

Development And Characterization Of A Tretinoin-Loaded Thermosensitive In Situ Gel For Sustained Topical Drug Delivery In Psoriasis

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ABSTRACT

Background: Psoriasis is a chronic inflammatory skin disorder requiring effective topical drug delivery. Thermosensitive in situ gels may improve drug residence and provide sustained release compared with conventional topical preparations. **Aim/Objectives:** The study aimed to develop and characterize a tretinoin-loaded thermosensitive in situ gel using Poloxamer 407 and Poloxamer 188 and to evaluate its physicochemical properties, drug incorporation, release behaviour, anti-inflammatory activity, and short-term stability. **Materials and Methods:** Eight formulations (F1–F8) were prepared by the cold method using different concentrations and ratios of Poloxamer 407 and Poloxamer 188. The formulations were evaluated for pH, gelation temperature, gelation time, drug content, entrapment efficiency, *in-vitro* drug release, anti-inflammatory activity, and stability. **Results:** The formulations showed pH values of 6.68–7.19, gelation temperatures of 34–47°C, drug content of 90.68–98.52%, and entrapment efficiency of 95.2–99.2%. F3 showed $35.0 \pm 1.0^\circ\text{C}$ gelation temperature, 38 ± 0.8 s gelation time, $98.52 \pm 0.42\%$ drug content, $98.0 \pm 0.5\%$ entrapment efficiency, and 94.8% drug release at 24 h. Its IC₅₀ was 132.8 µg/mL. **Conclusion:** F3 demonstrated favourable physicochemical characteristics, sustained drug release, *in-vitro* anti-inflammatory activity, and satisfactory short-term stability, supporting further investigation as a topical tretinoin delivery system. **Keywords:** Tretinoin; Thermosensitive gel; Poloxamer 407; Poloxamer 188; Psoriasis; Sustained drug delivery. **How to cite this article:** Aruna P, Dr R Manivannan: Development And Characterization Of A Tretinoin-Loaded Thermosensitive In Situ Gel For Sustained Topical Drug Delivery In Psoriasis. Int J Drug Deliv Technol. 2026;16(86s): 1402-1410; DOI: 10.25258/ijddt.16.86s.121

Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disorder characterized by recurrent erythematous, scaly plaques and a substantial impact on patients' quality of life. Its global burden has continued to increase, highlighting the need for effective, acceptable, and patient-friendly therapeutic approaches [1]. For patients with localized or mild-to-moderate disease, topical therapy remains an important component of management, with retinoids such as tazarotene included among established topical treatment options [2,3]. However, conventional topical formulations may have limitations related to drug residence on the skin, repeated application, formulation wash-off, and local irritation. These factors can affect treatment acceptability and adherence, particularly when prolonged therapy is required.

Novel topical drug-delivery systems have therefore been investigated to improve local drug retention and provide more controlled drug release. In situ gelling systems are particularly attractive because they can be administered as low-viscosity formulations and subsequently undergo gel formation under

physiological conditions. Thermosensitive systems based on poloxamers exploit temperature-dependent micellization and sol-gel transition, allowing formulation characteristics such as gelation temperature, viscosity, and drug-release behaviour to be modified through polymer concentration and composition [4,5]. Recent investigations have demonstrated the potential of Poloxamer 407-based systems for localized drug delivery and controlled release, supporting their continued development as pharmaceutical delivery platforms [5,6].

Recent formulation studies further support the potential of advanced topical delivery systems for psoriasis, including tretinoin-containing vesicular systems, thermosensitive hydrogels, and biomaterial-integrated hydrogel platforms.

The present study aimed to develop a tretinoin-loaded thermosensitive in situ gel for sustained topical drug delivery in psoriasis. The objectives were to formulate the gel using Poloxamer 407 and Poloxamer 188, evaluate its physicochemical properties, drug content, entrapment efficiency, gelation behaviour and *in-vitro* drug release, assess

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its anti-inflammatory potential, and examine the short-term stability of the optimized formulation.

Materials And Methods

Study design: An experimental formulation-development study involving the preparation and evaluation of eight tretinoin-loaded thermosensitive in situ gel formulations (F1–F8).

