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Formulation Optimisation and Evaluation of a Turmeric Extract–Incorporated Emulgel Using a Simplex Lattice Approach

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Abstract

Turmeric (*Curcuma longa* L.) possesses well-established anti-inflammatory, antioxidant, antimicrobial, and wound-healing properties; however, its topical application is limited by poor solubility, instability, and inadequate skin penetration. The present study aimed to develop and optimise a turmeric extract–incorporated emulgel using a simplex lattice experimental design to overcome these limitations and achieve an effective topical delivery system. Preformulation studies, including FTIR and DSC analyses, were carried out to characterise the extract and assess compatibility with formulation excipients. Solubility screening was performed to select suitable oil, surfactant, and co-surfactant for nanoemulsion development. Nanoemulsions were prepared and incorporated into an HPMC-based gel to form Nanoemulgels, which were optimised using Design-Expert® software with particle size and viscosity as response variables. The optimised formulation (F6) exhibited a mean particle size of approximately 379 nm with acceptable polydispersity and zeta potential, indicating good physical stability. The nanoemulgel showed skin-compatible pH, desirable rheological behaviour, uniform drug content, good spreadability, and sustained in-vitro drug release. Accelerated stability studies confirmed formulation stability over the study period. Overall, the findings demonstrate that simplex lattice-based optimisation is an effective approach for developing a stable and efficient turmeric extract nanoemulgel suitable for topical therapeutic and cosmetic applications.

Keywords: *Turmeric extract, Nanoemulgel, Simplex lattice design, Topical drug delivery, Physicochemical evaluation, In-vitro release.*

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INTRODUCTION

Topical drug delivery systems are widely preferred for managing localised skin disorders due to their ability to deliver therapeutic agents directly to the site of action, while minimising systemic exposure and associated side effects. Among various topical formulations, emulgels have gained increasing attention as they combine the advantages of both emulsions and gels, offering improved stability, enhanced spreadability, better patient acceptability, and the ability to incorporate lipophilic as well as hydrophilic drugs. Owing to these benefits, emulgels are considered an efficient and versatile dosage form for dermatological and cosmetic applications [1-3].

Turmeric (Curcuma longa L.) is a well-known medicinal plant with established anti-inflammatory, antioxidant, antimicrobial, and wound-healing properties, largely attributed to its curcuminoid content. However, the topical application of turmeric extract is limited by poor solubility, instability, and inconsistent skin penetration. Formulating turmeric extract into an emulgel system can address these limitations by improving its dispersion, stability, and bioavailability at the application site. Since the performance of emulgels depends strongly on the proportion of formulation components, a simplex lattice design approach was employed in this study to optimise the formulation systematically [4, 5]. This mixture design method enables efficient evaluation of component interactions and identification of an optimised formulation with desirable physicochemical properties. The present work, therefore, focuses on

the formulation optimisation and physicochemical evaluation of a turmeric extract–incorporated emulgels to develop a stable and effective topical delivery system.

MATERIALS AND METHODOLOGY

Materials

Turmeric (*Curcuma longa*) extract was obtained from Herb Sky Bio-tech Co. Ltd., China. Liquid paraffin oil was purchased from Moychem Pvt. Ltd. Methanol, ethanol, chloroform, acetone, potassium dihydrogen phosphate (KH_2PO_4), sodium chloride, HPMC K4, PEG-200, and Tween 80 were procured from Loba Chem Pvt. Ltd., Mumbai. All chemicals were of analytical grade, and double-distilled water was used throughout the study.

Physical Characterisation and Identification

Preformulation Studies

Turmeric (*Curcuma longa*) extract was subjected to preliminary physical examination for appearance, color, and organoleptic characteristics to confirm its identity and suitability for formulation development.

Fourier Transform Infrared (FTIR) Analysis

FTIR spectroscopy was performed to identify functional groups present in the turmeric extract and to assess extract–excipient compatibility. Samples were prepared using the KBr pellet method, and spectra were recorded over the range of 4000-400 cm^{-1} using an FTIR spectrometer (Shimadzu, Japan) [6].

Differential Scanning Calorimetry (DSC)

Thermal analysis of turmeric extract and selected excipients was carried out using a DSC instrument (Mettler DSC 1-Star System, Mettler-Toledo, Switzerland). Samples were sealed in perforated aluminum pans and heated at a rate of 10 °C/min over a temperature range of 30–350 °C under a nitrogen purge of 20 mL/min [7,8].

