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Nanostructured Lipid Carrier-Based Hydrogel of Anisomeles malabarica for Enhanced Topical Management of Psoriasis

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Abstract:	Psoriasis is a chronic immunity based inflammatory skin disorder characterized by hyperproliferation of skin layer on keratinocytes and dysregulated immune responses, leading to significant impairment in patient quality of life. Conventional topical therapies are very limited by poor skin penetration, systemic toxicity, and reduced patient compliance. In the present study, a nanostructured lipid carrier (NLC)-based hydrogel incorporating Anisomeles malabarica leaf extract was developed to enhance topical delivery and therapeutic efficacy against psoriasis. The ethanolic extract of Anisomeles malabarica was prepared by cold maceration technique and it's characterized by using phytochemical screening, Fourier transform infrared spectroscopy (FTIR), and gas chromatography–mass spectrometry (GC–MS), confirming the presence of bioactive constituents including flavonoids, terpenoids, and phenolic compounds. NLCs were formulated using hot homogenization followed by ultrasonication and subsequently incorporated into a Carbopol-based hydrogel. The developed formulation was evaluating such as particle size, zeta potential, viscosity, spreadability, drug content, and stability. In vitro release studies demonstrated sustained and controlled release behaviour, indicating better activity on topical delivery and prolonged therapeutic effect. Furthermore, molecular docking analysis reflects the strong binding affinity,of anisomelic acid toward cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX),,suggesting the dual activity of anti-inflammatory and potential therapeutic activity that,relevance in psoriasis management. The optimized process of NLC-based hydrogel exhibited improve in the physicochemical stability, enhanced the permeation characteristics, and targeted drug delivery potency. These findings suggest that Anisomeles malabarica-loaded NLC hydrogel represents a promising, effective, and safer alternative for already existed topical psoriasis therapy, warranting further preclinical and clinical investigations best future Implemented Drug System for therapeutic activity,K

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Cover letter
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04.05.2026

RESPECTED REVIEWERS AND EDITORS,

We wish to submit an original research article entitled **"Development and Evaluation of Anisomeles malabarica-Loaded Nanostructured Lipid Carrier (NLC) Hydrogel for Enhanced Topical Delivery in Psoriasis Management"** for consideration in your esteemed journal.

We confirm that this work is original and has not been published elsewhere, nor is it currently under consideration for publication in any other journal.

In this study, we report the development of a nanotechnology-based topical drug delivery system incorporating *Anisomeles malabarica* extract into nanostructured lipid carriers (NLCs), further embedded into a hydrogel matrix. The formulation was comprehensively characterized through physicochemical evaluation, including particle size, zeta potential, entrapment efficiency, viscosity, spreadability, and stability. Advanced analytical techniques such as FTIR and GC–MS were employed to confirm the presence of bioactive phytoconstituents. The optimized formulation demonstrated nanoscale size distribution, high entrapment efficiency, and sustained drug release following Higuchi kinetics. Additionally, antimicrobial activity against *Staphylococcus aureus* was observed.

Furthermore, molecular docking studies revealed that anisomelic acid exhibits strong binding affinity toward key inflammatory targets, COX-2 and 5-LOX, supporting a dual anti-inflammatory mechanism relevant to psoriasis pathogenesis. The integration of phytotherapy with nanostructured lipid carriers provides both mechanistic and therapeutic justification for enhanced efficacy.

This work is significant as it addresses the major limitations of conventional psoriasis therapy, including poor skin penetration and systemic side effects, by introducing a stable, controlled, and targeted topical delivery system. The study establishes a strong correlation between phytochemical composition, nanocarrier characteristics, and therapeutic performance.

We believe this manuscript is appropriate for publication in your journal as it aligns with the focus on novel drug delivery systems, nanotechnology-based therapeutics, and translational pharmaceutical research. The multidisciplinary approach integrating phytochemistry, nanotechnology, and computational biology will be of considerable interest to the journal's readership.

The novelty of this work lies in the development of a dual-function NLC-based hydrogel system combined with mechanistic validation through molecular docking, demonstrating simultaneous modulation of COX-2 and 5-LOX inflammatory pathways using a natural bioactive compound.

We have no conflicts of interest to disclose.

Please address all correspondence concerning this manuscript to me at sreenathmithwinner@gmail.com.

Thank you for your time and consideration.

Sincerely,

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Graphical abstract

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Anisomeles malabarica–Loaded Nanostructured Lipid Carrier (NLC) Hydrogel: A Promising Topical Nanotherapeutic Approach for Psoriasis Management

1. PLANT SOURCE & EXTRACTION

Anisomeles malabarica (Leaf)

Ethanolic Extract

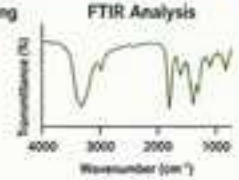
(Cold Maceration)

2. PHYTOCHEMICAL CHARACTERIZATION

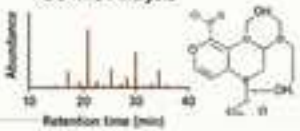
Phytochemical Screening

- ✓ Flavonoids
- ✓ Terpenoids
- ✓ Phenolics
- ✓ Tannins
- ✓ Saponins
- ✓ Alkaloids

FTIR Analysis



GC–MS Analysis



Bioactive constituents: Flavonoids, Terpenoids, Phenolic compounds, Anisomelic acid

3. FORMULATION OF NLC & HYDROGEL

NLC Preparation (Hot homogenization + Ultrasonication)

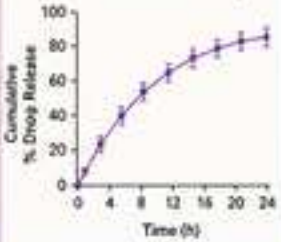
Incorporation into Carbopol Hydrogel

NLC Structure

4. EVALUATION OF NLC HYDROGEL

- Particle size
- Zeta potential
- Viscosity
- Spreadability
- Drug content
- Stability studies

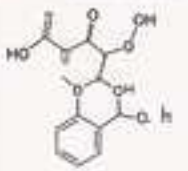
In vitro Release Study

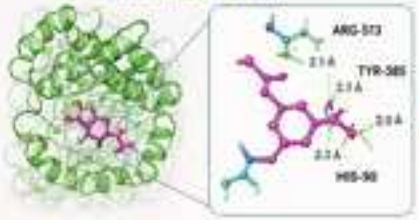


- ✓ Sustained & controlled release
- ✓ Prolonged therapeutic effect
- ✓ Enhanced topical delivery

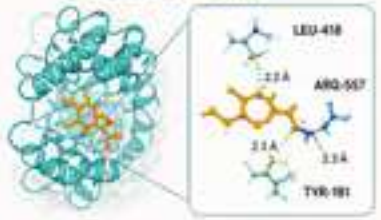
5. MOLECULAR DOCKING STUDY

Anisomelic acid





Binding Affinity: -9.2 kcal/mol



Binding Affinity: -9.2 kcal/mol

Strong binding affinity towards COX-2 and 5-LOX → Dual anti-inflammatory activity
Potential therapeutic relevance in psoriasis management

6. THERAPEUTIC BENEFIT IN PSORIASIS

Reduce inflammation • Relieves scaling, redness & itching • Improves quality of life

7. ADVANTAGES OF NLC HYDROGEL

- Improved physicochemical stability
- Enhanced skin permeation
- Targeted drug delivery
- Sustained release & prolonged therapeutic effect
- Safer alternative with better patient compliance

8. CONCLUSION

Anisomeles malabarica-loaded NLC hydrogel demonstrates enhanced stability, controlled release, strong anti-inflammatory potential, and superior topical delivery, making it a promising, effective, and **safer alternative for psoriasis therapy.**

9. FUTURE PERSPECTIVE

- Preclinical evaluation
- Clinical investigations
- Regulatory approval
- Best future implemented drug system

An Innovative & Promising Nanotherapeutic System for Effective & Safer Psoriasis Management

Declaration of interests

☒The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Nanostructured Lipid Carrier-Based Hydrogel of *Anisomeles malabarica* for Enhanced Topical Management of Psoriasis

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ABSTRACT

Psoriasis is a chronic immunity based inflammatory skin disorder characterized by hyperproliferation of skin layer on keratinocytes and dysregulated immune responses, leading to significant impairment in patient quality of life. Conventional topical therapies are very limited by poor skin penetration, systemic toxicity, and reduced patient compliance. In the present study, a nanostructured lipid carrier (NLC)-based hydrogel incorporating Anisomeles malabarica leaf extract was developed to enhance topical delivery and therapeutic efficacy against psoriasis. The ethanolic extract of Anisomeles malabarica was prepared by cold maceration technique and it's characterized by using phytochemical screening, Fourier transform infrared spectroscopy (FTIR), and gas chromatography–mass spectrometry (GC–MS), confirming the presence of bioactive constituents including flavonoids, terpenoids, and phenolic compounds. NLCs were formulated using hot homogenization followed by ultrasonication and subsequently incorporated into a Carbopol-based hydrogel. The developed formulation was evaluating such as particle size, zeta potential, viscosity, spreadability, drug content, and stability. In vitro release studies demonstrated sustained and controlled release behaviour, indicating better activity on topical delivery and prolonged therapeutic effect. Furthermore, molecular docking analysis reflects the strong binding affinity of anisomelic acid toward cyclooxygenase-2 (COX-2) and 5-lipoxygenase (5-LOX), suggesting the dual activity of anti-inflammatory and potential therapeutic activity that relevance in psoriasis management. The optimized process of NLC-based hydrogel exhibited

improve in the physicochemical stability, enhanced the permeation characteristics, and targeted drug delivery potency. These findings suggest that Anisomeles malabarica-loaded NLC hydrogel represents a promising, effective, and safer alternative for already existed topical psoriasis therapy, warranting further preclinical and clinical investigations best future Implemented Drug System for therapeutic activity

Keywords:
Anisomeles malabarica, Psoriasis, Nanostructured Lipid Carriers (NLC), Hydrogel, Topical drug delivery, Molecular docking.

1. INTRODUCTION

Psoriasis is a persistent inflammatory skin condition affect by the immune system, is distinguished by an accelerated proliferation of keratinocytes, atypical differentiation, and the presence of inflammatory mediators. Cases on roughly over 2–3% of the worldwide population, psoriasis substantially suppresses the quality of life on people from society for those afflicted. the development on stems from intricate interactions involving immune cells and cytokines like TNF-α, IL-17, and IL-23, and oxidative stress pathways are l ultimately resulting in the formation of red, scaly plaques on the skin.

Traditional treatment methods, encompassing the corticosteroids, vitamin D analogues, and systemic immunosuppressants, present with various drawbacks, including inadequate skin penetration, systemic toxicity, long-term adverse effects, and hide the patient adherence. These limitations under focus on the necessity for safer conditions, more efficacious, and more targeted drug delivery systems, especially in topical application

Nanotechnology-based drug delivery systems have recently become a focus of interest in dermatological applications over past years. Nanostructured Lipid Carriers in particular, present several advantages, it including improved drug loading capacity, enhances the stability, controlled release profiles, and superior on skin permeation action its result of their nanoscale dimensions and lipid compatibility with the stratum corneum. Furthermore, the incorporation of NLCs into hydrogel systems improves topical delivery by enhancing spreadability, hydration, and the duration of drug retention at the application site.

Anisomeles malabarica, a plant with medicinal properties, is commonly used in traditional medicine in Indian system of medicine. It's as anti-inflammatory, antioxidant, and antimicrobial effects are due to its rich phytochemical profile, which includes flavonoids, terpenoids, and phenolic compounds. These active ingredients have shown promise in affecting inflammatory processes related to psoriasis therapy.

Therefore, this study focusses towards to create and assess a hydrogel system with nanoparticles that contains Anisomeles malabarica extract, using nanostructured lipid carriers. This formulation is designed to improve skin absorption, provide the controlled drug release, and increase therapeutic effectiveness while reducing side effects. The developed hydrogel was

carefully evaluated for its physical and chemical properties, the drug release patterns, and stability to determine its suitability as a new topical treatment for psoriasis.

2. MATERIALS AND METHODS

2.1 COLLECTION AND AUTHENTICATION OF PLANT MATERIAL

Fresh plant material of *Anisomeles malabarica* was collected from a North Tamil Nadu geographical location of Arcot area. The plant was identified and authenticated by a qualified by the botanist. The collected material was washed with distilled water to remove dirt and dried under shade at room temperature. The dried plant material was then coarsely powdered with feathery in nature and stored in an airtight container for further use.

2.2 PREPARATION OF PLANT EXTRACT (COLD MACERATION)

The powdered plant material was subjected to cold maceration using a hydroalcoholic solvent system (ethanol: water, 70:30 v/v). Powdered drug was soaked in a solvent and kept for 72 hours with occasional stirring. The extract was filtered using muslin cloth followed by Whatman filter paper. The filtrate was concentrated under reduced pressure using a rotary evaporator and dried to obtain a crude extract. The extract was stored at 4°C until further use.

2.3 PHYTOCHEMICAL SCREENING

Preliminary phytochemical screening of the extract was performed using standard qualitative tests:

Table 1. Preliminary phytochemical screening of the extract was performed using standard qualitative tests

Phytoconstituent	Test	Observation
Alkaloids	Mayer's test	Cream precipitate
Flavonoids	Shinoda test	Pink/red colour
Phenols	Ferric chloride test	Blue-green colour
Tannins	Gelatin test	White precipitate
Glycosides	Keller kiliani test	Reddish brown ring formation
Terpenoids	Salkowski test	Reddish-brown layer

These tests confirmed the presence of bioactive compounds responsible for therapeutic activity.