Study population: The study focused on laboratory-prepared tretinoin thermosensitive in situ gel formulations using Poloxamer 407 and Poloxamer 188.

Sample size: Eight formulations (F1–F8) were prepared and evaluated.

Study duration: The study was conducted during the academic year 2025–2026.

Study setting/location: Department of Pharmaceutics, Excel College of Pharmacy, Komarapalayam, Tamil Nadu.

Inclusion criteria:

1. Formulations containing tretinoin as the active pharmaceutical ingredient.
2. Formulations prepared using Poloxamer 407 and/or Poloxamer 188.
3. Formulations suitable for physicochemical, drug-release, entrapment-efficiency, and stability evaluation.

Exclusion criteria:

1. Formulations not containing the required drug or polymers.
2. Preparations showing visible instability, phase separation, or non-uniformity.
3. Formulations unsuitable for further evaluation based on predefined quality parameters.

Statistical Analysis

All experimental observations were recorded and summarized using appropriate descriptive statistical methods. Continuous variables, including pH, gelation temperature, gelation time, drug content, entrapment efficiency, viscosity, and cumulative drug release, were expressed as mean $\pm$ standard deviation (SD), based on replicate measurements. Formulation-wise results were compared descriptively to assess the influence of Poloxamer 407 and Poloxamer 188 concentration and ratio on the physicochemical and release characteristics of the gels. The concentration-dependent anti-inflammatory activity of formulation F3 was evaluated using percentage inhibition and IC_{50} values, while stability was assessed by comparing changes in pH, gelation temperature, gelation time, and viscosity between baseline and day 7 under different storage conditions. Since the source study did not report inferential statistical tests or calculated p-values for the formulation comparisons, no unsupported statistical significance values were introduced. A p-value of <0.05 may be considered statistically significant for any future inferential analysis of these experimental data.

Result

Table 1. Composition and Basic Characteristics of Tretinoin Thermosensitive In Situ Gel Formulations

Formulation	Tretinoin (g)	Total polymer (%)	Poloxamer 407 (g)	Poloxamer 188 (g)	Water (mL)	pH
F1	0.005	5	1	–	20	6.9
F2	0.005	5	–	1	20	6.96
F3	0.005	10	2	–	20	6.9
F4	0.005	10	–	2	20	7.19
F5	0.005	15	2.25	0.75	20	6.75
F6	0.005	15	0.75	2.25	20	6.68
F7	0.005	20	3.4	0.6	20	7.15
F8	0.005	20	0.6	3.4	20	6.9

Table 2. Physicochemical Evaluation of Tretinoin In Situ Gel Formulations

Formulation	Gelation temperature (°C)	Gelation time (sec)	Drug content (%)	Entrapment efficiency (%)
F1	45.0 $\pm$ 1.0	62 $\pm$ 1.2	90.68 $\pm$ 0.82	97.4 $\pm$ 0.5
F2	47.0 $\pm$ 1.0	55 $\pm$ 0.9	92.74 $\pm$ 0.65	98.0 $\pm$ 0.5
F3	35.0 $\pm$ 1.0	38 $\pm$ 0.8	98.52 $\pm$ 0.42	98.0 $\pm$ 0.5
F4	36.0 $\pm$ 1.0	70 $\pm$ 1.5	95.70 $\pm$ 0.54	99.2 $\pm$ 0.5
F5	35.0 $\pm$ 1.0	65 $\pm$ 1.1	96.98 $\pm$ 0.61	95.2 $\pm$ 0.5
F6	37.0 $\pm$ 1.0	48 $\pm$ 1.0	94.28 $\pm$ 0.73	99.0 $\pm$ 0.5
F7	34.0 $\pm$ 1.0	75 $\pm$ 1.4	97.89 $\pm$ 0.38	98.0 $\pm$ 0.5

F8	36.0 ± 1.0	68 ± 1.3	93.62 ± 0.91	98.0 ± 0.5
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Table 3. *In Vitro* Cumulative Drug Release from Tretinoin In Situ Gel Formulations