Extract–Excipient Compatibility Study

Compatibility between turmeric extract and formulation excipients (HPMC K4, liquid paraffin oil, Tween 80, and PEG-200) was evaluated using FTIR and DSC analyses. Physical mixtures were prepared in a 1:1 ratio, and their spectra and thermograms were compared with those of the pure extract and individual excipients to identify possible interactions [9,10].

Screening of Oil, Surfactant, and Co-surfactant (Solubility Study)

Solubility studies were conducted to select suitable formulation components. Excess turmeric extract was added to 5 mL of various oils (oleic acid, liquid paraffin oil, olive oil), surfactants (Tween 80, Span 20, Tween 20), and co-surfactants (PEG-200, ethanol, propylene glycol). The mixtures were vortexed for 15 min, equilibrated for 24 h, and centrifuged at 3000 rpm for 15 min. The supernatant was filtered, diluted with methanol, and analyzed at 415 nm using a UV–visible spectrophotometer. All experiments were performed in triplicate [11, 12].

Formulation of Nanoemulsion

Nanoemulsions were prepared using the selected oil, surfactant, and co-surfactant based on solubility studies. The oil phase containing turmeric extract was mixed with the aqueous phase containing surfactant and co-surfactant under continuous stirring to obtain a homogeneous nanoemulsion.

Preparation of Nanoemulgel

Nanoemulgel was prepared by incorporating the optimized nanoemulsion into a gel base. HPMC K4 (1% w/w) was dispersed in distilled water and allowed to hydrate completely. The prepared nanoemulsion was then gradually added to the gel base with continuous stirring to obtain a uniform Nanoemulgel.

Experimental Design and Optimization

A simplex lattice design was employed to optimize formulation variables. Independent variables included concentrations of oil, surfactant/co-surfactant mixture, and gelling agent, while particle size and viscosity were selected as response variables. Data were analyzed using Design-Expert® software, and optimized formulation composition was determined based on desirability criteria [13, 14].

Characterization of Nanoemulsion and Nanoemulgel

Prepared formulations were evaluated for physical appearance, droplet size, polydispersity index, zeta potential, surface morphology, pH, viscosity, drug content, and spreadability using standard analytical methods [15, 16].

In-Vitro Drug Release Study

In-vitro drug release studies of nanoemulgel formulations were carried out using a Franz diffusion cell with phosphate buffer saline (pH 7.4) as the receptor medium maintained at 37 ± 0.5 °C. Samples were withdrawn at predetermined intervals and analysed using a UV–visible spectrophotometer [17].

Stability Studies

Accelerated stability studies of the optimized nanoemulgel were conducted under specified temperature and humidity conditions. Samples were evaluated periodically for changes in pH, viscosity, and drug content [18].

RESULT AND DISCUSSION

Preformulation Studies

The pre-formulation studies of turmeric extract were performed; the ginger extract was found as yellow brown resinous amorphous powder with pungent characteristic taste of ginger.

FTIR Analysis

In Figure 01, the FTIR spectra of turmeric extract is given, which show the characteristic band at 3568.41 cm-1 (O-H stretching), 3082.21 cm-1 (CH2 methylene stretch), 1637.61 cm-1 (C=O stretch) 1414.81 cm-1 (C=C aromatic ring stretch), 1048.26 cm-1 (C-OH stretch CH2OH) and 700.03 cm-1 (Phenolic O-H bond).

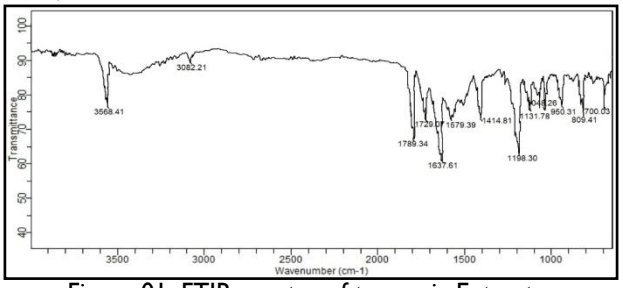

Figure 01: FTIR spectra of turmeric Extract

Differential Scanning Calorimetry

Differential Scanning Calorimetry (DSC) analysis of turmeric extract at a scanning rate of 10°C/min revealed a distinct melting endothermic peak at 159.39°C, as depicted in Figure 02. This peak indicates the transition from a semi-solid to a liquid state, showing the heat flow associated with this phase change. Furthermore, as the temperature increases, certain components of the plant extract may undergo decomposition, releasing energy in the process. This decomposition is evident on the DSC curve as an endothermic peak, corresponding to the heat absorbed during this specific thermal event.