3. FTIR SPECTRAL ANALYSIS OF ANISOMELES MALABARICA PLANT EXTRACT

Fourier Transform Infrared spectroscopy (FTIR) was used to identify the functional groups in the powdered extract of Anisomeles malabarica plant. The analysis was done using an FTIR spectrophotometer, covering the far-infrared, mid-infrared and near-infrared range of 4000–10 cm^{-1}. the sample was prepared and the dried polyherbal powder was finely ground with spectroscopic grade potassium bromide using the KBr pellet based method. This mixture was then compressed under high pressure to create a transparent pellet of sample . Then the spectrum was recorded at room temperature. The FTIR analysis was performed at IIT SAIF (Sophisticated Analytical Instrumentation Facility) using standard operating conditions.

4. GC–MS ANALYSIS OF *MALABARICA* PLANT EXTRACT

GC–MS analysis of a *Anisomeles malabarica* plant extract was carried out using an Agilent 8890 Gas Chromatograph coupled with Agilent 5977B Mass Selective Detector (MSD). Separation was achieved using an HP-5ms Ultra Inert capillary column (30 m × 0.25 mm × 0.25 µm) consisting of 5% phenyl and 95% dimethylpolysiloxane as the stationary phase.

Helium (99.999% purity) was used as the carrier gas (mobile phase) at a constant flow rate of 1.2 mL/min. The injection volume was 1 µL in split mode (15:1) with injector temperature maintained at 250°C.

The oven temperature program was set initially at 75°C (0.5 min hold), ramped at 5°C/min to 180°C (3 min hold), and further increased to 300°C (5 min hold). The total run time was 53.5 min. Mass spectrometric detection was performed using electron ionization (EI) mode at 70 eV with ion source temperature 230°C, quadrupole temperature 150°C, and transfer line temperature 280°C. The mass spectra were recorded in the m/z range of 50–600.

Sample Preparation

Dried Leaves of *Anisomeles malabarica* plant material was finely powdered using a mortar and pestle, approximately 10 g of powdered sample was extracted using cold maceration of ethanol (70:30 v/v) for 48 hours. The extract was filtered using Whatman No.1 filter paper and concentrated under reduced pressure using a rotary evaporator. The concentrated extract was reconstituted in HPLC-grade methanol and filtered through 0.45 µm syringe filter prior to GC–MS analysis.

Table 2. Conditions of GCMS

Parameter	**Condition**
Instrument	Agilent 8890 GC + 5977B MSD
Column	HP-5ms Ultra Inert (30 m × 0.25 mm × 0.25 µm)
Carrier Gas	Helium
Flow Rate	1.2 mL/min
Injection Volume	1 µL
Split Ratio	15:1
Injector Temp	250°C
Ionization Mode	EI (70 eV)
Mass Range	50–600 m/z

Transfer Line	280°C
Run Time	53.5 min

6. CHARECTERIZATION OF NLC BASED EMBEDDED HYDROGEL

6.1 Particle Size Analysis

Dynamic Light Scattering (DLS) was used to determine the size and poly-dispersity index (PDI) of the prepared Anisomeles malabarica NLC based embedded hydrogel. The prepared Anisomeles malabarica NLC based embedded hydrogel was suitably diluted with distilled water and analysed at 25°C. DLS measures the change in intensity of light that is scattered by the particles undergoing Brownian motion, thereby determining the hydrodynamic diameter of the nanoparticles. The average particle size is represented in nanometres.

6.2 Zeta Potential

Electrophoretic light scattering mobility was used to measure zeta potential to find out the surface charge and stability of the nanoparticles. The Anisomeles malabarica NLC in sample of embedded hydrogel was diluted properly and placed in a zeta potential cell. The zeta sizer was used to analyze, in which the velocity of charged particles when an electric field was applied was determined, and the values of zeta potential were taken in millivolts (mV).

6.3 Scanning Electron Microscopy (SEM)

The formulation was subjected to SEM analysis to assess surface morphology and particle structure. The dried specimen of Anisomeles malabarica NLC was attached to a metal stub with the help of the double-sided adhesive tape, and it was covered with a layer of gold by means of a sputter coater. The sample was then viewed under SEM to examine surface and shape of particles by magnification of 4000X-5000X, Range of 10 μm.

6.4 Transmission Electron Microscopy (TEM)

Transmission Electron Microscopy (TEM) was used to analyze the formulation's morphology and internal structure of the nanoparticles. A tiny portion of diluted, Anisomeles malabarica NLC dispersion was spread on a carbon-coated copper grid and left to dry. A negative staining with phosphotungstic acid was then done on the sample to increase contrast. TEM was used to view the prepared grid to determine the size, shape and distribution of the nanoparticles.

6.5 pH Measurement

The pH of the Anisomeles malabarica NLC embedded hydrogel formulation was measured using a calibrated digital pH meter at room temperature. About 1 g of the formulation was dispersed in 10 mL of distilled water and allowed to stand for equilibration. The electrode was immersed in the sample, and the pH was recorded at room temperature. This test is done to determine and ensure that the formulation's pH and skin pH are same, to prevent skin irritability.

7 6.6 Percentage Yield and Viscosity

Percentage yield was calculated to evaluate the efficiency of the Anisomeles malabarica NLC embedded hydrogel formulation. It was calculated by dividing the practical yield of the formulation prepared by the theoretical yield and multiplying it with 100 by the formula: Percentage yield = (Practical yield / Theoretical yield) × 100.

Brookfield viscometer was used to measure the viscosity of the formulation. A suitable sample was collected in a beaker and the spindle of interest was placed in the formulation. This was done at a given rotational speed (rpm) and temperature and the viscosity was measured in centipoise (cP).

6.7 Spreadability

The slip and drag method were used to determine the spreadability of the Anisomeles malabarica NLC embedded hydrogel, which was expressed in gm·cm². It is measured by placing a fixed amount of prepared formulation between two clean glass slides. A known weight was placed on the upper slide to enable uniform spreading. The spread formulation was measured at a given time in terms of diameter.

Spreadability was determined by dividing the weight attached to the upper slide by the length moved by the slide times the length of the slide by the time taken. **$S = (M \times L)/ T$.**

6.8 Homogeneity

To ensure that the formulation was even, devoid of lumps and is smooth, a small quantity of the formulation was rubbed between the thumb and the index finger. Visual assessment was also done for lumps, phase separation and syneresis in order to determine homogeneity.

6.9 . In Vitro Drug Diffusion Study

To measure cumulative drug released, in vitro drug release was evaluated by a diffusion cell system over a 420-minute period and the samples measured spectrophotometrically.

7.0 Entrapment Efficiency

Entrapment efficiency analysis was performed on the formulation to ascertain the quantity of drug entrapped in the nanostructured lipid carriers. The Anisomeles malabarica NLC preparation was centrifuged to differentiate the free (unentrapped) drug and the entrapped drug. Free drug in the supernatant was collected and subjected to usual analysis technique. Standard formula was then used to calculate the entrapment efficiency.

$$\%EE = \frac{\text{Total Drug Added} - \text{Free (Unentrapped) Drug}}{\text{Total Drug Added}} \times 100$$

7.1. **Zone of Inhibition:**

The antimicrobial activity of the embedded hydrogel on the Staphylococcus aureus was evaluated by the agar diffusion technique using the Anisomeles malabarica NLC embedded hydrogel. Nutrient agar plates were sterilized and inoculated uniformly with a standard bacterial suspension. A measured amount of the test formulation was added into the wells, and an appropriate control was maintained. The plates were incubated at 37 o C and left to incubate 24 hours. The incubation of the zone of inhibition around the wells was measured in millimetres using a calibrated ruler that was used to measure the antimicrobial activity of the formulation.

7.8 PREPARATION OF NANOSTRUCTURED LIPID CARRIERS (NLC):

The nanostructured lipid carrier (NLC) suspension was developed by incorporating a mixture of solid lipid (glycerol monostearate) and liquid lipid (caprylic triglyceride) to create the lipid backbone. Anisomeles malabarica extract was incorporated as the active component. To stabilize the system, poloxamer 188 was used as a surfactant and soy lecithin as a co-surfactant respectively, and distilled water was used as a continuous aqueous phase. The mixture was then ultra sonicated to reduce particle size, and cooled to form stable NLC.

TABLE 3: Preparation of NLC DISPERSION (250 mg)

Component	Amount (mg)	% w/w of total	Purpose
Glyceryl Monostearate	92.1	36.84%	Solid lipid (matrix)
Caprylic triglyceride (Miglyol 812)	39.5	15.79%	Liquid lipid (matrix modifier)
Anisomeles malabarica extract	19.7	7.89%	Active (herbal antioxidant)
Poloxamer 188 (surfactant)	39.5	15.79%	Steric stabilizer
Soy lecithin (emulsifier)	6.6	2.63%	Co-surfactant
Distilled water (continuous phase)	68.4	27.37%	Aqueous phase

7.9 PREPARATION OF NLC- EMBEDDED HYDROGEL:

The optimized NLC dispersion was placed in a gel matrix with Carbopol 974P and HPMC as gelling agents to prepare the NLC-based hydrogel. Glycerine was incorporated with continuous stirring, as a humectant to enhance skin moisturization and phenoxyethanol served as a preservative. To adjust pH to 6.0 to 6.7 and form gels, triethanolamine (TEA) was employed, and the vehicle was distilled water to complete the formulation.

TABLE 4: Preparation NLC BASED EMBEDDED HYDROGEL (100g)

Component	Amount (g)	% w/w of hydrogel	Purpose
NLC dispersion (prepared above)	0.10	0.10%	Encapsulated active
Carbopol 974P	0.00075	0.00075 %	Gelling agent
HPMC	0.00075	0.00075 %	Secondary polymer
Glycerine	4.00	4.00%	Humectant / skin feel
Propylene glycol	5.00	5.00 %	Preservative, Permeation enhancer
Phenoxyethanol	0.50	0.50%	Microbial control
TEA (Triethanolamine)	0.20–0.60	—	Neutralizer to pH 6.0–6.7
Distilled water	91.30	91.30 %	Vehicle

7.10. MOLECULAR DOCKING ANALYSIS OF ANISOMELIC ACID

a. Protein Validation:

COX-2 of chain (5KCI) and 5-LOX of chain (6NCF) structures were validated through the method of Ramachandran plots. Most of the residues fall in favoured regions of amino acids like glycine residues are flexible but allowed, and proline or pre-proline residues occupy proper acceptable regions. No significant structural errors are founded, then we confirming suitability for docking.

b. Docking with COX-2 (5KCI):

Anisomelic acid binds deep with active site, it can be stabilized by a hydrogen bond with Asn382, salt bridges with His207 and His386, and a hydrophobic contact with Val291. The best binding energy was found to be −8.7 kcal/mol, stronger than celecoxib (−8.2 kcal/mol). Key interactions are Arg120, Tyr355, Tyr385, Ser530, and Val349, contributing towards the

competitive inhibition of prostaglandin synthesis, which impels anti-inflammatory and analgesic effects.

c. Docking with 5-LOX (6NCF):

Anisomelic acid is superior phytochemical present in this plant it has shown strong binding affinity toward the allosteric pocket of 5-lipoxygenase (5-LOX), with a binding energy of −8.1 kcal/mol, which was superior to the standard 5-LOX inhibitor zileuton (−7.6 kcal/mol). The ligand binding was stabilized through hydrophobic bond interactions with Val107 and Val110, along with hydrogen bond formation involving Val110. Additionally, salt bridge forms the interactions with Arg101 and Glu134 further it can enhance binding stability.

Key catalytic residues are His367, His372, His550, and Ile673 were also involved in ligand stabilization within the binding pocket.

These interactions suggest that anisomelic acid binds to the allosteric site and stabilizes 5-LOX in an inactive conformation, thereby inhibiting leukotriene biosynthesis activity. Since leukotrienes play an important role in inflammatory skin disorders it can including psoriasis, inhibition of 5-LOX may contribute to reduced inflammatory responses. This result can support the potential of anisomelic acid as a promising phytochemical candidate for incorporation into nanostructured hydrogel formulations for topical psoriasis treatment.

d. Dual Inhibition Implication:

The ligand demonstrates potential activity of dual activity of COX-2/5-LOX inhibition, targeting both prostaglandin and leukotriene pathways. This suggests a synergistic anti-inflammatory effect, comparable to combination therapy with NSAID + LOX inhibitor, achieved with a single natural compound which can best for psoriasis treatment or therapeutic effect.

8 DESIGN EXPERT:

A factorial Design of Experiments was conducted using software of Stat-Ease Design-Expert to optimize topical gel formulation. Independent variables that included propylene glycol (A: 1-2 gm), Carbopol 974P (B: 1.1-1.6 gm), and triethanolamine (C: 1.3-1.9 gm), with responses measured as preservative content (R1, gm), gelling agent content (R2, gm), and pH adjuster probability (R3). Experimental conduct with proper runs generated response surface models experiments, including linear value for R1 and two-factor interaction (2FI) for R2

Stat-Ease Design-Expert software analysing a Design of Experiments (DoE) study for topical gel formulation optimization. Upcoming three factors are focused, A (propylene glycol, gm), B (Carbopol 974P, gm), and C (triethanolamine, gm), with responses R1 (preservative, gm), R2 (gelling agent, gm), and R3 (pH adjuster, analysed via logistic regression). This study shows the typical pharmaceutical DoE approach to verify the factor effects on formulation attributes

like preservative content, viscosity (gelling), and pH adjustment which make major role in formulation are to be selected. DoE enables systematic evaluation on multiple variables of independent and interactions with fewer runs than one-factor-at-a-time methods, aligning with Quality by Design (QbD) principles in pharma research.

