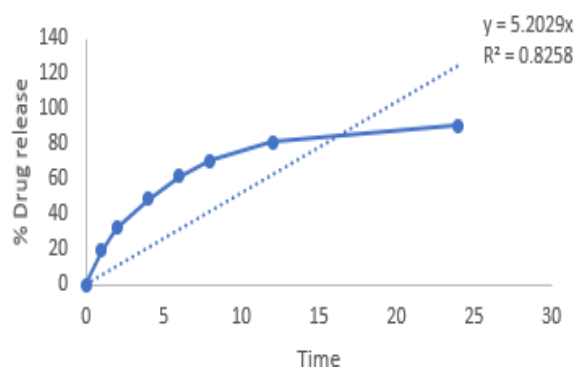
The drug content of the optimized F9 formulation was found to be 98.0%, indicating efficient and uniform incorporation of triamcinolone acetonide. The value was within the observed range of 96.2–98.2% for F1–F9.

In-vitro Drug Release Study

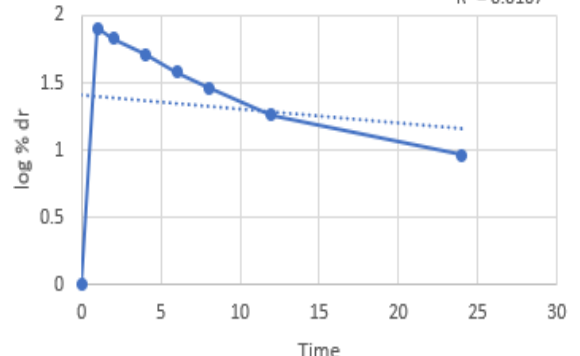
Time	Nanoemulsion (%drug release)	Plain gel with drug (% drug release)	Formulated-gel (%drug release)
0	0.0	0.0	0.0
1	19.8	25.4	14.2
2	32.6	40.8	24.7
4	48.9	57.6	36.8
6	61.7	68.9	46.9
8	70.8	75.8	54.7
12	81.6	84.7	64.9
24	90.8	94.1	76.8