Time (min)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)
0	0	0	0	0	0	0	0	0
5	14.2	16.5	11.45	13.2	7.8	9.4	4.5	6.2
15	22.8	25.4	18.3	21.1	12.6	15.2	8.1	11.5
30	35.6	38.9	27.6	31.4	19.5	23.8	13.4	18.2
60	49.1	53.2	38.9	44.5	28.4	34.1	21	27.6
120	68.4	72.8	52.1	59.3	41.2	48.7	32.5	39.8
240	84.5	89.1	66.8	74.6	56.3	64.2	46.8	54.1
360	94.2	98.4	78.5	86.2	68.9	76.5	58.2	66.4
480	98.1	99.2	86.4	93.8	78.4	85.1	67.9	75.8
1440	99.4	99.8	94.8	98.5	88.2	93.4	79.5	86.9

Table 4. *In Vitro* Anti-Inflammatory Activity of Optimized Formulation (F3) Compared with Diclofenac

Concentration (µg/mL)	F3 absorbance	F3 inhibition (%)	Diclofenac inhibition (%)
50	0.601	28.60 ± 0.74	32.40 ± 0.61
100	0.469	44.30 ± 0.52	49.80 ± 0.48
200	0.322	61.70 ± 0.85	67.50 ± 0.55
400	0.195	76.80 ± 0.63	82.30 ± 0.39
800	0.098	88.40 ± 0.41	93.60 ± 0.32
IC50 (µg/mL)	132.8	—	104.5

Table 5. Short-Term Stability Profile of Optimized Formulation F3

Storage condition	Parameter	Day 1	Day 7
25°C	pH	6.48	6.46
25°C	Gelation temperature (°C)	35	35.2
25°C	Gelation time (sec)	38	40
25°C	Viscosity (cps)	5.58	5.6
4 ± 1°C	pH	6.48	6.63
4 ± 1°C	Gelation temperature (°C)	35	35
4 ± 1°C	Gelation time (sec)	38	38
4 ± 1°C	Viscosity (cps)	5.58	5.47
37°C	pH	6.48	6.79
37°C	Gelation temperature (°C)	35	34.6
37°C	Gelation time (sec)	38	34
37°C	Viscosity (cps)	5.58	5.97

Table 6. Overall Formulation Screening and Selection Parameters

Parameter	F1	F2	F3	F4	F5	F6	F7	F8
pH	6.9	6.96	6.9	7.19	6.75	6.68	7.15	6.9
Gelation temperature (°C)	45	47	35	36	35	37	34	36
Gelation time (sec)	62	55	38	70	65	48	75	68
Drug content (%)	90.68	92.74	98.52	95.7	96.98	94.28	97.89	93.62
Entrapment efficiency (%)	97.4	98	98	99.2	95.2	99	98	98
24-h drug release (%)	99.4	99.8	94.8	98.5	88.2	93.4	79.5	86.9

Figure: 1. Time-Wise Recovery of F1–F8 (%)

