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Research Article

DEVELOPMENT AND OPTIMIZATION OF CLOBETASOL
PROPIONATE NANOCARRIER-BASED NANOGEL FOR
SELECTIVE EPIDERMAL TARGETING AND REDUCED
TRANSDERMAL PERMEATIONPremkumar. R^{*1}, Ranjani. G², Vasanthan. A³, Jeevanandham. S⁴¹ M. Pharm Scholar, Department of Pharmaceutics, Sri Vijay Vidyalaya College of Pharmacy, Nallampalli, Dharmapuri, affiliated to the TN Dr. MGR Medical University, Guindy, Chennai, Tamil Nadu, India.² Assistant Professor, Department of Pharmaceutics, Sri Vijay Vidyalaya College of Pharmacy, Nallampalli, Dharmapuri, affiliated to the TN Dr. MGR Medical University, Guindy, Chennai, Tamil Nadu, India.³ Associate Professor & HOD Department of Pharmaceutics, Sri Vijay Vidyalaya College of Pharmacy, Nallampalli, Dharmapuri, affiliated to the TN Dr. MGR Medical University, Guindy, Chennai, Tamil Nadu, India.⁴ Principal, Professor and Head, Department of Pharmaceutics, Sri Vijay Vidyalaya College of Pharmacy, Nallampalli, Dharmapuri, affiliated to the TN Dr. MGR Medical University, Guindy, Chennai, Tamil Nadu, India.

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Abstract:

Clobetasol propionate is a potent topical corticosteroid, and nanocarrier-based systems may improve localized skin delivery while reducing unnecessary transdermal permeation. The present study aimed to develop and optimize a clobetasol propionate nanocarrier-based nanogel for topical application. Four nanocarrier formulations were prepared using HPMC K100, PVA and Polysorbate 80 and evaluated for particle size, polydispersity index (PDI), zeta potential, entrapment efficiency and drug loading. The optimized nanocarriers were incorporated into Carbopol 934 nanogel and evaluated for appearance, pH, viscosity, spreadability and in vitro drug release. Clobetasol propionate showed a melting point of 196.7°C, with a UV λ_{max} of 238 nm and linearity over 1–5 $\mu\text{g/mL}$ ($R^2 = 0.9945$). Among the formulations, F2 showed the smallest particle size (124.6 nm), lowest PDI (0.09), highest entrapment efficiency (94.7%) and drug loading (24.4%), indicating favorable formulation characteristics. The F2 nanogel exhibited a pH of 7.0, viscosity of 19,458 cP and spreadability of 6.9 g-cm/s, with 96.12% drug release over 8 h. F4 also demonstrated favorable characteristics, with a particle size of 128.1 nm, PDI of 0.11 and 88.38% drug release over 8 h. Release kinetics showed the highest correlation with the first-order model, while Korsmeyer–Peppas analysis indicated predominantly Fickian diffusion. Overall, F2 demonstrated the most favorable physicochemical properties and controlled drug release, supporting its potential as a topical clobetasol propionate nanogel. Further ex vivo skin permeation and retention studies are required to confirm selective epidermal targeting and reduced transdermal permeation.

Keywords: Clobetasol propionate; nanocarrier; nanogel; topical delivery; epidermal targeting; controlled release; transdermal permeation.

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1. INTRODUCTION:

The skin is a complex biological barrier that protects the body from the external environment while regulating water loss, chemical penetration and interaction with the surrounding environment. It is composed principally of the epidermis, dermis and subcutaneous tissue. Among these layers, the epidermis, and particularly the stratum corneum, provides the major resistance to the entry of exogenous substances. The stratum corneum consists of corneocytes embedded within an organized intercellular lipid matrix and therefore acts as the principal barrier governing topical and transdermal drug disposition. The barrier characteristics of skin are highly relevant to the design of formulations intended either to remain within superficial cutaneous layers or to cross the skin and reach systemic circulation.