RESULTS:

9. PHYTOCHEMICAL SCREENING

Table 5: Result of Phytochemical Screening

S. NO.	PHYTOCONSTITUENT	TEST PERFORMED	PRESENCE/ABSENCE (+ / –)
1	ALKALOIDS	DRAGENDORFF'S TEST	+
2	GLYCOSIDES	KELLER–KILLIANI TEST	+
3	FLAVONOIDS	SHINODA TEST	+
4	PHENOLIC COMPOUNDS	FERRIC CHLORIDE TEST	+
5	TANNINS	GELATIN TEST	+
6	TERPENOIDS	SALKOWSKI TEST	+

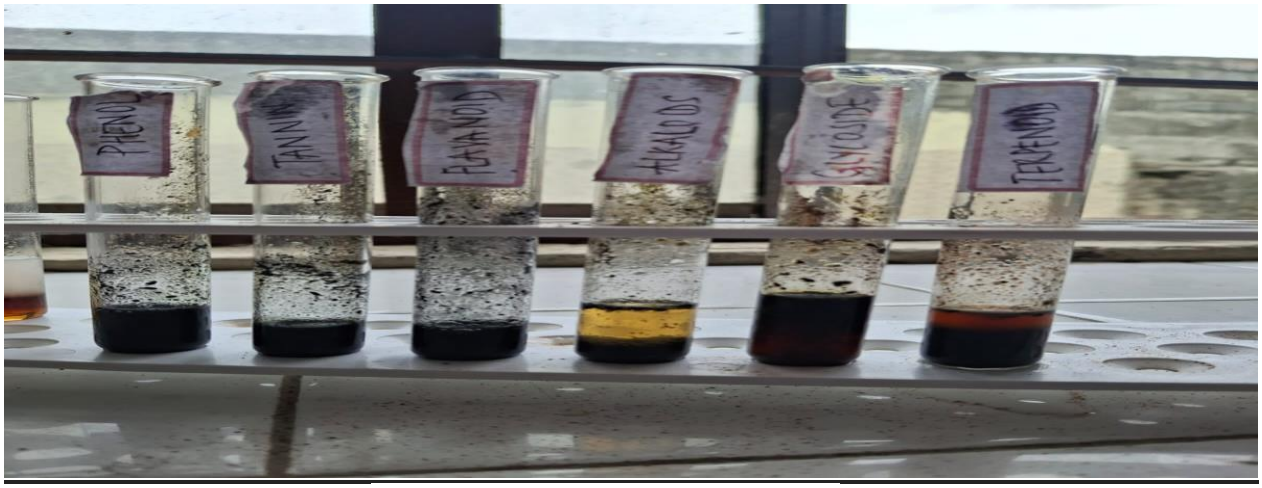

Figure 1. Phytochemical screening

9.1 FTIR SPECTRAL ANALYSIS OF *Anisomeles malabarica* POWDERED EXTRACT:

The full-range FTIR spectrum was chosen for comprehensive interpretation due to its superior resolution and detailed interpretation of Psoriasis specific and significant functional groups.

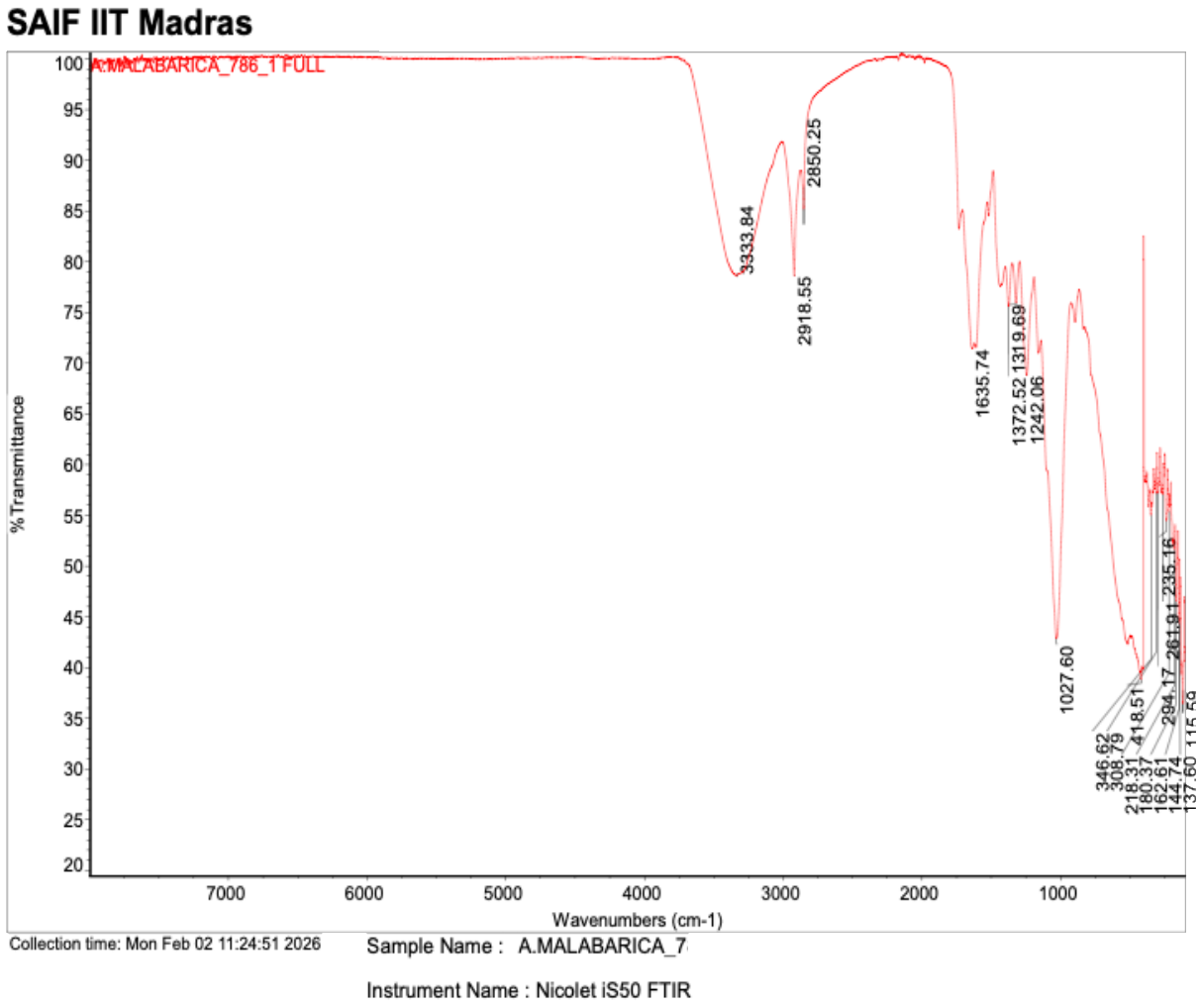

Figure no 25. FTIR Spectrum Showing Functional Group Identification in the Ethanolic Extract of *Anisomeles malabarica*

Table 6. FTIR Spectrum Showing Functional Group Identification in the Ethanolic Extract of *Anisomeles malabarica*

WAVENUMBER	FUNCTIONAL GROUP	BOND TYPE	ROLE IN PSORIASIS MANAGEMENT
3333.84 cm^{-1}	Hydroxyl	O–H stretching	Antioxidant, Reduction of ROS and eliminates keratinocyte hyperproliferation behaviour
2918.55 cm^{-1}	Alkane	C–H asymmetric stretch	Barrier protection activity and enhanced skin permeation

2850.25 cm^{-1}	Alkane	C–H symmetric stretch	Barrier protection activity, Reduces dryness and scaling
1733.59 cm^{-1}	Ester carbonyl	C=O Stretching	Potent Anti-inflammatory activity
1635.74 cm^{-1}	Carbonyl/aromatic group	C=C stretching	Anti-inflammatory activity by inhibiting COX, LOX pathways
1519.75 cm^{-1}	Aromatic ring	C=C stretching	Anti-inflammatory activity by suppressing NF-κB & cytokines (TNF-α, IL-17).
1327.52 cm^{-1}	Phenolic / amine	C–N stretching vibrations	Anti-inflammatory signalling modulation.
1242.06 cm^{-1}	Phenol / ester	C-O stretching	Enhanced drug stability and activity
1160.48 cm^{-1}	Secondary alcohol	C-O stretching	Increased solubility and enhanced interaction with skin proteins
1027.60 cm^{-1}	Ether / glycoside	C–O-C stretching vibrations	Enhancing bioavailability and improving sustained release

The FTIR spectrum of the Anisomeles malabarica powdered extract exhibited distinct absorption peaks corresponding to various different types functional groups of bioactive phytoconstituents in our formulation sample. Some of the peaks involved and their evidence in terms of Psoriasis management include:

1. A broad absorption band observed at **3333.84 cm^{-1}** is attributed to O–H stretching vibrations, indicating the presence of hydrogen bonded phenolic compounds and alcohols , which are may relates the action proportional to the antioxidant, reduction of ROS and eliminates keratinocyte hyperproliferation behaviour.
2. The peaks at **2918.55 cm^{-1}** and **2850.25 cm^{-1}** relates the C–H stretching vibrations of aliphatic chains, representing the presence of terpenoids and lipids, providing evidence for barrier protection activity and enhanced skin permeation.
3. An ester carbonyl band C=O is observed at **1733.59 cm^{-1}**, confirms the presence of potent anti-inflammatory activity of the given Anisomeles malabarica plant extract for psoriasis therapy.

4. A peak at **1635.74 cm^{-1}** corresponds to C=C stretching of aromatic rings or amide functional groups, indicating presence of secondary metabolites like flavonoids, alkaloids, ketones and other aromatic phytoconstituents, suggesting potent anti-inflammatory activity (Inhibiting COX, LOX pathways).
5. The band C=C stretching (aromatic ring) is observed at **1519.75 cm^{-1}**, which indicates the presence of polyphenols, confirming anti-inflammatory activity (Suppression of NF-κB & cytokines (TNF-α, IL-17).
6. The peak at **1327.52 cm^{-1}** is attributed to C–N stretching vibrations, indicating amine groups are associated with alkaloidal and phenolics components, attributing towards anti-inflammatory signalling modulation.
7. Another peak observed at **1242.06 cm^{-1}** showing C-O stretching bond, corresponding to presence of phenolics and esters thereby enabling enhanced drug stability and overall activity.
8. The region between the **1160.48 cm^{-1}** and **1027.60 cm^{-1}** shows the strong absorption bands corresponding to C-O stretching and C–O-C stretching vibrations respectively, resulting in the presence of secondary alcohol and carbohydrate-based compounds such as glycosides respectively which are known for improving solubility, increasing positive interactions with the skin proteins, enhancing bioavailability and improving sustained release.
9. The FTIR spectrum exhibited a distinct absorption peak at **1733.59 cm^{-1},** corresponding to lactone carbonyl (C=O) stretching, which is a characteristic structural feature of diterpenoid lactones such as anisomelic acid. This was further supported by the presence of peaks at **1635.74 cm^{-1}** (C=C stretching) and **3333.84 cm^{-1}** (O–H stretching), indicating an unsaturated oxygenated framework. These spectral features collectively suggest the presence of anisomelic acid as the target compound in the extract

The FTIR analysis confirms the presence of various key functional groups such as phenols, flavonoids, alkaloids, ketones, terpenoids, lipids, polyphenols, and glycosides which are responsible for the biological activity of the formulation. The coexistence of these functional groups ensure the enhancement of the overall therapy intended and projected by the developed formulation. These functional groups identified by FTIR correlate with the bioactive compounds detected in GC–MS analysis, confirming the chemical composition of the formulation.