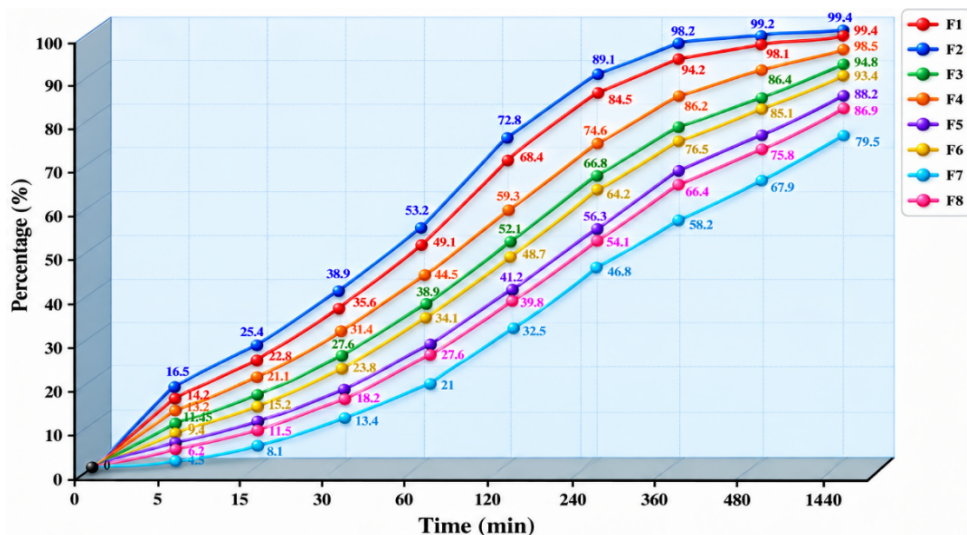
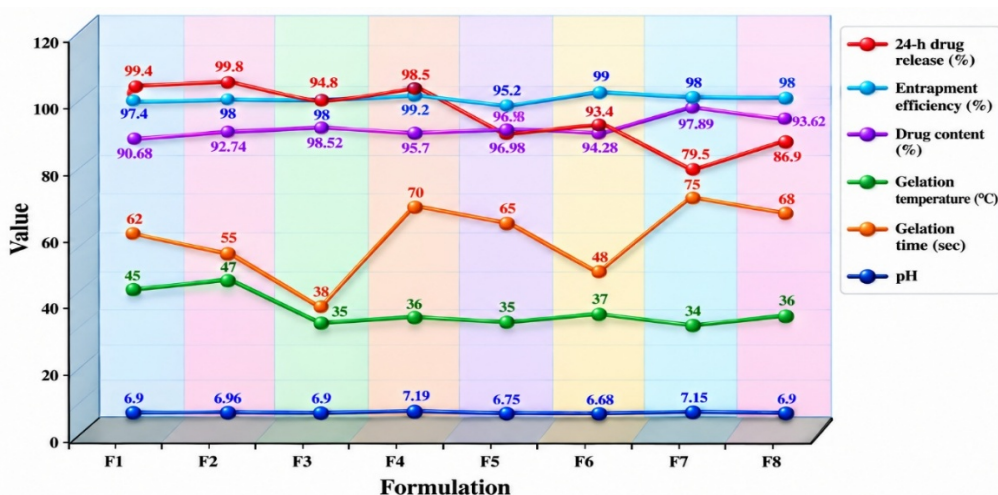


Figure 2. Comparative Evaluation of F1–F8 Formulations



Eight tretinoin-loaded thermosensitive in situ gel formulations (F1–F8) were prepared by varying the concentration and relative proportion of Poloxamer 407 and Poloxamer 188 while maintaining the drug quantity and other formulation components constant. The total polymer concentration ranged from 5% to 20%. F1 and F2 contained 5% polymer, F3 and F4 contained 10%, F5 and F6 contained 15%, and F7 and F8 contained 20%. The pH of the formulations ranged from 6.68 to 7.19, with the highest value observed for F4 (7.19) and the lowest for F6 (6.68). Formulations containing Poloxamer 407 alone and those containing Poloxamer 188 alone showed different pH profiles, while the mixed-polymer formulations remained within a relatively narrow range. Overall, the prepared formulations showed suitable basic physicochemical characteristics for further evaluation as topical thermosensitive systems.

The physicochemical evaluation demonstrated clear differences among the eight formulations with respect to gelation temperature, gelation time, drug content, and entrapment efficiency. Gelation temperature ranged from $34.0 \pm 1.0^\circ\text{C}$ in F7 to $47.0 \pm 1.0^\circ\text{C}$ in F2. F3 showed a gelation temperature of $35.0 \pm 1.0^\circ\text{C}$ and

a relatively rapid gelation time of 38 ± 0.8 seconds. Drug content varied from $90.68 \pm 0.82\%$ in F1 to $98.52 \pm 0.42\%$ in F3, while entrapment efficiency ranged from $95.2 \pm 0.5\%$ in F5 to $99.2 \pm 0.5\%$ in F4. F3 therefore demonstrated high drug incorporation together with a gelation temperature close to physiological skin temperature and rapid gel formation. The source study did not report formal statistical comparison or p-values for these formulation-wise parameters.