Topical drug delivery is attractive for dermatological therapy because it permits application directly at the site of disease and can reduce the need for systemic administration. However, topical treatment does not automatically ensure localization within the desired skin layer. Drug molecules may partition into the stratum corneum, diffuse into viable epidermis and dermis, or, depending on their physicochemical properties and formulation, proceed further toward systemic circulation. The balance between local therapeutic action and unnecessary deeper penetration is especially important for highly potent drugs, for which excessive exposure can increase the possibility of adverse effects.

Topical corticosteroids remain important agents in the management of inflammatory and hyperproliferative skin disorders. They exert anti-inflammatory and immunomodulatory actions and are used in conditions such as psoriasis, eczema and other inflammatory dermatoses. Clobetasol propionate is a highly potent topical corticosteroid selected when a strong local anti-inflammatory response is required. Its potency makes efficient local delivery desirable, but it also emphasizes the importance of controlling the extent and duration of drug exposure. Local adverse effects associated with potent corticosteroids may include skin atrophy and

other steroid-related changes, while systemic exposure may occur when conditions favor absorption.

The formulation of clobetasol propionate therefore represents a useful challenge in topical drug delivery: the formulation should provide sufficient drug availability at the application site while avoiding unnecessary rapid movement into deeper tissues. Conventional semisolid formulations may provide acceptable topical application, but their drug release and disposition can be influenced by the properties of the vehicle, drug solubility, skin condition and duration of contact. Modification of the drug into a carrier system provides another approach to regulate drug release and potentially create a localized drug reservoir.

Nanocarriers have received considerable attention in topical drug delivery because their small size and large interfacial area allow interaction with the drug and formulation environment at the application site. Depending on the carrier composition, drug loading and surface characteristics, nanocarriers can influence release, retention and the interaction of the formulation with the stratum corneum. Polymeric systems are particularly useful because polymer composition and concentration can be adjusted to influence particle size, drug entrapment, stability and release behavior.

Nanogels provide a complementary formulation environment by combining nanoscale delivery concepts with a hydrated polymeric gel matrix. A nanocarrier dispersed in a Carbopol-based gel can provide a formulation that is easy to apply, has suitable viscosity and spreadability, and remains in contact with the skin for an appropriate period. The gel matrix can also act as an additional diffusion barrier and may help regulate drug release from the incorporated nanocarrier. The combination of a nanocarrier and nanogel is therefore a rational approach when prolonged local residence and controlled release are desired.

In the present study, HPMC K100 and polyvinyl alcohol (PVA) were selected as polymeric components of the clobetasol propionate nanocarrier, with Polysorbate 80 used as a surfactant and acetone as the organic solvent for drug

incorporation. The resulting nanocarrier formulations were evaluated using particle size, PDI, zeta potential, entrapment efficiency and drug-loading measurements. These parameters were used collectively to identify the most favorable formulations rather than relying on particle size alone.

The selected nanocarrier systems were subsequently incorporated into a Carbopol 934 nanogel containing triethanolamine, EDTA sodium and methylparaben. The final nanogels were assessed for appearance, pH, viscosity, spreadability and in vitro drug release. Release data were analyzed using zero-order, first-order, Higuchi and Korsmeyer–Peppas models to understand the pattern and probable mechanism of drug release.

The overall formulation objective was to create a controlled topical drug-delivery platform that could potentially maintain clobetasol propionate at the application site and reduce unnecessary transdermal movement. Importantly, formulation characteristics and in vitro release can support this objective but cannot independently prove selective epidermal targeting. Quantitative ex vivo skin permeation and skin-retention studies are required to establish the distribution of drug among the different skin compartments. The present manuscript therefore interprets epidermal targeting and reduced transdermal permeation as formulation objectives and potential advantages rather than as conclusively demonstrated outcomes.

2. AIM AND OBJECTIVES

The aim of the study was to develop and optimize a clobetasol propionate nanocarrier-based nanogel intended for localized topical delivery, prolonged cutaneous residence and reduced unnecessary transdermal permeation.