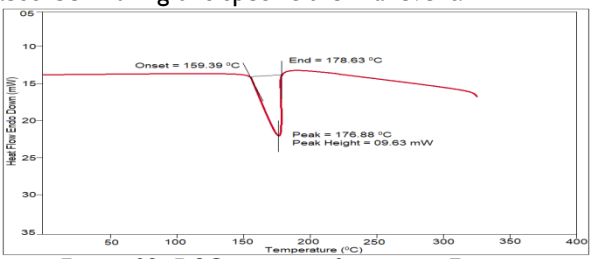

Figure 02: DSC spectra of turmeric Extract

Extract-Excipients Compatibility Study

FTIR Analysis

The FTIR spectra of turmeric extract and its physical mixture showed identical characteristic peaks corresponding to O–H, C–H, C=O, C=C, and C–O functional groups, with no significant shifts or new bands, confirming the chemical stability of the extract and its compatibility with formulation excipients (Figure 03).

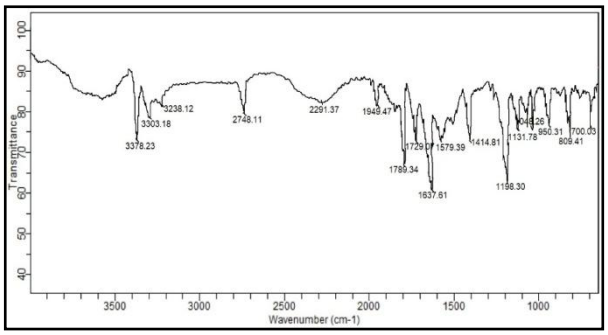

Figure 03: FTIR spectra of Turmeric Extract and Physical Mixture

Differential Scanning Calorimetry

The DSC thermogram of the turmeric extract–physical mixture showed a melting endotherm around 158–178 °C with no significant shift or new peaks, indicating no interaction between the extract and excipients and confirming their compatibility (Figure 04).

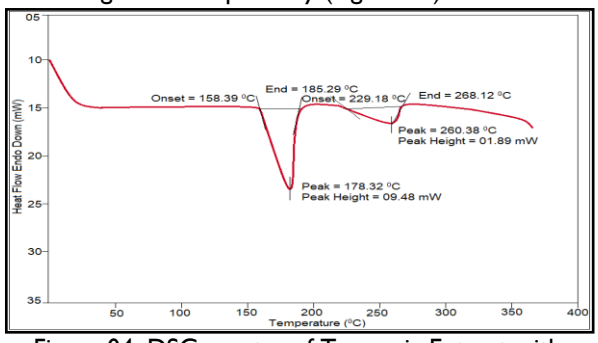

Figure 04: DSC spectra of Turmeric Extract with Physical Mixture

Screening of Oil, Surfactant and Co-surfactant (Solubility Study)

Screening of oils, surfactants and co-surfactants is based on their solubility profile for turmeric extract as shown in Table 1. The LPO was selected, oil, Tween 80 as surfactant and PEG-200 as co- surfactant.

Table 01: Solubility of turmeric extract

Name of Excipients	Solubility (mg/ml)
Liquid paraffin oil	34.12
Tween 80	37.02
PEG-200	35.58

Formulation and selection of Nanoemulsion and Nanoemulgel

On the basis of their visual observation, such as transparency and viscosity, 14 formulations were selected out as per a factorial design for preparing ginger extract-loaded nanoemulsion. For the preparation of nanoemulgel, HPMC K4 was used as gelling agent in a ratio 1.0% (gels made with a specified concentration range in the water).

Formulation Design

The two factors with lower, middle and upper design points in coded and un-coded. The ranges of responses Y1 and Y2 were 321-470 d.nm and 1421-

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1834 cps, respectively. All the responses observed for the nine formulations prepared were fitted to the main effect model, which was found as the best-fitted model for Y1 and Y2, using Design Expert® software. The values of R^2, SD and % CV are given in Table 2, along with the regression equation generated for each response. The results of ANOVA in Table 2, for the dependent variables, demonstrate that the model was significant for all the response variables. It was observed that independent variables X1, X2 and X3 had a positive effect on the entrapment efficiency and a desired particle size of nano-formulation i.e. nano-emulsion was achieved.