The *in vitro* release study showed a progressive increase in tretinoin release with increasing time for all eight formulations. At 60 minutes, cumulative drug release ranged from 21.00% in F7 to 53.20% in F2. At 240 minutes, release increased to 46.80–89.10%, while at 480 minutes it ranged from 67.90% to 99.20%. After 24 hours, F1 and F2 showed the highest cumulative release at 99.40% and 99.80%, respectively, whereas F7 showed the lowest release at 79.50%. Formulation F3 demonstrated a sustained release pattern, reaching 38.90% at 60 minutes, 66.80% at 240 minutes, 86.40% at 480 minutes, and 94.80% at 24 hours. The progressive reduction in release rate with increasing polymer concentration was

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particularly evident in the higher-polymer formulations, supporting the influence of polymer concentration and composition on drug-release behaviour. No formal p-value for between-formulation release comparison was reported in the source data.

The anti-inflammatory activity of the optimized F3 formulation was assessed at concentrations ranging from 50 to 800 µg/mL and compared with diclofenac. F3 produced a concentration-dependent increase in inhibition of protein denaturation, with inhibition increasing from $28.60 \pm 0.74\%$ at 50 µg/mL to $88.40 \pm 0.41\%$ at 800 µg/mL. The corresponding inhibition produced by diclofenac increased from $32.40 \pm 0.61\%$ to $93.60 \pm 0.32\%$ over the same concentration range. Thus, increasing the concentration of F3 was associated with progressively greater anti-inflammatory activity. The IC₅₀ of F3 was 132.8 µg/mL, compared with 104.5 µg/mL for diclofenac. Although F3 showed slightly lower inhibition than diclofenac at each tested concentration, the findings demonstrated measurable concentration-dependent *in vitro* anti-inflammatory activity of the formulation. The study did not report a p-value for the comparison between F3 and diclofenac.

The optimized F3 formulation was subjected to short-term stability assessment under refrigerated conditions ($4 \pm 1^\circ\text{C}$), room temperature (25°C), and a humidity chamber (37°C) for seven days. At room temperature, the pH changed only slightly from 6.48 to 6.46, while gelation temperature changed from 35.0°C to 35.2°C , gelation time from 38 to 40 seconds, and viscosity from 5.58 to 5.60 cps. Under refrigeration, the pH increased from 6.48 to 6.63, whereas gelation temperature and gelation time remained unchanged at 35.0°C and 38 seconds, respectively. At 37°C , the pH increased to 6.79, gelation temperature decreased slightly to 34.6°C , gelation time decreased to 34 seconds, and viscosity increased to 5.97 cps. The formulation remained visually clear during the assessment, with only slight translucency noted after seven days at 37°C . Overall, the observed changes were relatively small during the seven-day study period, indicating satisfactory short-term physical stability. No statistical p-values were reported for the stability comparisons.

When the formulation characteristics were considered together, F3 showed a favourable overall profile. It contained 10% Poloxamer 407 and demonstrated a gelation temperature of 35.0°C , gelation time of 38 ± 0.8 seconds, drug content of $98.52 \pm 0.42\%$, and entrapment efficiency of $98.0 \pm 0.5\%$. Its cumulative drug release reached 94.80% at 24 hours, indicating sustained release over the study period. These findings, together with the short-term stability observations, led the source study to select F3 as the optimized formulation for further consideration as a tretinoin thermosensitive *in situ* gel.

Discussion

The present study was undertaken to develop and characterize tretinoin-loaded thermosensitive *in situ* gel formulations using different concentrations and ratios of Poloxamer 407 and Poloxamer 188. Eight formulations (F1–F8) were prepared and evaluated with respect to pH, gelation temperature, gelation time, drug content, entrapment efficiency, drug-release behaviour, *in-vitro* anti-inflammatory activity, and short-term stability. The overall findings demonstrate that modification of polymer concentration and composition produced measurable differences in the physicochemical and release characteristics of the formulations. This observation is consistent with the established role of poloxamers as thermoresponsive pharmaceutical polymers, in which polymer concentration, temperature, molecular characteristics, and polymer blending influence micellization, gel formation, rheological behaviour, and drug-release characteristics [7]. Recent work has further emphasized that blending different poloxamers can modify their thermodynamic and rheological properties and thereby alter gelation behaviour [8].