- To characterize clobetasol propionate by organoleptic, solubility and melting-point studies.
- To develop and validate a UV spectrophotometric method for estimation of clobetasol propionate.
- To assess drug–excipient compatibility by FTIR studies.
- To prepare clobetasol propionate-loaded polymeric nanocarrier formulations using HPMC K100, PVA and Polysorbate 80.
- To characterize the nanocarriers for particle size, PDI, zeta potential, entrapment efficiency and drug loading.
- To select the most favorable nanocarrier formulation based on the combined characterization results.
- To incorporate the selected nanocarrier into a Carbopol 934-based nanogel.
- To evaluate the prepared nanogel for appearance, pH, viscosity, spreadability and in vitro drug release.

- To analyze the release data using different mathematical kinetic models and identify the predominant release mechanism.
- To establish a formulation basis for future ex vivo evaluation of skin permeation and skin retention.

3. MATERIALS AND METHODS:

3.1 Materials

Clobetasol propionate was used as the active pharmaceutical ingredient. HPMC K100 and polyvinyl alcohol (PVA) were used as polymeric carrier components. Polysorbate 80 was used as the surfactant and acetone as the organic solvent. Carbopol 934 was used as the gel-forming polymer, while triethanolamine was used as the neutralizing agent. EDTA sodium and methylparaben were incorporated as formulation excipients, and purified water was used as the aqueous vehicle. The formulation composition and processing approach were based on the supplied M.Pharm thesis.

3.2 Preformulation Studies

The drug was examined for physical appearance and solubility in selected solvents. The saturation solubility study was used to identify a suitable solvent for the organic phase of nanocarrier preparation. Melting point was determined by the capillary method and compared with the reported range in the thesis. The drug was obtained as a white to off-white crystalline powder and showed practical insolubility in water, partial solubility in ethanol and good solubility in acetone, dichloromethane and DMSO. Approximately 10 mg/mL solubility in acetone was reported after 30 min of bath sonication. A UV spectrophotometric method was established for quantitative estimation of clobetasol propionate. The maximum absorption wavelength was identified at 238 nm. A calibration curve was prepared over 1–5 µg/mL. Linearity, precision, accuracy, robustness and ruggedness were evaluated as part of the analytical method development. The method was subsequently used to support quantitative formulation evaluation.

3.3 Drug–Excipient Compatibility

Fourier-transform infrared spectroscopy (FTIR) was employed to compare the characteristic spectra of clobetasol propionate, selected formulation components and their physical mixture. The purpose was to identify major changes in characteristic functional-group regions that could indicate possible incompatibility. The compatibility assessment was used as a preliminary basis for proceeding with the selected polymeric carrier system.

3.4 Preparation of Clobetasol Propionate Nanocarriers

Four nanocarrier formulations (F1–F4) were prepared. All formulations contained 0.05% clobetasol propionate and 0.75% Polysorbate 80, while the concentrations of HPMC K100 and PVA were varied systematically. Clobetasol propionate

was dissolved in acetone to form the organic phase. HPMC K100 was hydrated in purified water and PVA was prepared separately. The polymer solutions were subsequently combined with Polysorbate 80 to obtain the aqueous polymer phase. The organic phase was added slowly to the aqueous polymer phase under stirring to produce a preliminary oil-in-water emulsion. The preliminary

emulsion was homogenized at 4000 rpm for 5 min per cycle for three cycles, with short cooling or rest periods between cycles. Probe sonication was then performed under controlled temperature conditions. Acetone was removed by gentle stirring/controlled evaporation, and the resulting nanocarrier dispersions were allowed to equilibrate before characterization.

Ingredient	F1	F2	F3	F4	Function
Clobetasol propionate	0.05%	0.05%	0.05%	0.05%	Active drug
HPMC K100	0.50%	1.00%	0.50%	1.00%	Polymeric carrier
PVA	0.50%	0.50%	1.00%	1.00%	Polymeric carrier
Polysorbate 80	0.75%	0.75%	0.75%	0.75%	Surfactant
Acetone	q.s.	q.s.	q.s.	q.s.	Organic solvent
Purified water	q.s.	q.s.	q.s.	q.s.	Aqueous vehicle

Table 1. Composition of clobetasol propionate nanocarrier formulations.