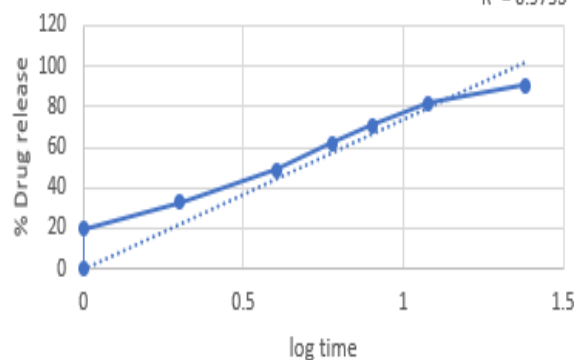
zero order kinetics for Nano-emulsion



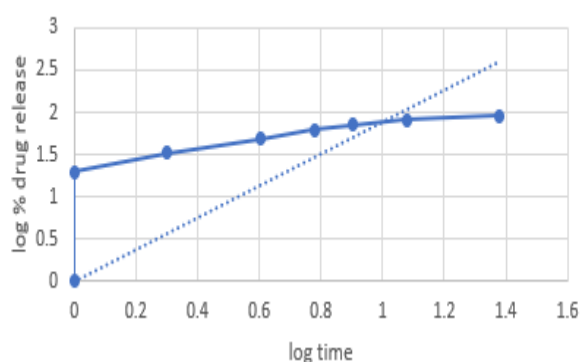
First order Nanoemulsion

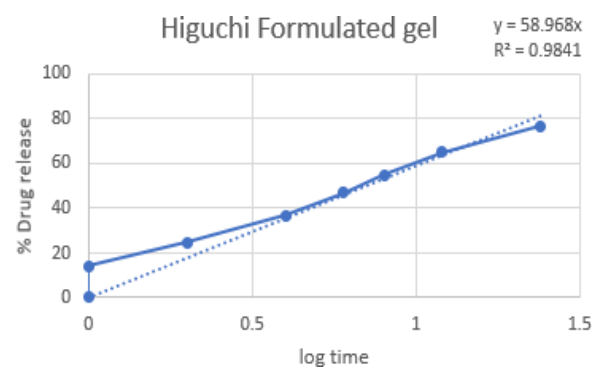
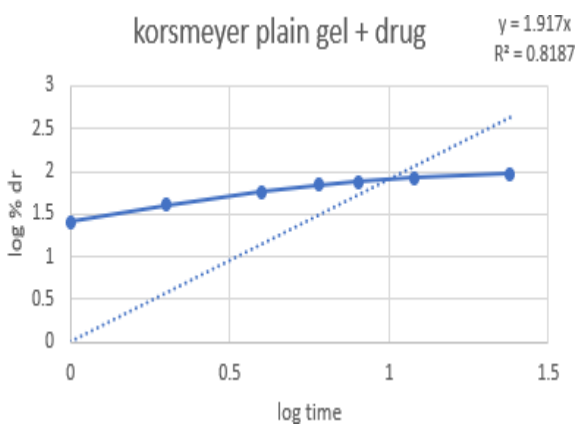
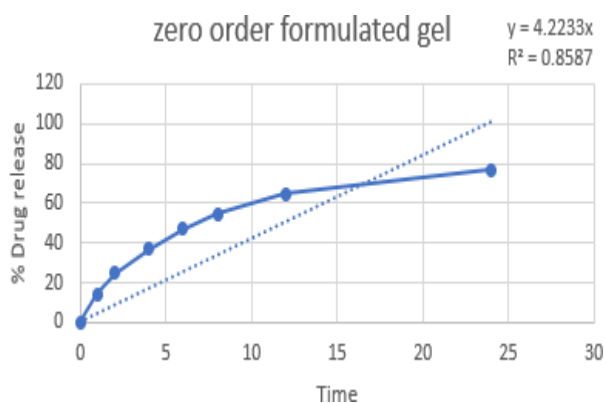
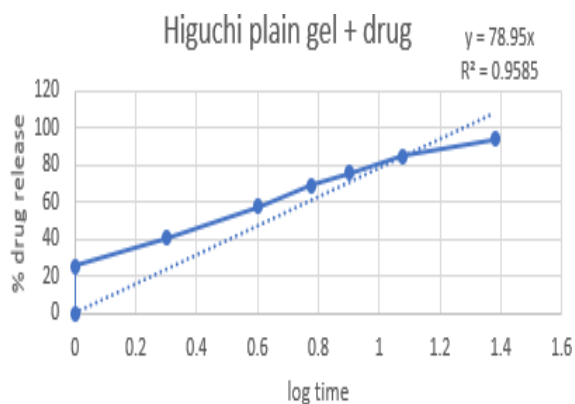
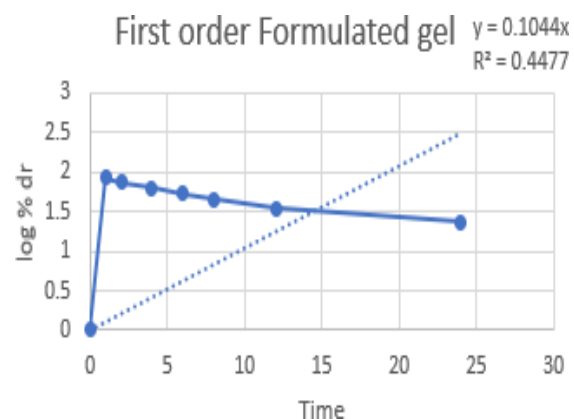
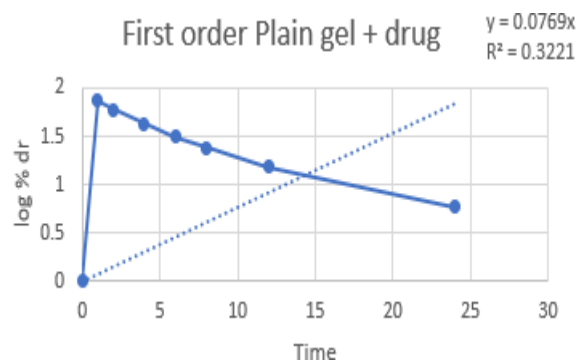
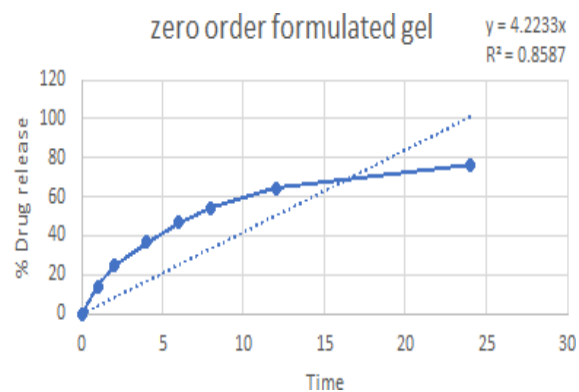
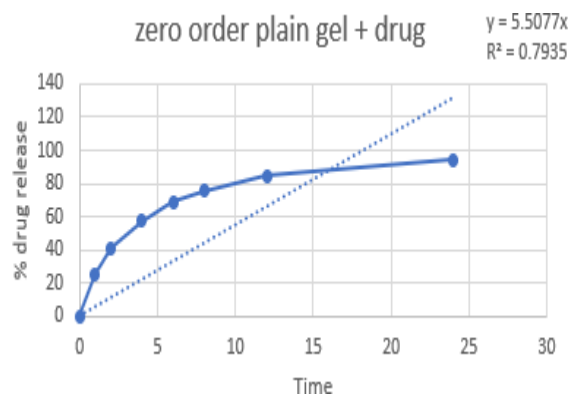