The pH of the prepared formulations ranged from 6.68 to 7.19. The relatively narrow pH range observed across F1–F8 indicates that variation in Poloxamer 407 and Poloxamer 188 concentration did not result in major changes in the overall formulation environment. The observed pH values are also relevant to the development of topical formulations because excessive deviation from the physiological skin environment may contribute to irritation and reduced acceptability. Previous work on thermosensitive topical systems has similarly emphasized the importance of maintaining appropriate pH together with suitable gelation and rheological properties [7]. In the present study, F3 showed a pH of 6.90, indicating an acceptable physicochemical environment for further formulation evaluation.

A major finding of the present study was the variation in gelation temperature among the formulations. Gelation temperature ranged from $34.0 \pm 1.0^\circ\text{C}$ in F7 to $47.0 \pm 1.0^\circ\text{C}$ in F2. F3, containing 10% Poloxamer 407, demonstrated a gelation temperature of $35.0 \pm 1.0^\circ\text{C}$ and a relatively rapid gelation time of 38 ± 0.8 seconds. These characteristics are important for a thermosensitive *in-situ* gel because the formulation should remain sufficiently fluid during application and subsequently undergo gel formation at a temperature compatible with topical administration. The thermoresponsive behaviour of Poloxamer 407 is attributed to temperature-dependent micellization and subsequent organization of micelles into more ordered structures as temperature increases [7]. Qutub et al. similarly demonstrated that polymer concentration and blending influence poloxamer gelation through changes in micellization and rheological behaviour [8].

The present findings also showed that formulations containing higher total polymer concentrations

generally exhibited lower gelation temperatures. F7, which contained the highest total polymer concentration, showed the lowest gelation temperature of $34.0 \pm 1.0^\circ\text{C}$. This observation is in agreement with previous experimental evidence demonstrating that increasing Poloxamer 407 concentration can reduce gelation temperature and increase gel strength [9]. The effect of polymer concentration is particularly important for optimizing a topical thermosensitive system because excessive polymer concentration may result in premature gelation or excessively high viscosity, whereas insufficient polymer concentration may produce inadequate gel formation and poor residence at the application site. Therefore, the intermediate polymer concentration represented by F3 provided a useful balance between gelation temperature and gelation time in the present formulation series.

The drug-content analysis further demonstrated differences among the formulations. Drug content ranged from $90.68 \pm 0.82\%$ in F1 to $98.52 \pm 0.42\%$ in F3. F3 therefore showed the highest measured drug content among the eight formulations. Its entrapment efficiency was also high at $98.0 \pm 0.5\%$. These findings indicate efficient incorporation of tretinoin within the polymeric formulation. Tretinoin presents formulation challenges because of its poor aqueous solubility and instability, and recent work has therefore explored vesicular and other advanced topical delivery approaches to improve its skin delivery and retention [10]. Zhao et al. demonstrated that tretinoin-loaded fatty-acid vesicles could improve skin absorption and retention compared with tretinoin solution, highlighting the relevance of formulation strategies for improving topical tretinoin delivery [10].

The drug-release study demonstrated a progressive increase in cumulative tretinoin release with increasing time in all eight formulations. At 60 minutes, cumulative release ranged from 21.00% in F7 to 53.20% in F2. At 240 minutes, release ranged from 46.80% to 89.10%, while at 480 minutes it ranged from 67.90% to 99.20%. After 24 hours, F3 released 94.80% of the incorporated drug. In comparison, F1 and F2 showed higher cumulative release values of 99.40% and 99.80%, respectively, whereas F7 demonstrated the lowest release of 79.50%. The progressive differences between formulations indicate that both polymer concentration and polymer composition influenced tretinoin release.

The comparatively slower release observed with the higher-polymer formulations may be explained by the formation of a denser polymeric environment that provides greater resistance to drug diffusion. This interpretation is consistent with previous investigations of Poloxamer 407-based systems in which polymer concentration affected gel strength, gelation temperature, and drug-release behaviour [9]. General reviews of poloxamer hydrogels have also described the relationship between polymer

concentration, micelle formation, gel structure, and controlled drug release [11]. Similarly, thermosensitive hydrogel systems have been reported to retain incorporated drugs locally and provide prolonged release following temperature-triggered gel formation [12].