Model Assessment

After putting the data in Design Expert® software, the Fit summary applied to the data in that Main Effect Model was suggested by the software for all the responses. The statistical evaluation was performed by using ANOVA. Results are shown in Table 2. The

coefficients with more than one factor term in the regression equation represent interaction terms. It also shows that the relationship between factors and responses is not always linear. When more than one factor are changes simultaneously and used at different levels in a formulation, a factor can produce different degrees of responses.

Table 02: Results of Analysis of Variance for Measured Response (Particle Size and viscosity

Parameters	Results of Analysis of Variance for Measured Response (Particle Size)	Results of Analysis of Variance for Measured Response (Viscosity)
Model	Quadratic Model (Significant)	Quadratic Model (Significant)
Model p-value	0.045	0.039
Standard Deviation	7.82	7.19
Mean	77.67%	77.07%
CV	10.07%	10.39%
R^2	0.8179	0.8079
Adequate Precision	7.7072	7.6903
Regression Equation	Y1 = 764.63 X1 + 733.37 X2 + 643.37 X3 - 2789.60 X1 X2 – 2447.20 X1 X3 - 2477.87 X2 X3 +5494.40 X1 X2 X3	Y1 = 734.63 X1 + 723.37 X2 + 623.37 X3 - 2879.60 X1 X2 – 2437.20 X1 X3 - 2837.87 X2 X3 +5954.40 X1 X2 X3

Response Surface Plot Analysis

From the 3D response surface plot (Figure 5), the formulation exhibiting the smallest particle size was considered optimal. Among all design batches, F6—containing approximately 32% Smix and 2% liquid paraffin oil—showed the minimum particle size (352 nm) and was therefore selected as the optimized formulation. The response surface analysis and regression coefficients further revealed that nanoemulgel viscosity increased with higher concentrations of liquid paraffin oil and HPMC K4M, with no significant interaction or nonlinearity observed. Notably, HPMC K4M exerted a greater influence on viscosity compared to liquid paraffin oil.

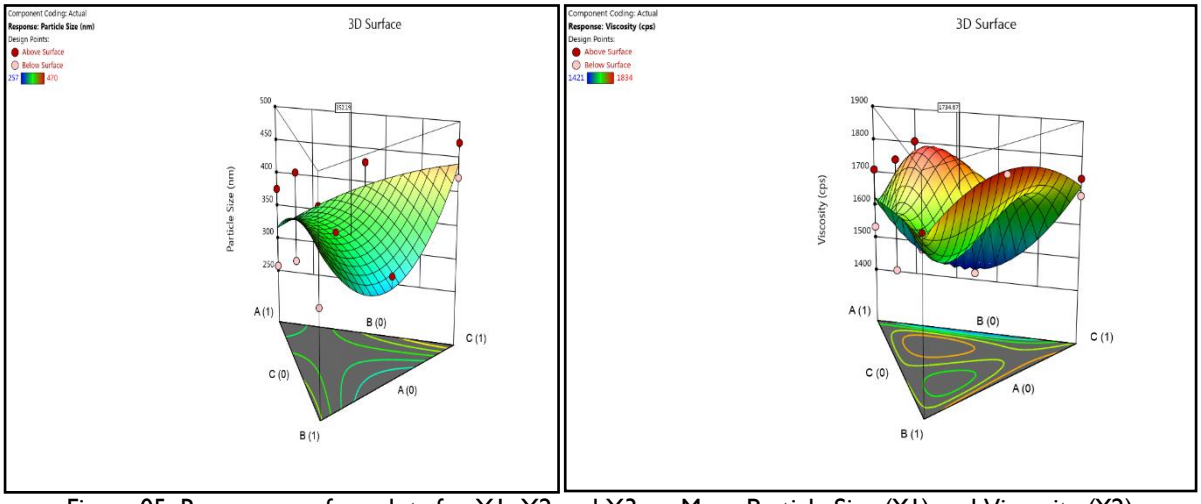

Figure 05: Response surface plots for X1, X2 and X3 on Mean Particle Size (Y1) and Viscosity (Y2)

Characterisation of Nanoemulsion

Physical characterization

All formulations are clear, transparent, and homogenous, and no grittiness and no clogs were found, and a suitable consistency was achieved.

Size Distribution, Zeta potential

Particle size strongly influences drug release and absorption, with smaller particles offering a larger surface area and improved bioavailability. The optimised formulation (F6) showed a mean particle size of 379 nm with a PDI of 0.412, indicating acceptable homogeneity (Figure 06). The nanoemulsion also exhibited a zeta potential of −22.3 mV, confirming good physical stability (Figure 06).