Higuchi Nanoemulsion



korsmeyer Nanoemulsion





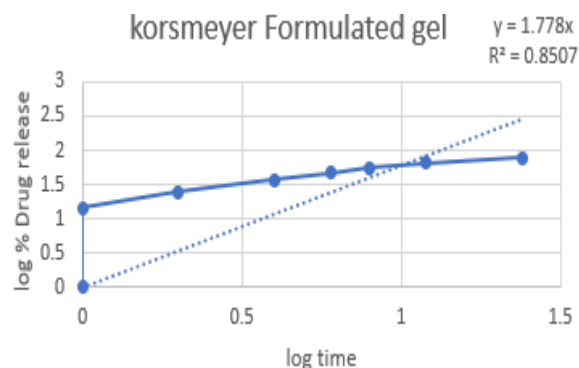
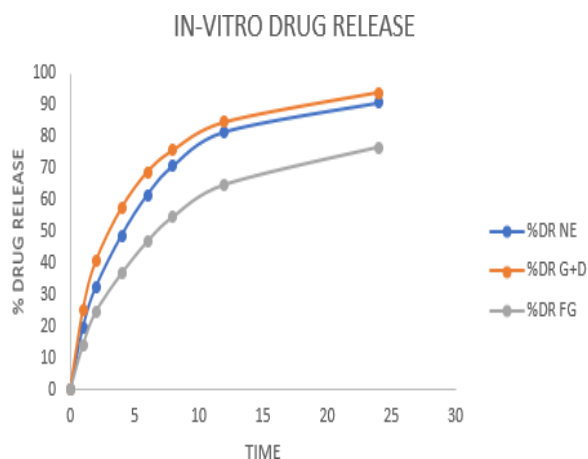