3.5 Nanocarrier Characterization

Particle size and PDI were determined by dynamic light scattering. Particle size was used to confirm the formation of nanoscale dispersions, whereas PDI provided information about the breadth of the particle-size distribution. Zeta potential was measured to characterize surface charge. Entrapment efficiency was calculated from the amount of drug associated with the carrier relative to the total drug used, while drug loading represented the amount of drug incorporated relative to the carrier system according to the calculation procedures described in the thesis.

3.6 Preparation of Nanocarrier-Based Nanogel

Carbopol 934 was used at 2% w/v as the primary gel-forming polymer. It was dispersed in purified

water maintained at approximately 60–70°C and allowed to hydrate for 3 h. EDTA sodium and methylparaben were incorporated with continuous stirring. Triethanolamine at 0.1% w/v was added dropwise under continuous stirring at approximately 400–500 rpm to develop the gel matrix. The selected nanocarrier dispersion was then added gradually to the gel under continuous stirring and mixed for a further 30 min.

The final nanogel was sonicated for approximately 15 min to reduce entrapped air and improve uniformity. The final pH was checked before the formulation was packed in airtight, light-resistant containers. The same basic nanogel platform was used for the selected F2 and F4 nanocarrier systems evaluated in the reported results.

Component	Concentration / quantity	Function
Carbopol 934	2% w/v	Gel-forming polymer
Triethanolamine	0.1% w/v	Neutralizing agent / gel formation
EDTA sodium	0.05–0.1%	Chelating / stabilizing excipient
Methylparaben	0.5%	Preservative
Optimized nanocarrier	As required	Clobetasol propionate-loaded carrier
Purified water	q.s.	Vehicle

Table 2. Composition of the nanocarrier-based Carbopol 934 nanogel platform.

3.7 Evaluation of Nanogel

The prepared nanogels were evaluated visually for colour, clarity, homogeneity and consistency. The pH was determined using a digital pH meter. Viscosity was measured using a Brookfield DV II PRO viscometer. Spreadability was assessed using the method reported in the thesis and expressed in g·cm/s. In vitro drug release was monitored over an 8 h period. The cumulative release data were fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas models to characterize the release pattern and probable mechanism.

3.8 Data Interpretation

Formulation selection was based on the collective performance of the nanocarriers rather than on a single response. Lower particle size and PDI were considered favorable for nanoscale dispersion characteristics, while high entrapment efficiency and drug loading indicated efficient incorporation of clobetasol propionate into the carrier system. For the nanogels, near-neutral pH, suitable viscosity and good spreadability were considered desirable for topical application. Release kinetics were interpreted from the correlation coefficients

obtained for the mathematical models, together with the Korsmeyer–Peppas release exponent.

4. RESULTS AND DISCUSSION:

4.1 Preformulation and Analytical Characterization

Clobetasol propionate was obtained as a white to off-white crystalline powder. Its solubility profile showed practical insolubility in water, partial solubility in ethanol and good solubility in acetone, dichloromethane and DMSO. The reported saturation solubility in acetone was approximately 10 mg/mL after 30 min of bath sonication. This finding was relevant to the preparation process because acetone provided a suitable medium for dissolving the drug before incorporation into the aqueous polymeric phase.

The observed melting point was 196.7°C, which was within the 195–197°C range cited in the thesis.

Agreement with the expected range supported the identity and physical suitability of the drug used for formulation development. The preformulation findings also provided a rational basis for using an organic solvent phase during nanocarrier preparation.

The UV spectrophotometric method showed a maximum absorption at 238 nm. The calibration range of 1–5 µg/mL produced a linear response with an R^2 value of 0.9945. Recovery was reported between 98.46% and 99.58%. The thesis further reported satisfactory precision, robustness and ruggedness. Collectively, these results indicated that the analytical method was suitable for estimation of clobetasol propionate during the formulation studies.