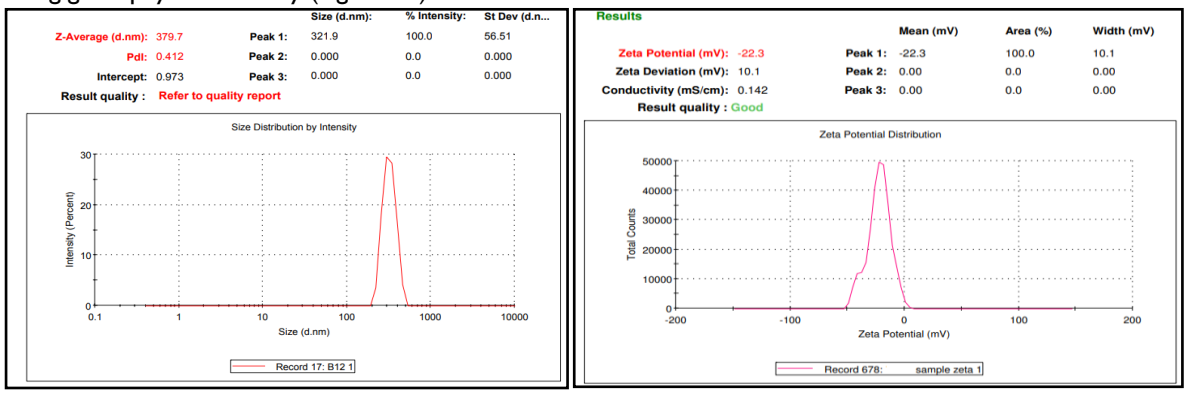

Figure 06: Particle size and Zeta potential of F6 formulation

Characterisation of Nanoemulsion Gel

pH and Viscosity Evaluation

The pH of the nanoemulsion (NE) and nanoemulgel formulations (F1–F14) ranged from 6.12–6.92 and 5.12–5.96, respectively, which lies within the physiological skin pH range, indicating suitability for topical application without irritation. Viscosity measurements using a Brookfield viscometer showed that all formulations exhibited shear-thinning behaviour, with viscosity decreasing as shear rate increased (Table 3). Among the formulations, F6 exhibited comparatively higher viscosity, indicating better consistency and spreadability for topical use.

Table 03: Characterisation of Nanoemulsion Gel

Formulation code	pH value of NE	pH value of NE gel	Viscosity (cps)
F1	6.92±0.02	5.53±0.03	1421±2.33
F2	6.54±0.03	5.96±0.07	1520±2.28
F3	6.55±0.04	5.63±0.04	1685±2.21
F4	6.98±0.01	5.76±0.01	1711±2.29
F5	6.12±0.03	5.30±0.03	1833±2.31
F6	6.93±0.02	5.93±0.05	1724±2.35
F7	6.45±0.01	5.94±0.02	1625±2.36
F8	6.57±0.04	5.60±0.04	1741±2.39
F9	6.25±0.06	5.67±0.07	1834±2.33
F10	6.83±0.03	5.12±0.01	1735±2.27
F11	6.56±0.02	5.58±0.05	1685±2.26
F12	6.48±0.04	5.36±0.03	1819±2.21
F13	6.29±0.05	5.94±0.02	1735±2.28
F14	6.69±0.03	5.15±0.03	1698±2.31

Drug Content of Nanoemulsion Gel and Spreadability

The drug content of the nanoemulgel formulations (F1–F14) ranged from 85.19% to 97.28%, indicating uniform and acceptable drug distribution across all batches. Spreadability values varied between 86.45% and 96.35%, demonstrating good spreading characteristics suitable for topical application. Among all formulations, F6 exhibited the highest drug content (97.28%) and maximum spreadability (96.35%), indicating optimal formulation performance (Table 4). Overall, all formulations met acceptable criteria for drug content and spreadability.