Table 5. Regression analysis of drug-release kinetic models

Formulation	Zero order R ²	First order R ²	Higuchi R ²	Korsmeyer peppas R ²
Nano-emulsion	0.8258	0.0167	0.9753	0.8358
Plain gel + drug	0.7935	0.3221	0.9585	0.8187
Formulated gel	0.8587	0.4477	0.9841	0.8507



Stability Study

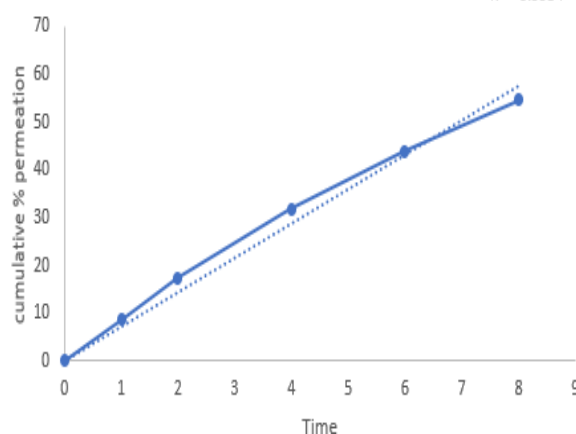
Evaluation	Initial 0 Day	After 15 days	After 1 month
Particle size	73.2	75.8	78.6
PDI	0.153	0.160	0.167
Zeta potential	-35	-34.4	-33.8
Drug content %	98.0	97.5	96.9
Entrapment efficiency %	94.5	93.9	93.2

Ex-Vivo Drug Permeation Study:

Time (h)	Cumulative drug permeated (%)
0	0.00 ± 0.00
1	8.6 ± 0.7
2	17.4 ± 1.1
4	31.8 ± 1.6
6	43.9 ± 1.8
8	54.7 ± 2.1

Ex-vivo permeation drug study

$y = 7.2033x$
 $R^2 = 0.9954$



VI. DISCUSSION

Identification of Triamcinolone Acetonide by FTIR: The FTIR spectrum of pure triamcinolone acetonide showed characteristic absorption bands at approximately 3577, 3388, 2930, 2875, 1728, 1636, 1609, 1453, 1412, 1215, 1164, 1125, 1080 and 1013 cm^{-1} . The broad absorption band in the 3500–3300 cm^{-1} region was attributed to O–H stretching vibrations. The bands observed around 2930 and 2875 cm^{-1} corresponded to aliphatic C–H stretching vibrations. The prominent band near 1728 cm^{-1} was associated with carbonyl (C=O) stretching, while the bands around 1636 and 1609 cm^{-1} were related to characteristic skeletal/double-bond vibrations of the corticosteroid structure. Absorption bands in the fingerprint region, particularly around 1215–1013 cm^{-1} , were attributed to C–O/C–O–C and C–F related vibrations. The observed characteristic bands were consistent with reported FTIR characteristics of triamcinolone acetonide, supporting the identity of the drug.(26)

Determination of λ_{max} of Triamcinolone Acetonide

The standard solution of triamcinolone acetonide was scanned in the UV-visible spectrophotometer over the wavelength range of 200–400 nm. The maximum absorption of triamcinolone acetonide was observed at 232 nm. Therefore, 232 nm was selected as the analytical wavelength for the estimation of triamcinolone acetonide in subsequent studies.

Standard Calibration Curve of Triamcinolone Acetonide

A calibration curve of triamcinolone acetonide was prepared in phosphate buffer pH 6.8 using standard concentrations of 2, 4, 6, 8 and 10 $\mu\text{g/mL}$. The absorbance values obtained at 232 nm were used to construct the calibration curve by plotting concentration against absorbance.

The calibration curve demonstrated a linear relationship between the concentration of triamcinolone acetonide and its absorbance. The coefficient of determination (R^2) was found to be 0.9998, indicating excellent linearity over the investigated concentration range. Therefore, the developed UV-visible spectrophotometric method was considered suitable for quantitative estimation of triamcinolone acetonide during the formulation studies.