Parameter	Observed result	Interpretation
Appearance	White to off-white crystalline powder	Consistent physical appearance
Water solubility	Practically insoluble	Supports use of suitable solvent system
Ethanol solubility	Partially soluble	Intermediate solubility
Acetone solubility	Freely soluble; ~10 mg/mL saturation study	Suitable for organic phase
Melting point	196.7°C	Within reported 195–197°C range
λ_{max}	238 nm	Selected analytical wavelength
Linearity	1–5 µg/mL; $R^2=0.9945$	Good linear response
Recovery	98.46–99.58%	Acceptable analytical recovery

Table 3. Summary of preformulation and analytical findings.

4.2 Drug–Excipient Compatibility

The FTIR compatibility study did not demonstrate significant spectral changes that were interpreted as evidence of incompatibility between clobetasol propionate and the selected formulation components. The compatibility findings supported the use of HPMC K100, PVA and the other selected excipients in the nanocarrier and nanogel systems. HPMC K100 and PVA were retained as polymeric components because their formulation roles were consistent with film-forming, adhesion and gel-forming behavior and their ability to influence drug release and topical applicability.

4.3 Effect of Polymer Composition on Nanocarrier Characteristics

All four formulations produced particles within the nanometric range, confirming successful formation of the intended nanoscale carrier system. However, clear differences were observed among the

formulations as the concentrations of HPMC K100 and PVA were varied. F1 showed the largest particle size of 197.2 nm and a PDI of 0.17. F3 showed an intermediate particle size of 162.6 nm and a PDI of 0.14. In contrast, F2 and F4 showed substantially smaller particles, measuring 124.6 and 128.1 nm, respectively, with PDI values of 0.09 and 0.11.

The lower PDI values of F2 and F4 indicate comparatively narrower particle-size distributions than F1 and F3. This difference suggests that the higher HPMC K100 concentration used in F2 and F4, in combination with the corresponding PVA concentration, produced a more favorable balance during the formation and stabilization of the nanocarrier dispersion. The data do not establish a single causal factor because HPMC K100 and PVA concentrations were varied as formulation variables; nevertheless, the overall formulation response clearly favored F2 and F4.

Formulation	Particle size (nm)	PDI	Zeta potential (mV)	Interpretation
F1	197.2	0.17	–19.2	Largest particle size; broader distribution
F2	124.6	0.09	–11.9	Smallest size; lowest PDI
F3	162.6	0.14	–17.7	Intermediate characteristics
F4	128.1	0.11	–14.2	Comparable to F2

Table 4. Particle-size, PDI and zeta-potential characteristics of nanocarrier formulations.

The zeta potential values were negative for all formulations and ranged from -11.9 to -19.2 mV. F1 showed the most negative value (-19.2 mV), followed by F3 (-17.7 mV), F4 (-14.2 mV) and F2 (-11.9 mV). Zeta potential provides information about surface charge characteristics, but the present study did not use this parameter alone to rank the formulations. Instead, it was interpreted together with particle size, PDI, entrapment efficiency and drug loading.

Formulation	Entrapment efficiency (%)	Drug loading (%)
F1	84.3	22.3
F2	94.7	24.4
F3	92.3	23.2
F4	89.1	23.9

Table 5. Entrapment efficiency and drug loading of clobetasol propionate nanocarriers.

The high entrapment efficiency observed for F2 indicates efficient association of clobetasol propionate with the polymeric carrier system. Its drug-loading value was also the highest among the four formulations. F4 was the second most favorable formulation in terms of particle size and showed a drug-loading value close to that of F2. The combined results therefore identified F2 as the most favorable candidate, with F4 retained as a close alternative for subsequent nanogel evaluation.

4.5 Overall Selection of F2 and F4

Selection of an optimized nanocarrier is a multidimensional decision because a formulation

4.4 Entrapment Efficiency and Drug Loading

The entrapment efficiency and drug-loading results further differentiated the formulations. F1 showed 84.3% entrapment efficiency and 22.3% drug loading. F2 showed the highest values, with 94.7% entrapment efficiency and 24.4% drug loading. F3 showed 92.3% entrapment efficiency and 23.2% drug loading, while F4 showed 89.1% entrapment efficiency and 23.9% drug loading.

with the smallest particle size may not necessarily provide the highest entrapment efficiency or the most appropriate release profile. In the present study, F2 combined the smallest particle size, lowest PDI, highest entrapment efficiency and highest drug loading. F4 showed a particle size close to F2 and a similarly low PDI, although its entrapment efficiency was lower. These combined characteristics justified the selection of F2 as the primary optimized formulation and F4 as a closely comparable formulation for nanogel evaluation.