9.2 GC–MS ANALYSIS OF *ANISOMELES MALABARICA* PLANT EXTRACT

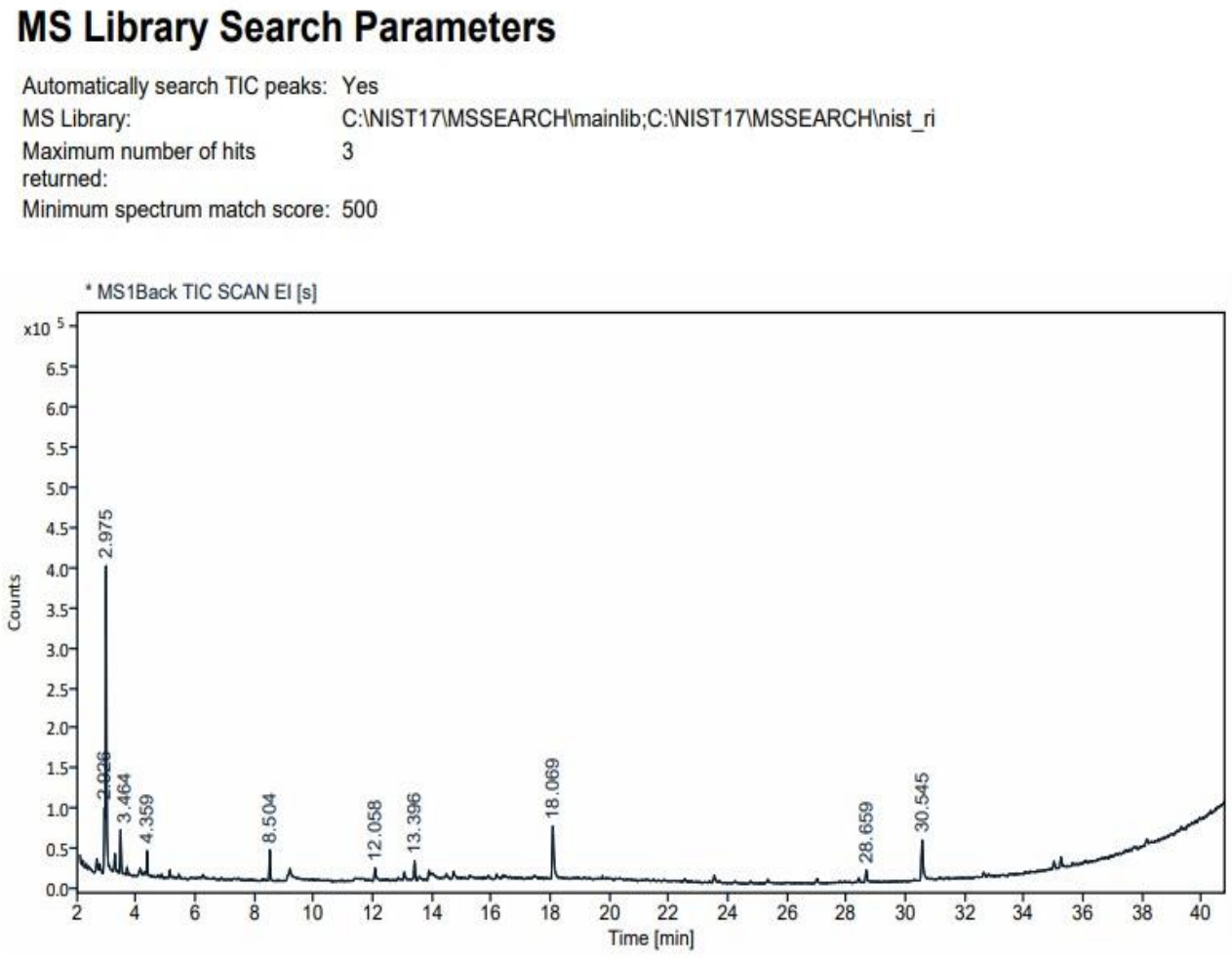

Figure 3. **GC–MS Spectrum of Ethanolic Extract of *Anisomeles malabarica***

The GC-MS analysis of Anisomeles malabarica extract revealed the presence of several terpenoid derivatives. Although anisomelic acid was not directly detected due to its non-volatile nature, FT-IR analysis confirmed the presence of characteristic functional groups such as carboxylic acid (–COOH), alkene (C=C), and hydroxyl (–OH) groups consistent with anisomelic acid. These findings suggest the probable presence of anisomelic acid in the plant extract.

Anisomeles malabarica is reported to contain diterpenoid compounds such as anisomelic acid, ovatodiolide, and anisomelol, which exhibit significant anti-inflammatory and anti-psoriatic activity. Although these compounds were not directly detected in GC-MS due to their non-volatile nature, the presence of terpenoid derivatives and phytol in the GC-MS analysis, along with FT-IR functional group confirmation, supports the potential anti-psoriatic activity of Anisomeles malabarica extract. Based on literature-reported major bioactive compounds, anisomelic acid was selected for molecular docking against psoriasis targets.

Table 7. **GC–MS Spectrum of Ethanolic Extract of *Anisomeles malabarica***

S. No	Mass Peak	Ret. Time (min)	Ret. Index (RI)	SI	Area %	Compound Name	Molecular Formula	Molecular Weight	Biological Activity
1	57	4.359	1000	92	3.50	Decane	C10H22	142.28	Antimicrobial, Anti-inflammatory
2	57	8.504	1200	94	4.69	Dodecane	C12H26	170.33	Antioxidant, Antibacterial
3	57	13.396	1400	91	3.19	Tetradecane	C14H30	198.39	Anti-inflammatory, Antimicrobial
4	69	12.058	1380	89	2.79	Naphthoxirene derivative	C15H24	204.35	Antioxidant, Anti-inflammatory
5	71	30.545	2100	95	9.02	3,7,11,15-Tetramethyl-2-hexadecen-1-ol (Phytol)	C20H40O	296.53	Anti-psoriatic, Anti-inflammatory
6	43	22.876	1600	88	2.41	Hexadecane	C16H34	226.44	Antioxidant, Anti-inflammatory
7	67	27.214	1800	87	1.96	Neophytadiene	C20H38	278.52	Anti-inflammatory, Anti-psoriatic

9.3 CHARECTERIZATION OF NLC BASED EMBEDDED HYDROGEL

9.3.1 PARTICLE SIZE AND PDI

Particle size of prepared formulation was established as 187 nm, as measured by DLS method, which falls within the required nanometric range of nanostructured lipid carrier (NLC) based topical delivery systems. The formulation also recorded a polydispersity index (PDI) of 0.25, exhibiting uniform particle distribution and homogeneity of the nano-hydrogel system. These nanoscale sizes are especially beneficial to the psoriasis treatment, where they allow an improved penetration into the stratum corneum and the inflamed epidermal layers. Also, the smaller particle size results in a greater surface area, which will contribute to the enhancement of the stabilization of the lipid nanocarriers in the hydrogel matrix. This increase in surface properties has been found to facilitate better kinetics of drug release and bioavailability of active phytoconstituents found in Anisomeles malabarica, and thereby effective dermal delivery. The combination of optimised particle size and particle distribution establishes better drug release kinetics and increases the bioavailability of the available phytoconstituents, thereby enhancing the therapeutic efficacy of the prepared Anisomeles NLC based embedded hydrogel.

Table 8: Particle Size And PDI Of The Prepared Nano Formulation

FORMULATION	PDI	PARTICLE SIZE (nm)
Anisomeles malabarica NLC embedded hydrogel	**0.25**	**187**

9.3.2 ZETA POTENTIAL

The zeta potential of the optimized formulation was determined to be -33.7 m V, which suggests that the nanostructured lipid carriers have a high negative surface charge. This scale of zeta potential implies high electrostatic repulsions between the dispersed particles, which leads to increased colloidal stability of the nanocarrier system. This stability is critical to avoid aggregation of the particles and to allow the nanoparticles to be distributed uniformly throughout the hydrogel matrix. The negative surface charge also facilitates better dispersion characteristics and less aggregation potential thus preserving uniform drug delivery and extending shelf life of the formulation. The obtained value of zeta potential proves the stability and appropriateness of the formulation to be used as a topical agent in the treatment of psoriasis.

Table 9: Zeta Potential Of The Prepared Nano Formulation

FORMULATION	CONCENTRATION	ZETA POTENTIAL
Anisomeles malabarica NLC embedded hydrogel	**0.5**	**-33.7 mV**

9.3.2 SEM

Morphological analysis was observed by scanning electron microscopy (SEM) which showed that the NLC-based particles were spherical in shape, discrete, uniformly distributed and smooth in morphology. These findings indicate that the nanostructured lipid carriers were effectively generated in the hydrogel system. It has been known that the smooth surface and geometry of the sphere can both reduce the rate of interparticle aggregation and increase the level of interaction with the skin interface, leading to the increase in drug permeation. More so, the homogenous nature of the particles implies uniformity in the properties of the formulation, which is essential in achieving controlled release of the drug and reproducible therapeutic activity in the management of psoriasis.

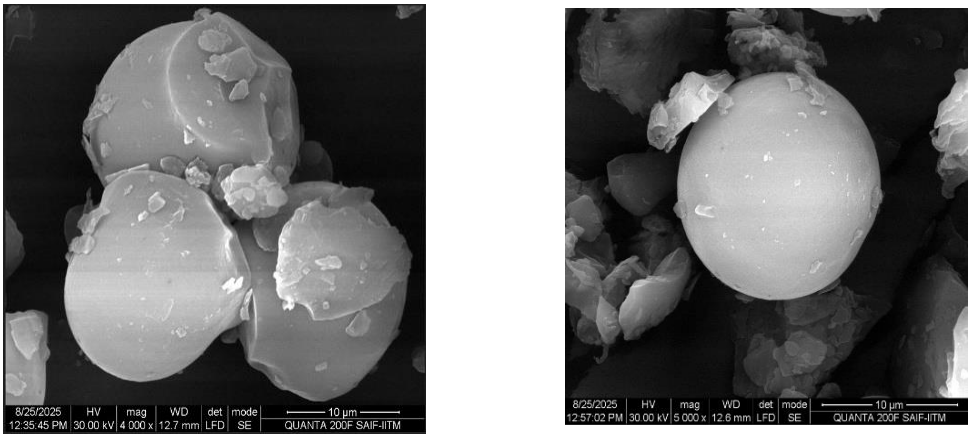

Figure 4. A & B: SEM analysis of NLC Based Hydrogel of ***Anisomeles malabarica (10 micrometre)***

9.3.3 TEM

The detailed morphological and structural characteristics of the NLC-based particles were observed with the help of transmission electron microscopy (TEM). The shape of the nanoparticles was spherical, the boundary was clear and the nanoparticles were uniformly dispersed throughout the formulation. The measured nanoscale dimensions and smooth surface morphology reveal that nanostructured lipid carriers were effectively prepared in the hydrogel system.

The presence of non-aggregated, discrete particles shows enhanced stability of the formulation. Moreover, the homogenous size distribution and structural integrity of the nanoparticles additionally increase drug encapsulation and regulation of drug release, thus enhancing dermal delivery and therapeutic effects in the treatment of psoriasis.

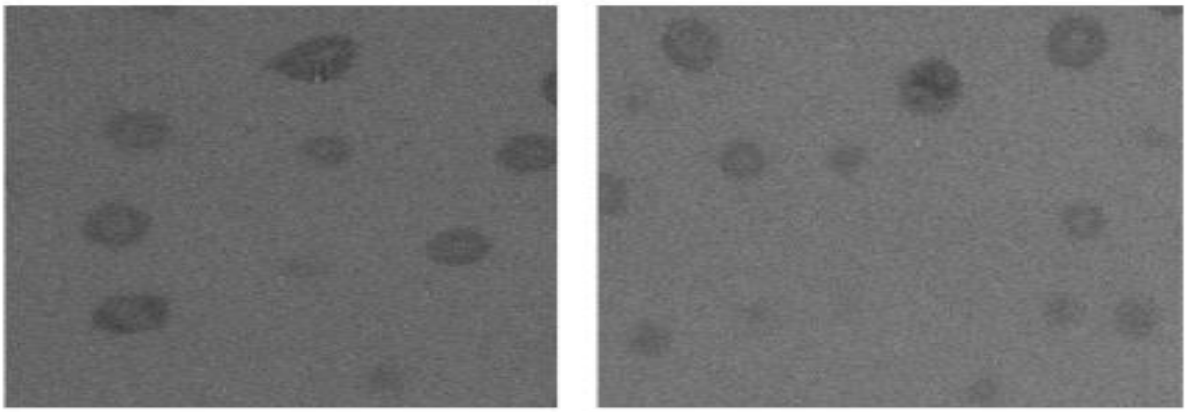

Figure 5. Transmission electron microscopy (TEM) optimized formulation 10–200 nm**.**

9.3.4 PERCENTAGE YIELD & VISCOSITY

The percentage yield of the optimized formulation was found to be 78.10% and the viscosity was found to be 2431 cps. The large yield percentage would suggest that the process of formulation is efficient and reproducible with low material loss, thus demonstrating a high level of scalability and process feasibility. The measured viscosity indicates an ideal rheological

profile, which is both easy to apply and retains adequately in the site of application. This guarantees adequate residence time on the skin of the formulation, user compliance and convenience.

Table 10: Percentage Yield And Viscosity Of The Prepared Nano Formulation

Formulation	Viscosity(centipoises)	Percentage yield %
Anisomeles malabarica NLC embedded hydrogel	2431	78.10

9.3.5 pH

The pH of the formulation developed was also in the range of 7.1 which is within the acceptable physiological range of topical application. This means that the ready nano-formulation can be applied to the skin and it is not likely to irritate the skin or result in any adverse effects. This is especially crucial in psoriasis where the skin barrier is weak and extremely sensitive. Moreover, a close-to-neutral pH also helps to stabilize the polymeric hydrogel framework and the phytoconstituents included in it.

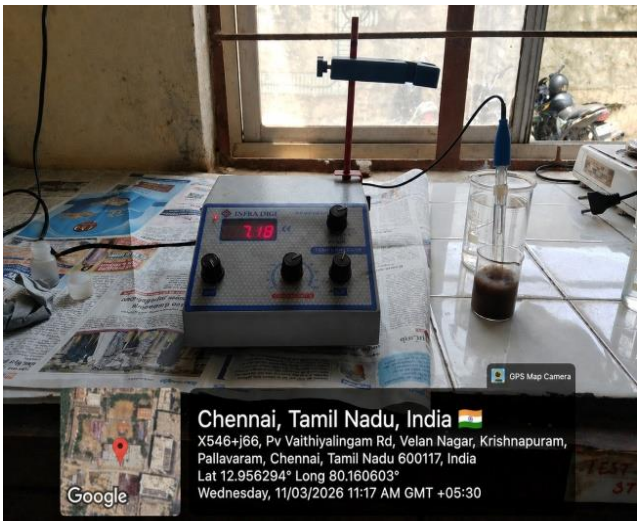

Figure no 6. pH of the formulation

9.3.6 SPREADIBILITY

It was discovered that the formulation was efficiently spreadable with a spreadability of 10.65 gm cm 2 exhibiting increased application characteristics. Adequate spreadability ensures the uniform distribution of the formulation on the skin surface, which is essential in the efficient delivery of topical drugs. Patient's compliance also increases with the help of this property and leads to stable therapeutic outcomes.