Evaluation of Triamcinolone Acetonide Nanoemulgel Formulations

Nine formulations (F1–F9) of triamcinolone acetonide nanoemulsion were prepared by varying the concentrations of Tween 80 and propylene glycol while maintaining oleic acid at 1 mL. The prepared formulations were evaluated for particle size, polydispersity index (PDI), zeta potential, pH, viscosity, drug content and entrapment efficiency.

Particle Size

The particle size of the prepared formulations ranged from 73.2 to 142.6 nm. Formulation F1 exhibited the highest particle size of 142.6 nm, whereas F9 showed the lowest particle size of 73.2 nm.

A progressive reduction in particle size was observed from F1 to F9 with increasing concentrations of Tween 80 and propylene glycol. The particle size decreased from 142.6 nm in F1 to 118.9 nm in F3 when Tween 80 was increased from 2 to 4 mL at a constant propylene glycol concentration of 1 mL. A

similar reduction was observed in the subsequent formulation groups.

The reduction in particle size indicates improved dispersion of the oil phase within the aqueous phase with increasing surfactant and cosurfactant concentrations. The optimized formulation F9 exhibited a particle size of 73.2 nm, confirming the formation of a nanosized dispersion.(27)

Polydispersity Index

The PDI values of the formulations ranged from 0.153 to 0.342. F1 exhibited the highest PDI of 0.342, whereas F9 showed the lowest value of 0.153. A progressive reduction in PDI was observed across the formulation batches. The decrease in PDI indicates a comparatively narrower particle-size distribution as the concentration of surfactant and cosurfactant was increased.(28)

The optimized formulation F9 exhibited a PDI of 0.153, indicating a relatively uniform nanosized dispersion.

Zeta Potential

The zeta potential values of the formulations ranged from -18.4 to -35.0 mV. F1 exhibited a zeta potential of -18.4 mV, while F9 showed the most negative value of -35.0 mV.

The progressive change toward a more negative zeta potential across the formulations indicates an increase in the surface charge of the dispersed droplets. The optimized formulation F9 exhibited a zeta potential of -35.0 mV, demonstrating a comparatively high magnitude of surface charge.(29) The zeta-potential results, together with the low PDI and nanosized particle size, support the physical characterization of F9 as the optimized nanoemulsion formulation.

pH

The pH values of the prepared formulations ranged from 6.4 to 6.8. F1 exhibited a pH of 6.4, whereas F7, F8 and F9 showed a pH of 6.7, 6.8 and 6.8, respectively.

The gradual increase in pH across the formulations remained within a relatively narrow range. The optimized formulation F9 exhibited a pH of 6.8.

Viscosity

The viscosity of the formulations ranged from 8,950 to 12,550 cP. F1 exhibited the lowest viscosity of

8,950 cP, while F9 showed the highest viscosity of 12,550 cP.

An increasing trend in viscosity was observed from F1 to F9. The increase in viscosity may contribute to improved retention of the formulation at the intended site of administration and is particularly relevant to the development of a mucoadhesive nanoemulgel. The optimized F9 formulation exhibited a viscosity of 12,550 cP.(30)

Spreadability

The optimized F9 nanoemulgel showed a mean spreading diameter of 58.6 ± 1.1 mm, corresponding to a spreading area of 2697 ± 101 mm². The satisfactory spreadability may be attributed to the balanced viscosity of 12,550 cP and the homogeneous Carbopol 934 gel matrix, allowing uniform application over the oral mucosal surface while maintaining adequate formulation consistency.

Drug Content

The drug content of the prepared formulations ranged from 96.2% to 98.2%.

F1 showed a drug content of 96.2%, whereas the highest drug content of 98.2% was observed with F8. F9 showed a drug content of 98.0%.

The relatively high drug-content values observed across all formulations indicate consistent incorporation of triamcinolone acetonide during formulation development. The optimized F9 formulation showed a drug content of 98.0%.