Key parameter	F2	F4	Preferred observation
Particle size	124.6 nm	128.1 nm	F2
PDI	0.09	0.11	F2
Zeta potential	-11.9 mV	-14.2 mV	Comparable; not sole selection criterion
Entrapment efficiency	94.7%	89.1%	F2
Drug loading	24.4%	23.9%	F2

Table 6. Comparative basis for selecting F2 and F4 for nanogel development.

4.6 Nanogel Appearance and Physical Properties

The selected nanocarriers were incorporated into Carbopol 934 nanogel systems. The prepared nanogels were described as half-white, clear or translucent, with smooth and elastic consistency. Such physical appearance is relevant to topical application because a uniform semisolid preparation is easier to spread and can provide consistent contact with the skin surface.

Both F2 and F4 nanogels showed a pH of 7.0, indicating a near-neutral formulation environment. A near-neutral pH was considered favorable from the perspective of topical application and was consistent across the two formulations. The viscosity values were 19,458 cP for F2 and 21,007

cP for F4. The slightly higher viscosity of F4 may contribute to its slower release profile by providing greater resistance to drug movement through the gel matrix, although the present data do not establish viscosity as the sole determinant of release. Spreadability values were $6.9 \text{ g}\cdot\text{cm/s}$ for F2 and $7.0 \text{ g}\cdot\text{cm/s}$ for F4. The close similarity between the two values indicates that the higher viscosity of F4 did not produce a major difference in measured spreadability under the test conditions. The combination of near-neutral pH, relatively high viscosity and satisfactory spreadability supported the practical topical characteristics of both nanogel formulations.

Parameter	F2 nanogel	F4 nanogel	Interpretation
Appearance	Half-white, clear/translucent	Half-white, clear/translucent	Smooth and elastic consistency
pH	7.0	7.0	Near-neutral
Viscosity	19,458 cP	21,007 cP	F4 slightly higher
Spreadability	6.9 g·cm/s	7.0 g·cm/s	Closely similar

Table 7. Physical evaluation of the selected nanocarrier-based nanogels.

4.7 In Vitro Drug Release

The in vitro release study was performed over 8 h to compare the release behavior of the selected nanogel formulations. Both F2 and F4 exhibited progressive drug release with time rather than an abrupt release pattern. F2 released 12.07% of the drug at 15 min, 26.04% at 30 min, 41.67% at 60 min, 58.48% at 120 min, 76.94% at 240 min and 96.12% at 480 min. F4 released 10.85%, 23.54%, 37.38%, 53.07%, 70.15% and 88.38% at the corresponding time points.

Time (min)	F2 cumulative release (%)	F4 cumulative release (%)
15	12.07	10.85
30	26.04	23.54
60	41.67	37.38
120	58.48	53.07
240	76.94	70.15
480	96.12	88.38

Table 8. In vitro cumulative release of clobetasol propionate from F2 and F4 nanogels.

The difference between the two formulations became more evident with increasing time. At 8 h, F2 achieved 96.12% release, whereas F4 achieved 88.38%. Thus, F4 exhibited a slower overall release profile. The slightly higher viscosity of F4 and its different polymer composition may have contributed to the slower drug liberation. Nevertheless, both formulations showed extended release over the 8 h study period, which is consistent with the objective of providing a controlled release environment rather than rapid drug liberation.

From a formulation-development perspective, the release profile of F2 was particularly attractive because it combined high drug entrapment with a relatively rapid but still prolonged release over 8 h. F4 provided a slower release profile and may be useful where a greater degree of release retardation is desired. The choice between these profiles should ultimately be linked to skin retention and permeation data, because an in vitro release profile by itself does not indicate how much drug will remain within the epidermis or cross into deeper tissue.