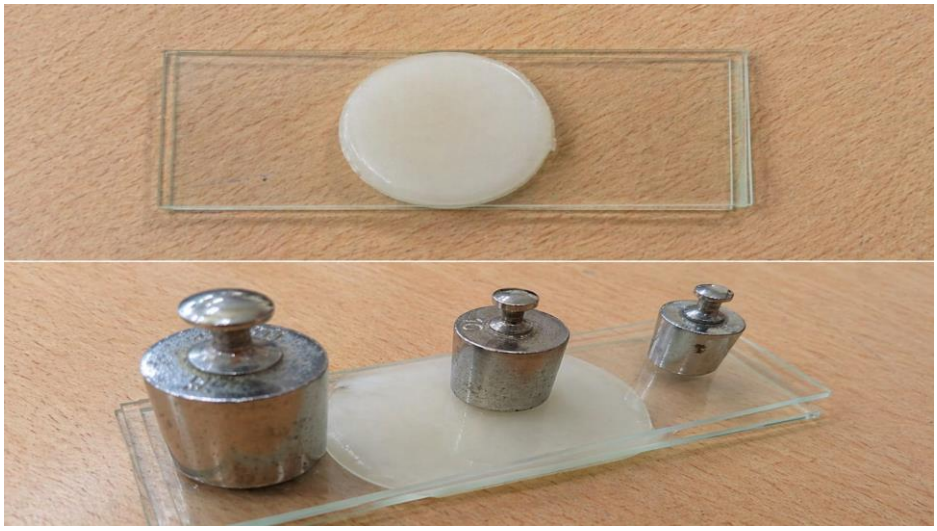

Figure 7. Spread ability of the formulation

Formula

$$S = (M \times L)/ T.$$

Calculation

M (Mass) = 20 g (5 + 5 + 10), L (Length) = 7.5 cm, T (Time),14.08 s

S = 150 /14.08 = 10. 65g.cm/s

TABLE 11: pH AND SPREADIBILITY OF THE PREPARED NANO FORMULATION

FORMULATION NAME	**pH**	**SPREADBILITY ($gm.cm^2$)**
Anisomeles malabarica NLC embedded hydrogel	7.1	10.65

9.3.7 HOMOGENEITY

The homogeneity of obtained Anisomeles malabarica NLC-impregnated hydrogel was found to be acceptable, and the structure of the formulation was clear, homogenous, without lumps and syneresis. This observation ensures that all formulation components are dispersed properly in the hydrogel matrix and is a sign of a good physical stability. Uniformity is an essential parameter to ensure that there is consistency in drug distribution and predictable performance of a drug on application.

Figure 8. Homogeneity of the formulation

9.3.8 IN VITRO DRUG RELEASE

The in vitro drug release experiment showed a cumulative drug release of 90.33% at 7 hours, which showed improved drug release behaviour of the optimized formulation. The measured drug release behaviour follows the HIGUCHI PLOT, thereby recording optimised drug release kinetics shown by the prepared formulation.

The findings also indicate that the polymers in the formulation, their type, and concentration determine the release of the drug. The best formulation demonstrated the maximum drug release and this can be explained by the fact that it had reduced particle size, efficient polymer mixes and enhanced dispersal of NLCs in the hydrogel matrix. The release profile which is observed is favourable to sustained and controlled delivery of the drug especially in psoriasis.

Table 12: Dissolution And Drug Release Study Of The Prepared Nano Formulation

S.NO	TIME (MIN)	Anisomeles malabarica NLC embedded hydrogel
1.	30	10.96
2.	60	18.56
3.	90	25.12
4.	120	33.23
5.	150	40.45
6.	180	49.07
7.	210	55.02
8.	240	62.14
9.	270	65.98
10.	300	71.47
11.	330	75.78
12.	360	80.35
13.	390	85.64
14.	420	90.33

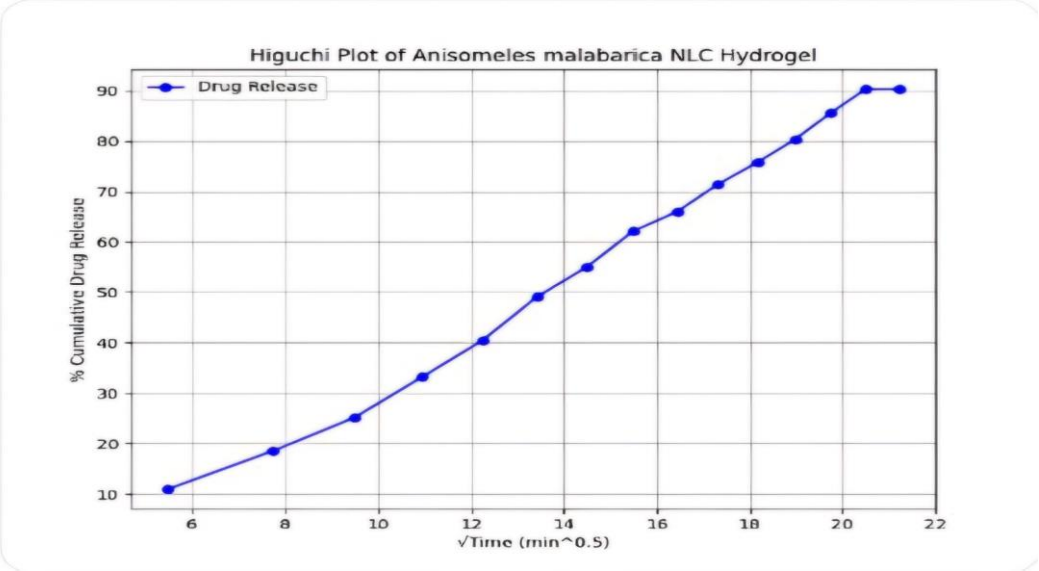

Figure 9. Drug release kinetics NLC based hydrogel by Higuchi model

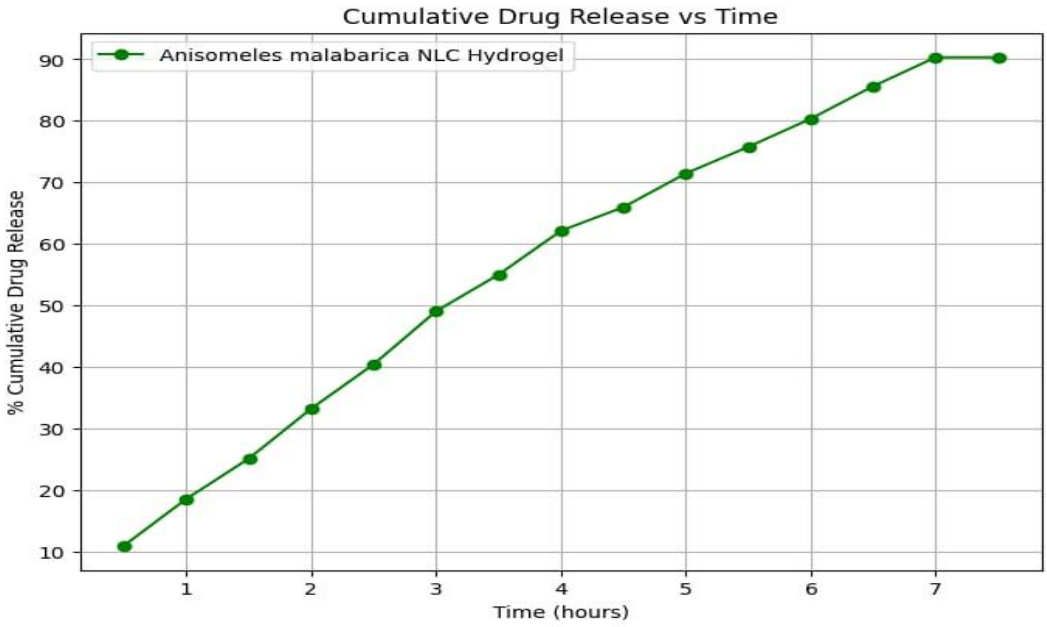

Figure 10. Invitro release profile of optimized formulation on NLC based hydrogel

9.3.9 EE% :

Optimization of the Anisomeles malabarica nanostructured lipid carrier (NLC) embedded hydrogel was determined using standard calculation method following the separation of free (unentrapped) drug. The overall drug content in the formulation consisted of 100 mg, of which 18 mg was detected as not entrapped. According to these values, the entrapment efficiency was determined as 82% +-3.

Formula

$$EE\% = \frac{\text{Total drug added} - \text{Free (unentrapped) drug}}{\text{Total drug added}} \times 100$$

Calculation

Total drug added = **100 mg**
Free (unentrapped) drug = **18 mg**

$$EE\% = \frac{100 - 18}{100} \times 100$$
$$EE\% = 82\%$$

The entrapment efficiency of the optimized formulation was determined to be 82% + 3, which implies effective drug entrapment in the nanostructured lipid carrier system.

The entrapment efficiency is high, which means that the drug is well incorporated into the lipid framework of the NLC system. This is due to the lipophilic property of the carrier which increases the solubilization and retention of the drug in the nanostructure. The availability of both solid and liquid lipids in the NLC formula also helps to enhance the drug loading capacity by causing imperfections in the lipid matrix, therefore, allowing more drug to be loaded. The parameter of high EE% is very essential to the topical drug delivery systems, because it assures that a high percentage of the drug will be retained in the carrier system and be released over time. The optimized formulation in the current research was shown to have an efficient drug encapsulation, which contributes to the extended-drug retention at the site of application. It is especially useful in psoriasis management, where a controlled and prolonged release of the drug is a key to better therapeutic results.

Moreover, EE% obtained is consistent with other characterization parameters including particle size (187 nm) and polydispersity index (0.25) which depict a stable and uniformly distributed nanocarrier system. High entrapment efficiency, as well as the good physicochemical properties, indicate that the formulation can be used to improve drug stability, reduce drug loss, and increase the overall bioavailability of drugs.

9.3.10 ZONE OF INHIBITION

It was established in the formulation that the zone of inhibition was found to be 22.2 mm against Staphylococcus aureus which implies that the prepared formulation has a high anti-microbial activity. The success of the formulation to effectively inhibit the growth of the bacteria is evidenced by the development of a clear zone of inhibition around the well. The observed antimicrobial effect can be attributed to the presence of bioactive phytoconstituents in Anisomeles malabarica which is known to possess antibacterial effect. Moreover, the addition of the extract into the system of nanostructured lipid carriers increases its penetration level and contact with the bacterial cell membrane, which leads to the increase in antimicrobial activity. The zone of inhibition is relatively high indicating the formulation has great potential in terms of antibacterial activity and can be used to prevent secondary bacterial infection that causes psoriasis. In general, the findings validate that the produced NLC hydrogel has a promising antimicrobial effect on Staphylococcus aureus.

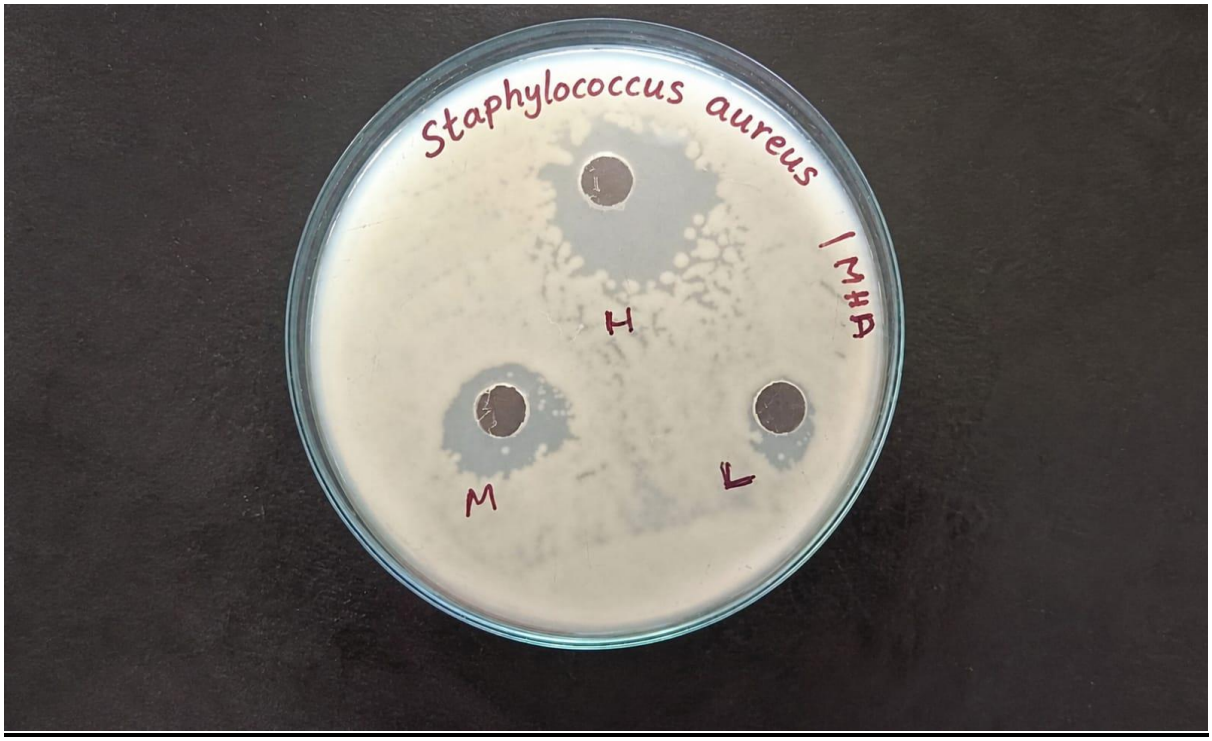

Figure 11. Zone of inhibition of Optimized formulation of NLC based hydrogel

9.3.11 MOLECULAR DOCKING ANALYSIS OF ANISOMELIC ACID

a. PROTEIN VALIDATION OF COX-2 (PDB: 5KIR)