The sustained release behaviour observed with F3 is particularly relevant to topical drug delivery. Conventional topical preparations may undergo removal from the skin surface because of washing, friction, evaporation, or other environmental factors. A formulation capable of undergoing *in-situ* gelation may potentially increase residence at the application site and provide more prolonged drug availability. Recent research in psoriasis has demonstrated that hydrogel-based delivery systems can improve drug retention and skin penetration compared with conventional formulations [13]. Yao et al. reported that a water-responsive gel increased skin retention and facilitated penetration of curcumin in a psoriasis model, illustrating the potential importance of formulation-mediated retention for topical treatment [13].

The present findings are also supported by recent psoriasis-specific thermosensitive hydrogel research. Chen et al. developed a thermosensitive hydrogel system for methotrexate delivery and demonstrated enhanced penetration through the stratum corneum together with prolonged skin retention in a psoriasis model [14]. Although the active drug and experimental system differed from the present tretinoin formulation, the study provides relevant evidence that thermosensitive hydrogel platforms can be used to modify topical drug deposition and release. Similarly, Flores-Pérez et al. developed a thermosensitive hydrogel containing nanostructured lipid carriers for topical delivery of anti-inflammatory phytochemicals in psoriasis and demonstrated enhanced formulation-dependent drug availability and skin retention [15].

Recent reviews have further emphasized the potential role of hydrogel-based systems in psoriasis because the thickened stratum corneum can restrict topical drug delivery [16]. Composite and biomaterial-based hydrogels have been investigated to overcome limitations related to drug loading, mechanical characteristics, penetration, and controlled release [16]. Lin et al. also highlighted the development of advanced topical delivery strategies, including nanocarriers and other systems designed to improve drug localization and penetration in psoriatic skin [17]. These findings provide a broader formulation context for the present study, although direct comparison of efficacy should not be made because the active ingredients, formulation compositions, experimental models, and endpoints differ substantially between studies.

The *in-vitro* anti-inflammatory evaluation of the optimized F3 formulation demonstrated a

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concentration-dependent increase in inhibition of protein denaturation. The inhibition increased from $28.60 \pm 0.74\%$ at $50 \mu\text{g/mL}$ to $88.40 \pm 0.41\%$ at $800 \mu\text{g/mL}$. The calculated IC_{50} of F3 was $132.8 \mu\text{g/mL}$. Diclofenac demonstrated greater inhibition at each corresponding concentration, with an IC_{50} of $104.5 \mu\text{g/mL}$. Thus, under the conditions of the present assay, F3 demonstrated measurable concentration-dependent anti-inflammatory activity, although its activity was lower than that of the reference drug.

The observed anti-inflammatory activity is consistent with the broader rationale for incorporating retinoids into advanced topical delivery systems. Erol et al. previously evaluated tazarotene-loaded thermosensitive *in-situ* gels for potential psoriasis management and reported physicochemical suitability together with anti-inflammatory and biocompatibility-related findings [4]. The present investigation extends this formulation concept to tretinoin. However, the protein-denaturation assay used in the present study represents an experimental *in-vitro* screening method and should not be interpreted as direct evidence of clinical anti-psoriatic efficacy. In particular, the present findings cannot establish therapeutic equivalence between tretinoin F3 and diclofenac or predict clinical outcomes.

The stability assessment demonstrated that F3 underwent only modest changes during the seven-day observation period under the tested storage conditions. At 25°C , pH changed from 6.48 to 6.46, gelation temperature changed from 35.0°C to 35.2°C , gelation time changed from 38 to 40 seconds, and viscosity changed from 5.58 to 5.60 cps. Under refrigeration at $4 \pm 1^{\circ}\text{C}$, the gelation temperature remained at approximately 35°C and gelation time remained at 38 seconds. At 37°C , somewhat greater changes were observed, including an increase in pH from 6.48 to 6.79 and viscosity from 5.58 to 5.97 cps. These changes were relatively small over the seven-day period, although the limited duration of the stability assessment must be considered when interpreting these findings.