4.8 Release Kinetics and Mechanism

Formulation	Zero-order R ²	First-order R ²	Higuchi R ²	Korsmeyer–Peppas R ²	n value
F2	0.9273	0.9949	0.9826	0.9862	0.456
F4	0.9312	0.9948	0.9845	0.9873	0.463

Table 9. Mathematical release-kinetic analysis of F2 and F4 nanogels.

The first-order model produced the highest correlation coefficients for both formulations, with R² values of 0.9949 for F2 and 0.9948 for F4. This indicates that, within the tested mathematical models, the release profile was best described by first-order kinetics. The high Higuchi correlations, 0.9826 for F2 and 0.9845 for F4, also indicate a substantial diffusion contribution to the release process.

The Korsmeyer–Peppas model provided R² values of 0.9862 for F2 and 0.9873 for F4. The corresponding release exponent values were 0.456 and 0.463. These values were close to the Fickian diffusion range described for the system in the thesis, supporting the interpretation that diffusion was the predominant mechanism. The slightly

higher n value of F4 may indicate a small contribution from polymer relaxation or matrix-related effects, but the overall interpretation remained predominantly diffusion-controlled.

F4 showed marginally higher Higuchi and Korsmeyer–Peppas correlation coefficients than F2, whereas F2 showed a marginally higher first-order correlation coefficient. The differences were small, indicating broadly similar release behavior. Therefore, the kinetic results alone do not provide a sufficient basis to replace F2 as the preferred formulation; rather, they complement the particle-size, PDI, entrapment-efficiency, drug-loading and nanogel-property findings.

4.9 Relationship Between Nanocarrier Properties and Release Behavior

The formulation data demonstrate that the properties of the nanocarrier and the final nanogel are interrelated. F2 had the smallest particle size and lowest PDI among the tested systems, together with the highest drug entrapment and loading. When incorporated into Carbopol 934 gel, these characteristics were associated with a controlled release profile extending over 8 h. F4, which had a closely similar particle size but slightly higher viscosity in the final gel, released the drug more slowly than F2.

The results also illustrate why optimization should consider both the nanoscale carrier and the final dosage form. A nanocarrier may exhibit favorable particle characteristics, but once incorporated into a semisolid gel, the surrounding polymer network becomes an additional factor influencing drug diffusion. Consequently, the final topical performance depends on the combined effect of carrier composition, gel structure, drug loading, viscosity and the interaction of the formulation with the skin surface.

4.10 Relevance to Localized Epidermal Delivery

The formulation strategy was designed around the concept of maintaining clobetasol propionate within the intended cutaneous region. The drug was incorporated into a polymeric nanocarrier and subsequently dispersed within a relatively viscous Carbopol 934 gel. The nanoscale particle size, high entrapment efficiency and prolonged in vitro release provide a rational basis for considering the formulation as a localized drug reservoir. Such a reservoir may help moderate the availability of drug at the skin surface and maintain drug delivery over an extended period.

However, selective epidermal targeting is a biological distribution outcome and cannot be inferred solely from particle size, viscosity or in vitro release. To establish epidermal localization, the amount of clobetasol propionate retained in the stratum corneum, viable epidermis and dermis should be measured separately after topical application. Similarly, reduced transdermal permeation requires quantitative measurement of the drug reaching the receptor compartment in an appropriate ex vivo skin model. Because these numerical endpoints were not reported in the available thesis results, they have not been presented as demonstrated findings in this manuscript.

The appropriate interpretation is therefore that the developed nanocarrier-based nanogel possesses formulation characteristics that may support localized topical delivery and controlled drug release. F2 is particularly promising because it combines the most favorable nanocarrier characteristics with high drug entrapment and satisfactory nanogel properties. Confirmation of the

intended targeting advantage remains an important next stage of development.