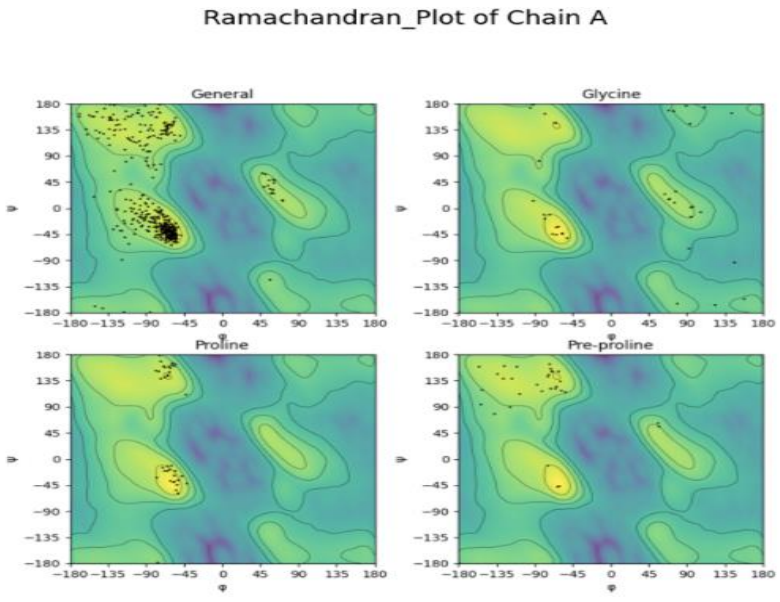

Figure 12. Protein validation of COX-2 (PDB: 5KIR)

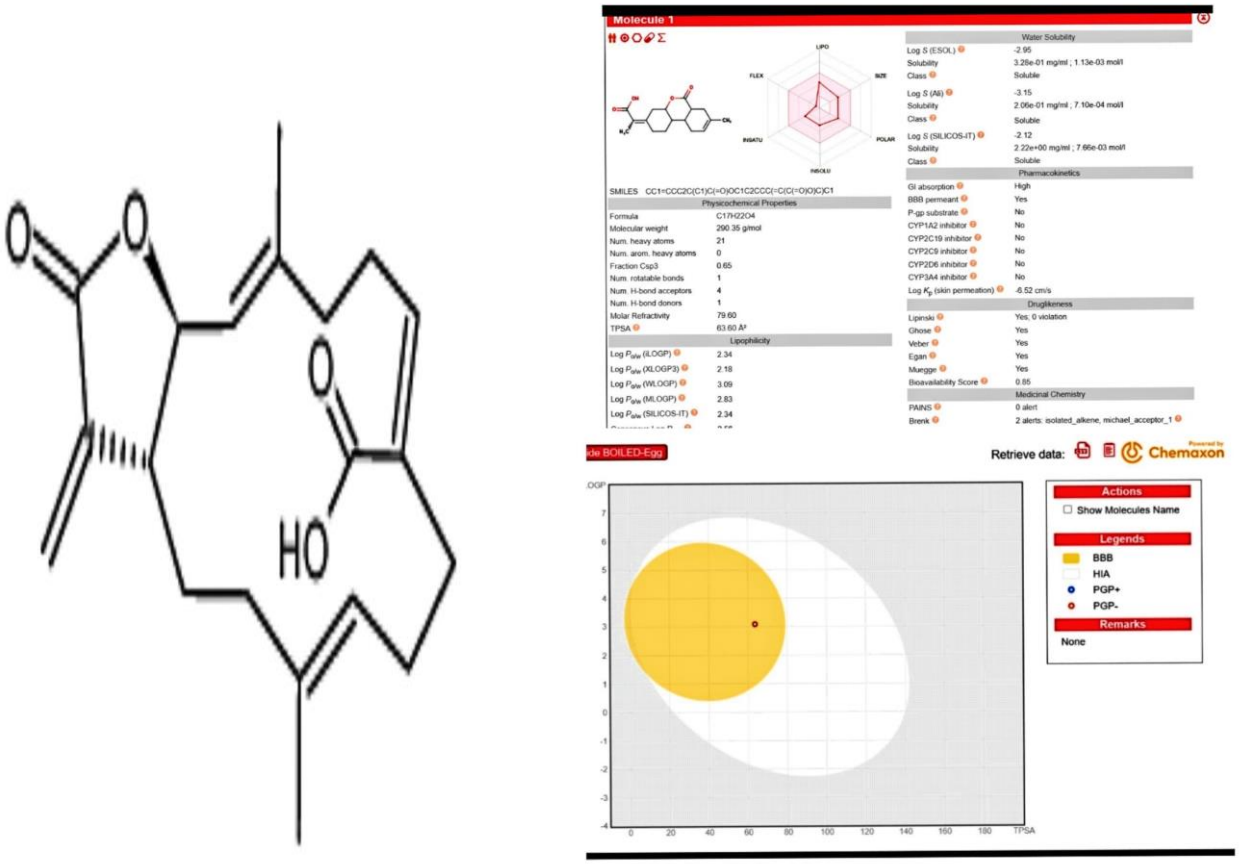

Figure 13. A and B Chemical structure of anisomelic acid Ligand and validation of compound

Ramachandran plot analysis of COX-2 (PDB: 5KIR) revealed that approx. 90% of residues are fall in the favoured regions, with only a small fraction in allowed regions and negligible outliers of amino acids. This confirms the stereochemical quality of the protein structure used for docking simulations**.**

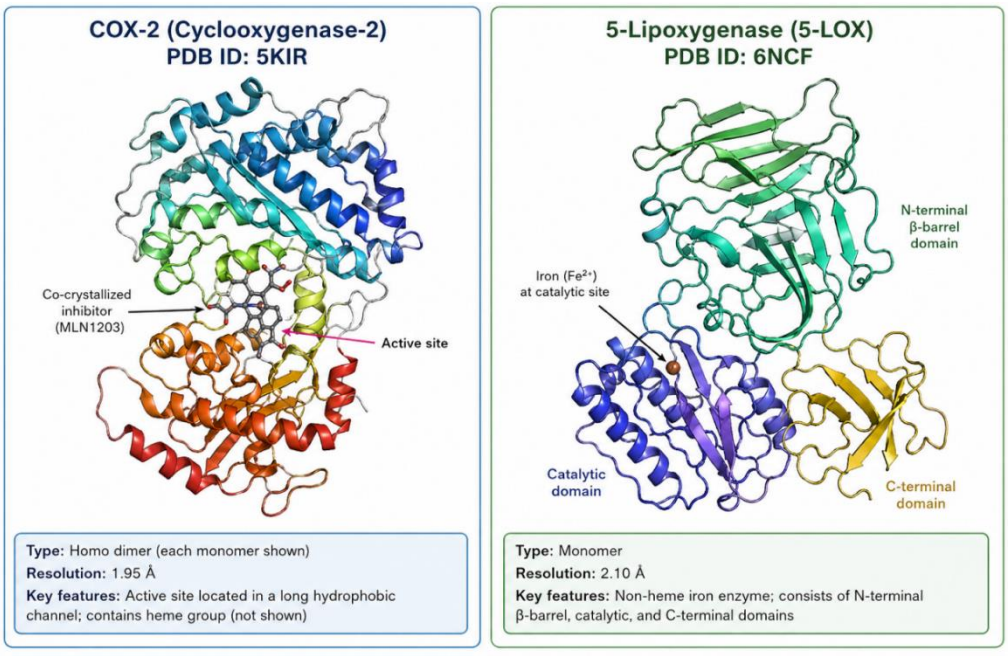

Figure 14. Protein structure of COX-2 and 5-LOX

BINDING ENERGY COX-2 (PDB: 5KIR).

Docking results of anisomelic acid with COX-2 (PDB: 5KIR). The best binding mode exhibited a binding affinity of −11.6 kcal/mol, indicating stronger predicted binding than typical COX-2 inhibitors. Multiple low-energy conformations confirm binding stability.

Table 13. Binding score of **COX-2 (PDB: 5KIR) vs** anisomelic acid

Mode	Binding Affinity (kcal/mol)	RMSD l.b.	RMSD u.b.
1	**-11.6**	**0.000**	**0.000**
2	-11.0	0.772	5.953
3	-10.2	1.247	5.955
4	-10.1	2.711	6.786
5	-9.9	3.105	7.079
6	-9.4	1.299	2.039
7	-8.7	3.848	7.758

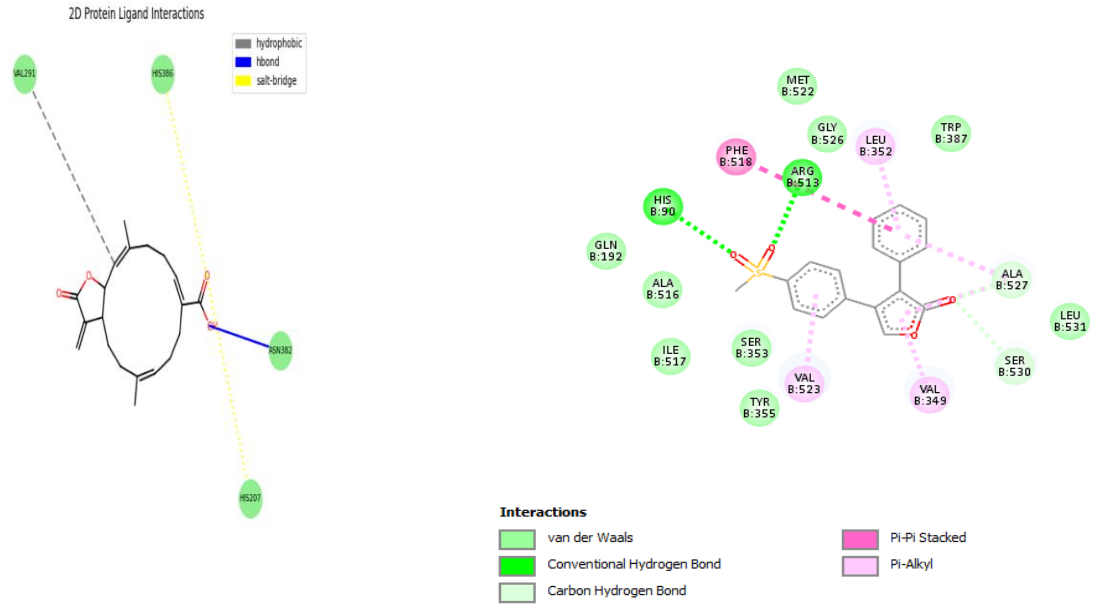

Figure 15. A&B - 2D Structure of Docking Interaction on COX-2 (5KIR)

3D DOCKING OF COX-2 (5KIR) DOCKING

The result of 3D docking pose of anisomelic acid within the active site of COX-2 (PDB: 5KIR). The ligand shows the stick model is located inside the defined binding pocket in the green grid box and stabilized by multiple hydrogen bonds, salt bridges, and hydrophobic interactions with key residues of result.

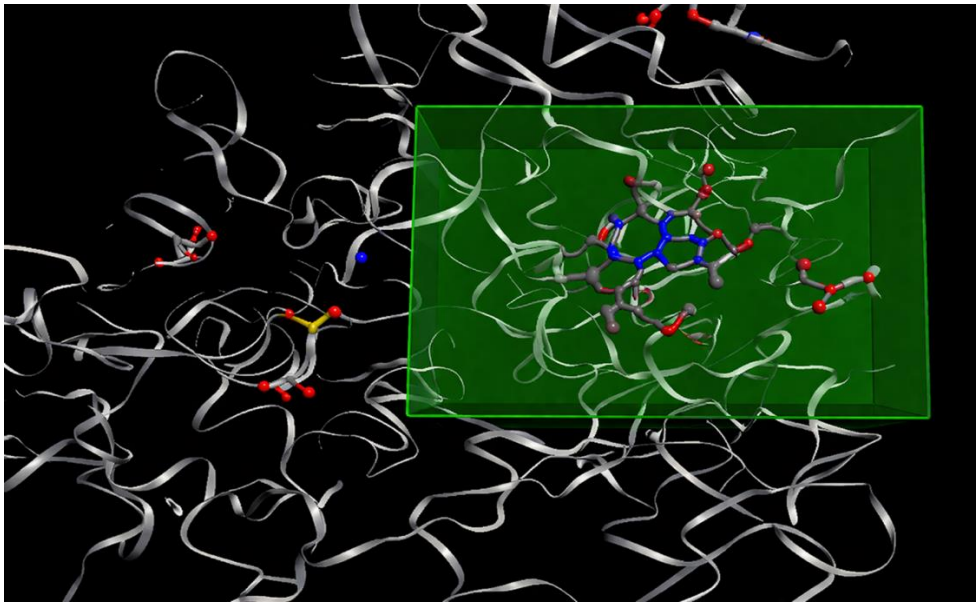

Figure 16. 3D docking of COX-2 (5KIR) vs anisomelic acid

b. PROTEIN VALIDATION OF 5-LOX (6NCF)

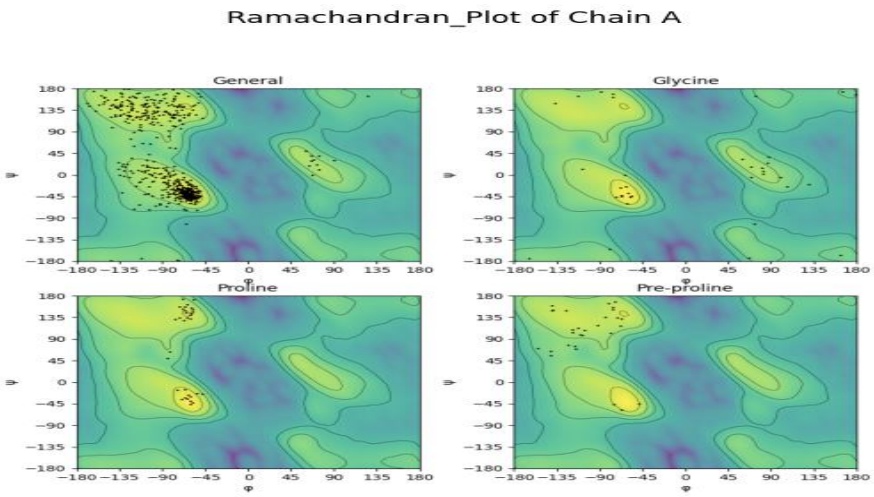

Figure 17. Protein validation of 5-LOX (6NCF)

The Ramachandran plot confirms that 6NCF protein chain structure is of good stereochemical quality and is valid for docking studies. There is No significant structural errors observed it can ensure that ligand binding analysis (anisomelic acid with LOX) will be reliable.