Stability and rheological characteristics are important considerations in thermosensitive formulations because changes in polymer organization may influence gelation, viscosity, drug release, and application characteristics [7]. Recent work on P407-based thermosensitive systems has also demonstrated that formulation composition can influence gelation and physical properties [8]. In addition, recent *in-situ* hydrogel research has demonstrated the potential of Poloxamer 407-containing systems to provide prolonged release while maintaining a temperature-responsive formulation structure [18]. These studies support the importance of evaluating both short-term physical stability and formulation performance during development.

The recent literature also indicates that advanced hydrogel systems are increasingly being investigated specifically for psoriasis. Xiao et al. described the development of biomaterial-based hydrogels designed to overcome limitations associated with drug loading, release control, mechanical properties, and penetration through psoriatic skin [16]. Cao et al. similarly reviewed hydrogels as therapeutic platforms for inflammatory skin diseases and emphasized their potential for controlled drug delivery, tunable properties, and improved skin-barrier interaction [19]. Lai et al. further demonstrated that a borneol-embedded hydrogel could enhance topical delivery of a tyrosine kinase 2 inhibitor and improve drug permeability in experimental models of psoriasiform dermatitis [20]. These studies reinforce the growing interest in hydrogel-based topical delivery but also emphasize that formulation performance is highly dependent on the incorporated drug, polymeric matrix, penetration strategy, and experimental model.

Taken together, the present results indicate that polymer concentration and composition substantially influenced the physicochemical and release characteristics of tretinoin-loaded thermosensitive *in-situ* gels. Among the eight formulations, F3 demonstrated a combination of $35.0 \pm 1.0^{\circ}\text{C}$ gelation temperature, 38 ± 0.8 seconds gelation time, $98.52 \pm 0.42\%$ drug content, $98.0 \pm 0.5\%$ entrapment efficiency, and 94.80% cumulative drug release at 24 hours. The formulation also demonstrated concentration-dependent *in-vitro* anti-inflammatory activity and relatively small changes during seven days of stability assessment.

The findings should nevertheless be interpreted within the limitations of the experimental design. The study was primarily a formulation-development investigation and did not include animal efficacy studies, human skin permeation studies, long-term or formal accelerated stability testing, histopathological assessment, or clinical evaluation. Furthermore, the source data did not report inferential statistical comparisons or p-values between formulations; therefore, the observed numerical differences should not be interpreted as statistically significant differences. Future studies should investigate optimized F3 using appropriate *ex-vivo* skin permeation and retention models, *in-vivo* psoriasis models, longer-term stability protocols, and ultimately controlled clinical investigations. Such studies would help determine whether the favourable physicochemical and release characteristics observed in the present formulation translate into meaningful therapeutic performance.

Overall, the present study provides formulation-level evidence supporting F3 as an optimized candidate within the tested formulation series. Its combination of near-physiological gelation temperature, relatively rapid gel formation, high drug incorporation, sustained tretinoin release, measurable *in-vitro* anti-

inflammatory activity, and short-term physical stability provides a rational basis for further preclinical investigation. Importantly, these findings support further investigation, rather than establishing clinical efficacy of the formulation in patients with psoriasis.

Conclusion

The present study successfully developed and evaluated a tretinoin-loaded thermosensitive in situ gel using Poloxamer 407 and Poloxamer 188 for sustained topical drug delivery in psoriasis. Eight formulations were prepared and demonstrated acceptable physicochemical characteristics, with pH values ranging from 6.68 to 7.19. Among them, F3 showed a favourable overall profile, with a gelation temperature of $35.0 \pm 1.0^\circ\text{C}$, rapid gelation time of 38 ± 0.8 seconds, high drug content of $98.52 \pm 0.42\%$, and entrapment efficiency of $98.0 \pm 0.5\%$. It provided sustained tretinoin release, reaching 94.8% at 24 hours, and demonstrated concentration-dependent *in-vitro* anti-inflammatory activity. Short-term stability testing showed only minor changes under the tested storage conditions. Overall, the findings support F3 as a promising thermosensitive topical delivery system for tretinoin, although longer-term stability studies and appropriate *in-vivo* and clinical investigations are required to establish its therapeutic effectiveness and practical applicability.

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