Entrapment Efficiency

The entrapment efficiency of the formulations ranged from 88.4% to 94.5%.

F1 exhibited the lowest entrapment efficiency of 88.4%, whereas F9 exhibited the highest entrapment efficiency of 94.5%. An overall increasing trend in entrapment efficiency was observed with increasing concentrations of Tween 80 and propylene glycol.

The increase in entrapment efficiency suggests improved incorporation of triamcinolone acetonide within the nanoemulsion system. The optimized F9 formulation demonstrated an entrapment efficiency of 94.5%, indicating efficient incorporation of the drug into the nanosystem.(31)

In-vitro Drug Release Study

The in-vitro drug release study of the developed formulations was carried out using the data obtained

at predetermined time intervals up to 24 h. The cumulative percentage drug release was evaluated at 1, 2, 4, 6, 8, 12 and 24 h.

The in-vitro drug release study demonstrated a progressive increase in cumulative drug release with increasing time for all three investigated formulations.

The Nano-Emulsion formulation showed a cumulative drug release of 19.8% at 1 h, which gradually increased to 70.8% at 8 h, 81.6% at 12 h and 90.8% at 24 h.

The plain gel with Drug formulation exhibited 25.4% drug release at 1 h and showed a progressive increase to 75.8% at 8 h and 84.7% at 12 h. The cumulative drug release reached 94.1% at 24 h.

The Formulated Gel formulation showed comparatively slower drug release, with 14.2% release at 1 h, increasing to 54.7% at 8 h and 64.9% at 12 h. At 24 h, the cumulative drug release reached 76.8%.

The observed release profiles indicate that the three formulations exhibited different rates of drug release. Among the investigated formulations, G+D demonstrated the highest cumulative drug release at 24 h, whereas FG exhibited the slowest release profile.

The comparatively slower release observed with FG may be associated with the formulation matrix providing greater resistance to drug diffusion. The gradual release over the investigated period indicates prolonged drug availability compared with a rapid initial release.(32)

Drug-Release Kinetic Study

The drug-release data were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models to understand the release behaviour of the formulations. The Higuchi model showed the highest R² value for all three formulations, with R² values of 0.9753 for nanoemulsion, 0.9585 for plain gel + drug, and 0.9841 for formulated gel.

Among the tested formulations, the formulated gel showed the highest Higuchi R² (0.9841), indicating that its drug-release profile was most closely described by the Higuchi diffusion model. The lower R² values obtained with the zero-order and first-order models suggest that the release was not predominantly governed by constant-rate or concentration-dependent release kinetics.

The Korsmeyer–Peppas model showed R^2 values of 0.8358, 0.8187, and 0.8507 for nanoemulsion, plain gel + drug, and formulated gel, respectively. Overall, the higher Higuchi correlation suggests that diffusion through the formulation matrix was an important mechanism contributing to triamcinolone acetonide release, particularly from the formulated gel.

Stability Study

The optimized formulation F9 was subjected to a one-month stability study to evaluate changes in its physical and formulation characteristics during storage. The formulation was evaluated initially and after 15 days and 1 month for particle size, polydispersity index (PDI), zeta potential, drug content, and entrapment efficiency.

The optimized F9 formulation showed relatively small changes in the evaluated parameters during the one-month storage period. The particle size increased gradually from 73.2 nm initially to 75.8 nm after 15 days and 78.6 nm after one month. The PDI showed a slight increase from 0.153 to 0.167, indicating a small change in particle-size distribution during storage.

The zeta potential changed from -35.0 mV initially to -34.4 mV after 15 days and -33.8 mV after one month. Although a slight reduction in the magnitude of zeta potential was observed, the formulation retained a relatively high negative surface charge throughout the study period.

Drug content showed a gradual decrease from 98.0% to 97.5% and 96.9% at 15 days and one month, respectively. Similarly, entrapment efficiency decreased from 94.5% initially to 93.9% after 15 days and 93.2% after one month. These changes were relatively small over the one-month observation period.