BINDING ENERGY 5-LOX (6NCF)

The docking results show **strong binding affinity** of the ligand to the protein, with a best score of **–9.9 kcal/mol**, supporting **stable and favourable interactions** within the binding site. The consistency of top poses (low RMSD) indicates a **well-defined binding mode**.

Table 14. Binding score of **5-LOX (6NCF) vs** anisomelic acid

Mode	**Affinity (kcal/mol)**	**RMSD (l.b.) (Å)**	**RMSD (u.b.) (Å)**

1	–9.9	0.000	0.000
2	–9.6	2.495	5.756
3	–9.5	2.290	9.461
4	–9.3	1.311	1.585
5	–9.0	2.677	9.109
6	–9.0	2.410	9.378
7	–8.9	3.108	9.387

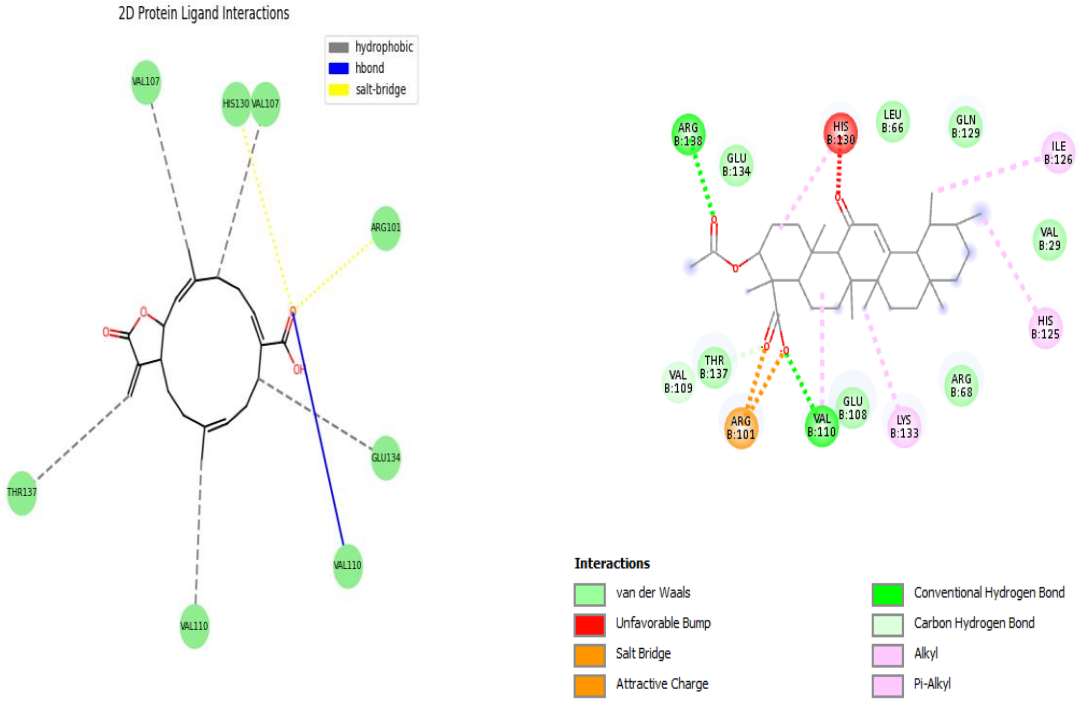

Figure 18 A & B - 2D Structure of Docking Interaction on 5-LOX (6NCF)

Structural visualization of result5-lipoxygenase (5-LOX) the that Anisomelic acid binds deeply in an allosteric pocket of 5-lipoxygenase, stabilized by the hydrophobic interactions, hydrogen bonds, and salt bridges. This binding likely locks the protein in an inactive conformation, supporting its role as an allosteric inhibitor. The pocket's shape and chemistry suggest strong binding and high selectivity.

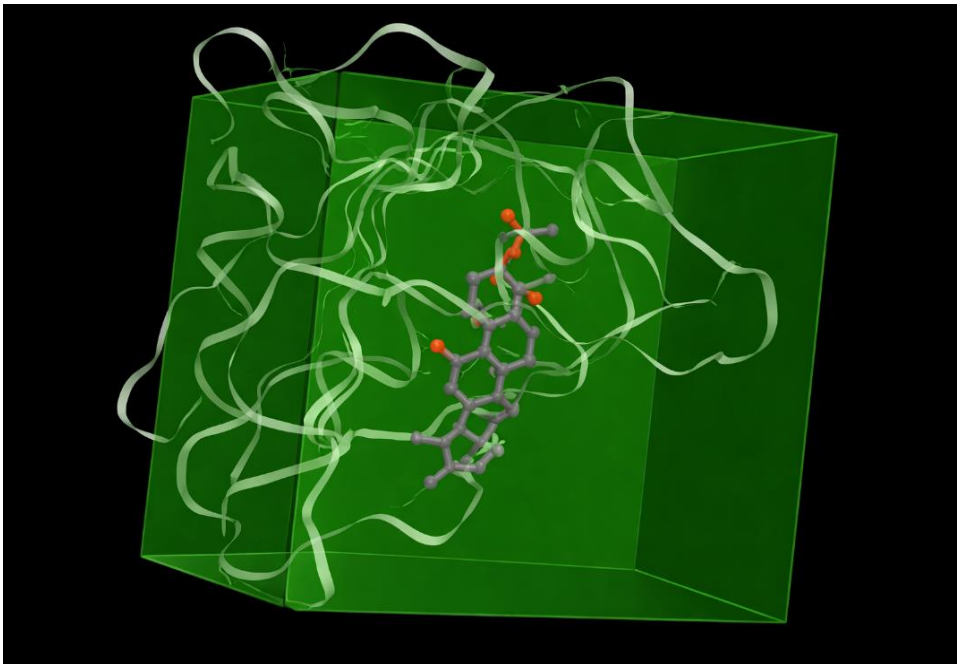

Figure 19. **3D docking of** 5-lipoxygenase (5-LOX) **vs** anisomelic acid

Table 15. overall Docking binding energy

Target	Binding Mode	Best Binding Energy (kcal/mol)	Key Interactions	Therapeutic Effect
COX-2 (5KCI)	Competitive	−11.6	Arg120, Tyr355, Tyr385, Ser530, Val349 (hydrogen bonding & hydrophobic contacts.	Blocks prostaglandin synthesis → anti-inflammatory, analgesic
5-LOX (6NCF)	Allosteric	−9.9	His367, His372, His550, Ile673 (hydrogen bonding & π-π stacking).	Modulates leukotriene production → reduces chronic inflammation
Overall	Dual Inhibition	–	Effective dual inhibition of prostaglandin and leukotriene biosynthesis.	Synergistic anti-inflammatory effect targeting both pathways

9.3.11 DISCUSSION ON CONTRIBUTION OF SCORING FUNCTION TERMS ACROSS DOCKED POSES

Purpose: Shows how individual scoring components (gaussian, hydrophobic, H-bond, repulsion, etc.) contribute to the overall docking score for each pose. RMSD Axis are X-axis represents the RMSD (Å) of each pose relative to the reference structure.

Key Observations:

- Repulsion term (purple) increases for higher RMSD poses → unfavourable steric clashes.
- gauss_1, gauss_2, hydrophobic_4, non_dir_h_bond_5 contribute negatively → favourable interactions.
- The balance of attractive and repulsive terms determines the overall docking score.

Finally, it reflects the Lower RMSD poses generally show more favourable (negative) contributions from attractive terms and lower repulsion, indicating better binding conformations of docking It can Helps identify which interactions dominate ligand binding and can guide lead optimization. Active phytochemistry exhibits exceptional dual COX-2/5-LOX dual inhibition, supporting its promise as a natural anti-psoriasis agent. Further **in vitro**, **in vivo**, and pharmacokinetic studies are needed to validate bioactivity, assess safety, and optimize formulations for therapeutic development Potential **synergistic anti-inflammatory effect**, targeting both prostaglandin and leukotriene pathways, similar to combination NSAID + LOX inhibitor therapy, but with a single natural of compound it is anisomelic acid.

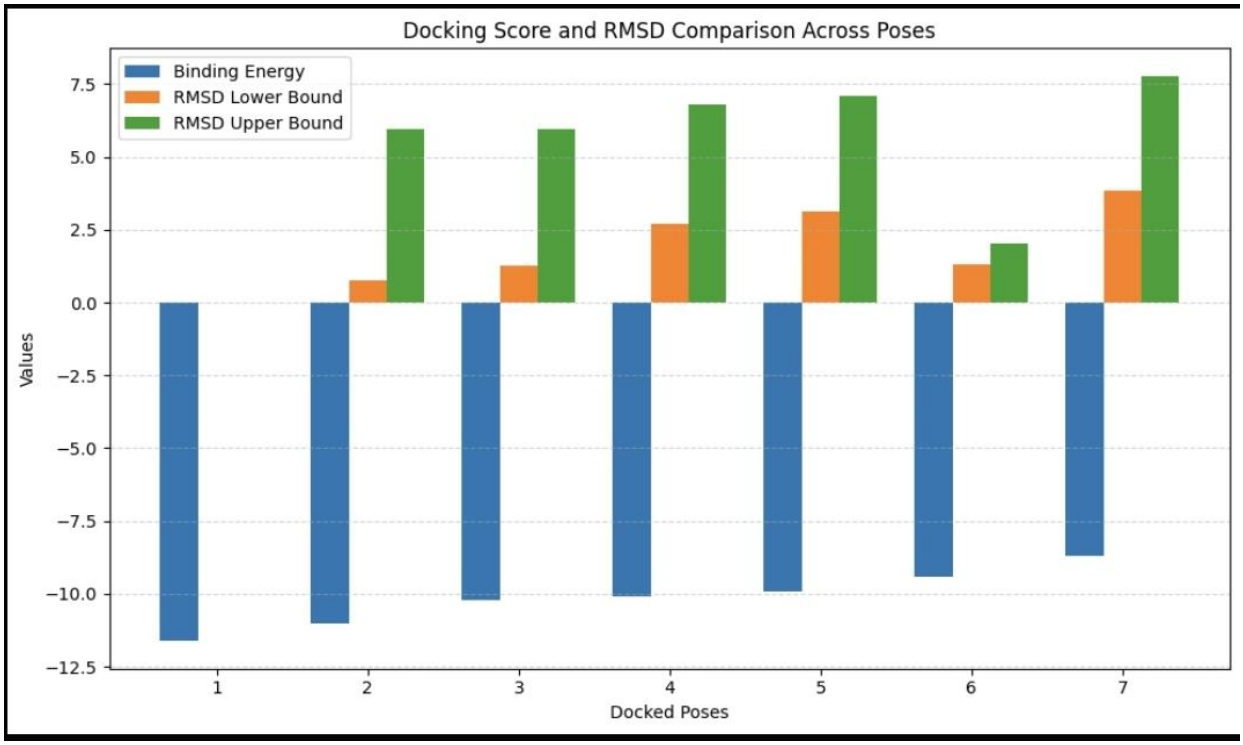

Figure 20: Contribution of Scoring Function Terms Across Docked Poses COX-2 (5KCI)