4.11 Comparison of F2 and F4

F2 and F4 were the strongest formulations across the reported nanocarrier and nanogel evaluation parameters. F2 had a particle size of 124.6 nm, PDI of 0.09, zeta potential of -11.9 mV, entrapment efficiency of 94.7% and drug loading of 24.4%. F4 had a particle size of 128.1 nm, PDI of 0.11, zeta potential of -14.2 mV, entrapment efficiency of 89.1% and drug loading of 23.9%. The particle-size difference was small, but F2 had the advantage in PDI, entrapment efficiency and drug loading.

At the nanogel level, F2 showed 19,458 cP viscosity and 6.9 g·cm/s spreadability, whereas F4 showed 21,007 cP and 7.0 g·cm/s. The release study showed a higher cumulative release for F2 at every reported time point, reaching 96.12% at 8 h compared with 88.38% for F4. Thus, F2 provided a somewhat faster overall release while maintaining controlled release characteristics, whereas F4 provided greater release retardation. Considering the complete dataset, F2 was retained as the most favorable formulation, while F4 remained a useful comparator and alternative candidate.

4.12 Study Strengths and Limitations

A major strength of the study is the systematic evaluation of multiple formulation variables and responses. The nanocarriers were not selected only on the basis of particle size; PDI, zeta potential, entrapment efficiency and drug loading were considered together. The selected nanocarriers were then evaluated after incorporation into the final Carbopol 934 nanogel, allowing the formulation to be assessed in the dosage form intended for topical use. In addition, the release data were examined using multiple kinetic models rather than relying on cumulative release alone.

The principal limitation is the absence of reported quantitative ex vivo skin permeation and skin-retention results. These studies are necessary to demonstrate whether the formulation actually increases drug retention in the epidermis and decreases movement into deeper skin layers or the receptor compartment. Other biological performance parameters, such as comparative pharmacodynamic efficacy and long-term stability, would also strengthen the development of the formulation. Accordingly, the present work should be considered a formulation-development and in vitro characterization study with a clear basis for subsequent ex vivo evaluation.

4.13 Future Work

Future studies should compare the optimized nanogel with a suitable conventional clobetasol propionate topical formulation using an ex vivo Franz diffusion-cell model. Quantification of drug in the donor formulation, skin tissue and receptor phase would provide a complete mass-balance assessment. Tape stripping or validated skin-layer

separation could be used to estimate drug retention in superficial and deeper skin compartments. Such experiments would directly address the intended objective of selective epidermal localization and reduced transdermal permeation.

Additional development work may include assessment of physical and chemical stability, rheological behavior under different shear conditions, drug-content uniformity, long-term storage stability and comparative topical efficacy. If future studies demonstrate increased epidermal retention with reduced receptor-compartment permeation, the formulation strategy would have stronger evidence for achieving the intended therapeutic localization of clobetasol propionate.

5. CONCLUSION:

The present study demonstrated the feasibility of developing a clobetasol propionate-loaded polymeric nanocarrier and incorporating the optimized carrier into a Carbopol 934-based nanogel. The preformulation and analytical studies confirmed the suitability of the drug and selected formulation components, while FTIR findings did not indicate significant incompatibility. All four nanocarrier formulations exhibited nanoscale particle sizes, with F2 providing the most favorable overall combination of particle size, PDI, entrapment efficiency and drug loading.

F2 showed a particle size of 124.6 nm, PDI of 0.09, entrapment efficiency of 94.7% and drug loading of 24.4%. The corresponding nanogel exhibited a near-neutral pH, viscosity of 19,458 cP and spreadability of 6.9 g/cm/s. F4 also demonstrated favorable characteristics and produced a slightly more retarded release profile. Both selected nanogels showed controlled release over 8 h, with first-order kinetics providing the highest correlation and Korsmeyer–Peppas analysis indicating predominantly Fickian diffusion.

Overall, F2 was the most favorable formulation based on the reported physicochemical and in vitro performance parameters. The nanocarrier-based nanogel provides a rational platform for localized topical delivery of clobetasol propionate and has potential to act as a controlled local drug reservoir. Nevertheless, selective epidermal targeting and reduced transdermal permeation cannot be confirmed from the present data alone. Ex vivo skin permeation and skin-retention studies are required

before these targeted-delivery outcomes can be stated conclusively.

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