Table 04: Characterisation of Nanoemulsion Gel and Spreadability

Formulation code	Drug Content (%)	Spreadability (%)
F1	85.19±0.27%	88.18±1.10%
F2	86.91±0.29%	86.45±1.14%
F3	87.92±0.30%	87.36±1.16%
F4	89.38±0.31%	88.91±1.22%
F5	95.91±0.32%	93.21±1.25%
F6	97.28±0.26%	96.35±1.27%
F7	91.38±0.28%	90.89±1.29%
F8	92.47±0.32%	92.26±1.28%
F9	93.21±0.31%	91.65±1.32%
F10	90.38±0.30%	92.78±1.26%
F11	91.36±0.28%	88.89±1.24%
F12	88.38±0.29%	94.65±1.22%
F13	89.65±0.35%	91.45±1.29%
F14	89.35±0.39%	93.36±1.32%

In-vitro Release Study

In-vitro drug release studies of turmeric extract–loaded emulgels (F1–F14) were performed using a Franz diffusion cell in phosphate buffer saline (pH 7.4) at 37 °C. The cumulative drug release ranged from 82.47 ± 1.98% to 96.38 ± 2.96%. An initial burst release was observed, attributed to the small particle size and large surface area of the nanoemulgel, as well as rapid diffusion of drug from the outer gel matrix (Table5 and Figure 7).

Table 05: *In-vitro* release profile of nanoemulgel

Time (Min.)	nanoemulgel (F6)
0	0
60	24.49±1.36
120	48.42±2.41
180	54.89±1.69
240	69.98±2.32
300	93.29±2.56
360	96.38±2.96

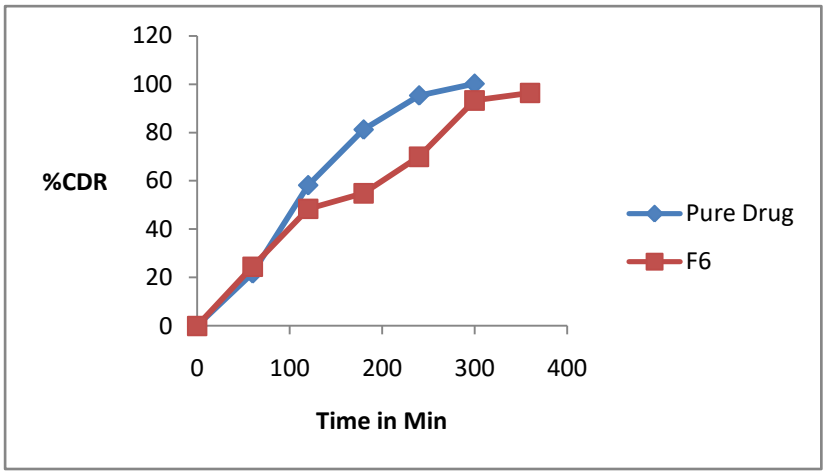

Figure 07: In-vitro drug release study of F6

Accelerated Stability Study

The optimised emulgel was subjected to stability studies, and the results are given in Table 6. Based on these results, it is revealed that Turmeric-loaded nanoemulgel(Formulation batch F6) was found to be a stable formulation at the given temperature and humidity conditions.

Table 06: Stability study of parameters of the optimised formulation (F6)

Parameters	Initial Month	1st Month	2nd Month	3rd Month
pH	5.93 ± 0.03	5.96 ± 0.04	5.83 ± 0.02	5.90 ± 0.03
Viscosity (cps)	1724 ± 2.31	1712 ± 2.28	1729 ± 2.33	1728 ± 2.30
Drug content (%)	97.28 ± 0.32	97.35 ± 0.35	97.39 ± 0.31	97.29 ± 0.39

CONCLUSION

In summary, the meticulous pre-formulation investigations, encompassing FTIR and DSC analyses, yielded essential insights into the physical and molecular attributes of turmeric extract. Compatibility examinations with excipients, followed by the formulation of nanoemulsion and nanoemulgel, demonstrated the viability of establishing a reliable delivery system for turmeric extract. The optimized formulation (F6) displayed positive features, including a mean particle size of 379.7 nm, a notable zeta potential, and sustained release characteristics. The all-encompassing assessment, covering pH, viscosity, drug content, and stability, collectively lays a strong foundation for developing a dependable and efficient delivery system for turmeric extract, with potential applications in both therapeutic and cosmetic formulations.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

ETHICAL APPROVAL

Not applicable

ETHICAL STATEMENT

The present study did not involve any experiments on humans or animals. Hence, ethical approval was not required.

AUTHOR CONTRIBUTION

Archana G. L.: Conceptualization, methodology, experimental work, data analysis, and manuscript preparation.

*K. Srisailam: Supervision, validation, and critical revision of the manuscript.

*M. Nagulu: Data interpretation, technical support, and final manuscript review.

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