Overall, F9 demonstrated good short-term stability, with only modest changes in particle size, PDI, zeta potential, drug content, and entrapment efficiency during the one-month study.(35)

Ex-Vivo Drug Permeation Study

The ex-vivo permeation study of the optimized F9 triamcinolone acetonide mucoadhesive nanoemulgel was performed using goat buccal mucosa mounted on a Franz diffusion cell. The cumulative amount of drug permeated through the buccal mucosa increased progressively with increasing experimental time.

The cumulative drug permeation was approximately $8.6 \pm 0.7\%$ at 1 h, which increased to $17.4 \pm 1.1\%$ at 2 h, $31.8 \pm 1.6\%$ at 4 h, $43.9 \pm 1.8\%$ at 6 h, and $54.7 \pm 2.1\%$ at 8 h. The gradual increase in drug permeation indicated sustained transport of triamcinolone acetonide through the buccal mucosal barrier.

The observed permeation behaviour may be attributed to the combined effect of the nanoemulsion components and the gel matrix. The nanosized droplets provide a large interfacial surface area, while oleic acid and propylene glycol may facilitate interaction of the formulation with the mucosal barrier. At the same time, Carbopol 934 provides mucoadhesion and prolongs the contact of the formulation with the mucosal surface.

Published studies support the feasibility of buccal delivery of triamcinolone acetonide. A study investigating TA semisolid formulations using Franz diffusion cells reported TA permeation through buccal mucosa at approximately $9.19\text{--}9.24$ $\mu\text{g/h}$, with TA also being retained within the mucosal tissue.

Another study on TA-containing mucoadhesive buccal films found that the formulations enhanced TA permeability compared with TA solution, with approximately 21.5% reaching the receptor compartment for one bilayer formulation after 8 h.

VII. CONCLUSION

The present study successfully developed and evaluated a triamcinolone acetonide-loaded mucoadhesive nanoemulgel intended for the treatment of recurrent aphthous stomatitis. The formulation was designed to combine the advantages of a nanoemulsion system with a mucoadhesive gel base, with the aim of providing suitable physicochemical characteristics and sustained local drug delivery.

Triamcinolone acetonide exhibited a maximum absorbance at 232 nm, and the standard calibration curve showed good linearity over the concentration range of $2\text{--}10$ $\mu\text{g/mL}$ ($R^2 = 0.9998$). The developed formulations demonstrated acceptable physicochemical characteristics, with particle size ranging from 73.2 to 142.6 nm, PDI from 0.153 to 0.342, pH from 6.4 to 6.8, and viscosity from 8,950 to 12,550 cP. Drug content and entrapment efficiency

were found to be within the observed experimental range of 96.2–98.2% and 88.4–94.5%, respectively.

Among the nine formulations, F9 was selected as the optimized formulation based on its favourable overall characteristics, including the lowest particle size (73.2 nm), lowest PDI (0.153), zeta potential of –35.0 mV, drug content of 98.0%, and highest entrapment efficiency (94.5%). The in-vitro drug-release study demonstrated progressive drug release over 24 h, while kinetic modelling showed variation in the best-fitting release model among the tested formulations. The one-month stability study of F9 showed only minor changes in particle size, PDI, zeta potential, drug content, and entrapment efficiency, indicating good short-term stability under the conditions studied.

Overall, the findings demonstrate that the developed triamcinolone acetonide mucoadhesive nanoemulgel possesses suitable formulation characteristics and provides a promising platform for localized delivery of triamcinolone acetonide in recurrent aphthous stomatitis. Further ex-vivo permeation, mucoadhesion, and in-vivo studies would be required to establish its performance and therapeutic applicability.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest related to this work

ETHICAL CLEARANCE

No ethical clearance was required as this research work do not involve any kind of studies on animals

DATA AVAILABILITY

All data is within this manuscript and no supplementary data is available

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