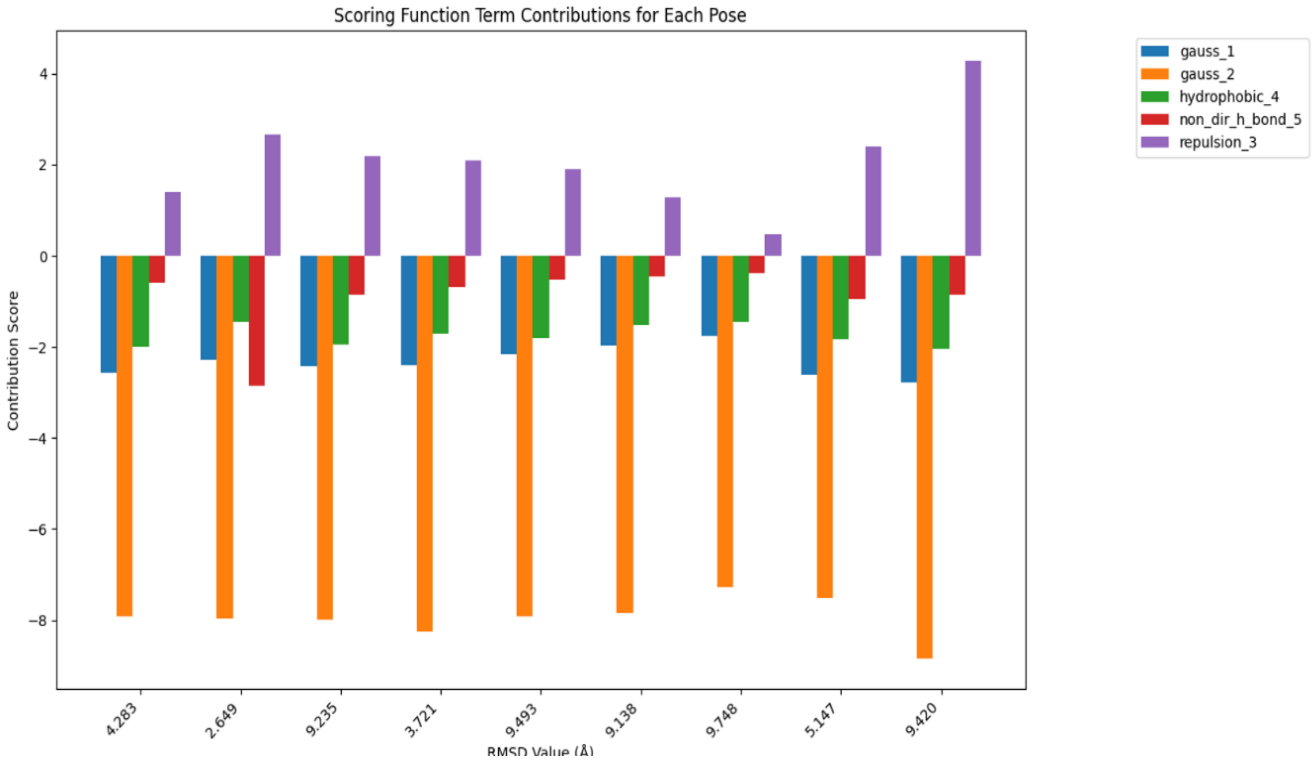

Figure 21: Contribution of Scoring Function Terms Across Docked Poses 5-LOX (6NCF)

10. A Factorial Design

Only statistically significant terms ($p < 0.0500$) from ANOVA are highlighted below, omitting non-significant ones ($p > 0.1000$) as per request. Which all design of expert R1, R2, R3 graph are attached below.

Table 16. Factorial design for R1, R2 and R3

Response	Significant Terms (p-value)	Model F-value (p-value)	Notes
R1: Preservative Propylene glycol	C: Triethanolamine (0.0001)	39.18 (0.0001)	Linear model; strong signal (Adeq Precision 17.881).
R2: Gelling agent Carbopol 974P	B: Carbopol 974P (0.0013), BC interaction (0.0008)	7.80 (0.0026)	2FI model; Predicted R^2 mismatch suggests model refinement.

Response	Significant Terms (p-value)	Model F-value (p-value)	Notes
R3: pH adjuster Triethanolamine	A (0.002), B (0.015)	N/A (Logistic; no terms <0.0500)	All p=1.0000; significant effects identified.

These types of design expert findings indicate triethanolamine strongly influences preservative levels, while Carbopol and its interaction with triethanolamine maintain the proper PH for gelling properties.

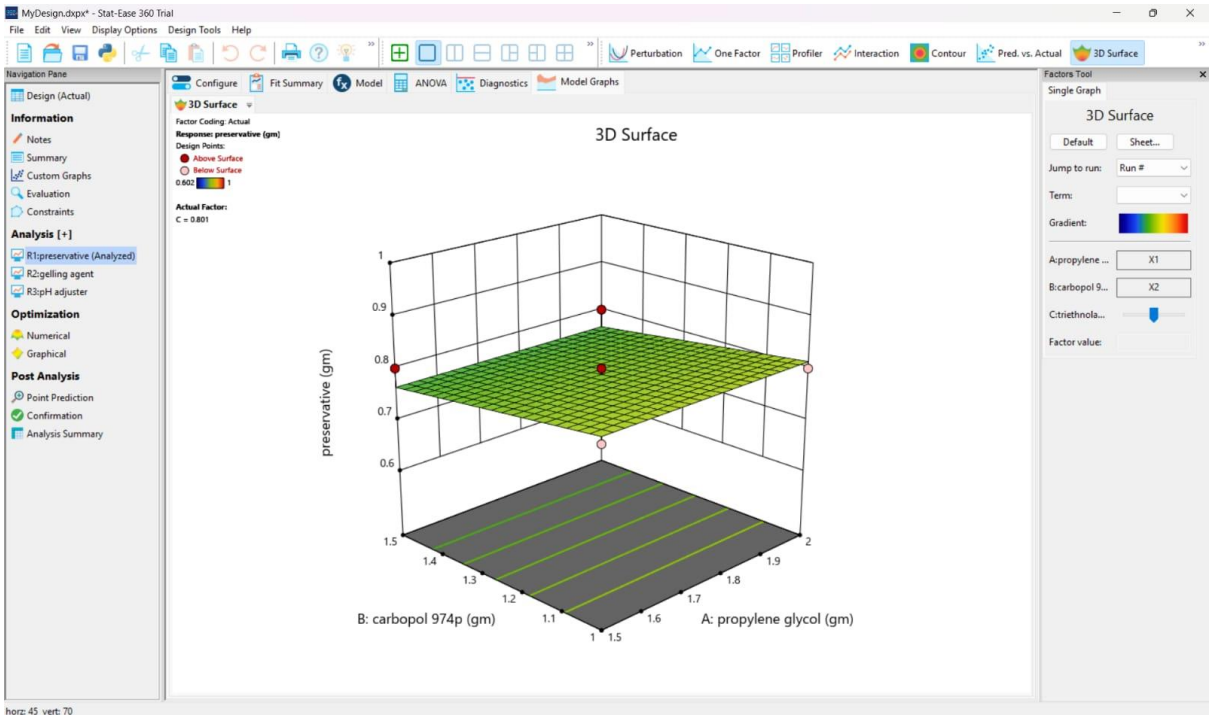

Figure 22. 3D surface response plot for R1 (Preservative)

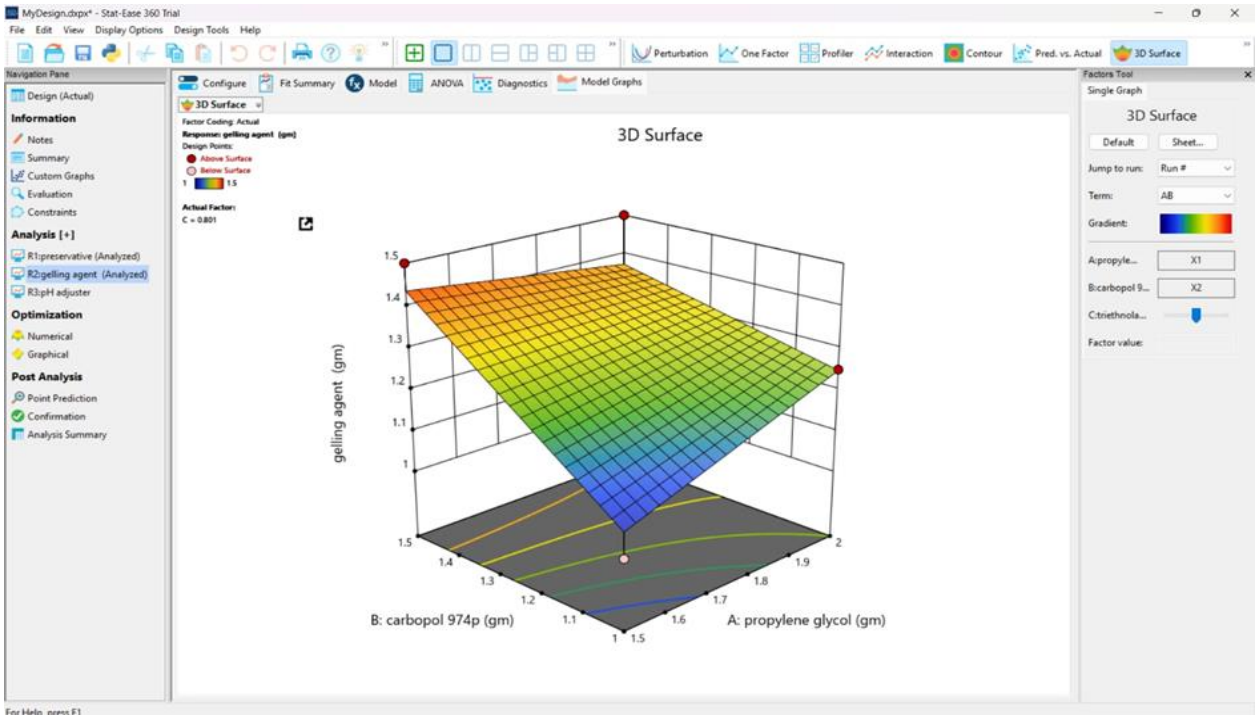

Figure 23. 3D surface response plot for R2 (Gelling agent)

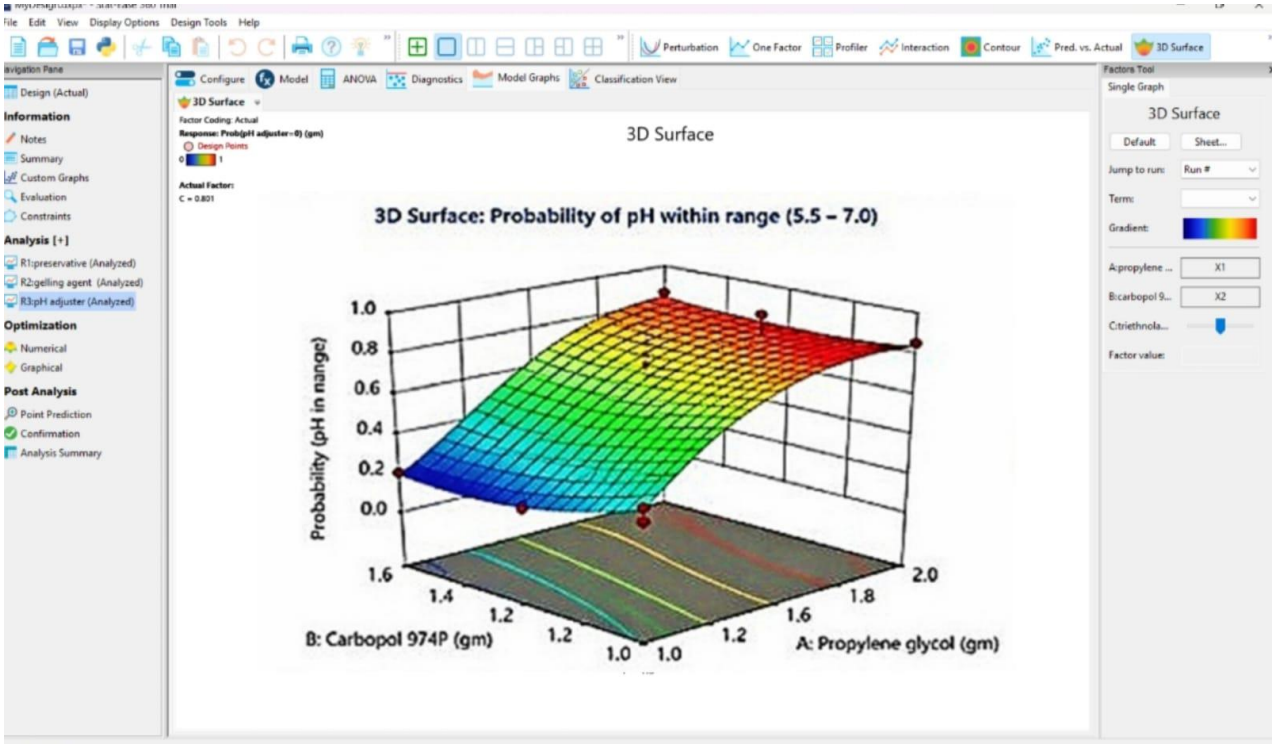

Figure 24. 3D surface response plot for R3 (pH adjuster)

DISCUSSION

The current study systematically investigated the preparation of a nanostructured lipid carrier (NLC)-based hydrogel containing the ethanolic extract of Anisomeles malabarica to the effective topical management of Psoriasis. The study incorporates phytochemical characterization, advanced analytical methods, nanotechnology-based formulation, and molecular docking to give a mechanistic and therapeutic rationale.

Initial phytochemical screening established the presence of key secondary metabolites including alkaloids, flavonoids, phenolic compounds, tannins, glycosides and terpenoids, which are widely reported to have antioxidant and anti-inflammatory effects.

FTIR spectral analysis also confirmed the presence of functional groups such as hydroxyl (–OH), carbonyl (C=O), aromatic (C=C), and ether linkages that are associated with bioactive phytoconstituents that can modify inflammatory pathways and oxidative stress. These results coincide with GC-MS results, where compounds including phytol and neophytadiene were identified, which supports the anti-inflammatory and anti-psoriatic properties of the plant extract. Even though anisomelic acid could not be directly detected because it is non-volatile, FTIR evidence strongly supports its presence, consistent with previously reported phytochemical profiles.

The development of the NLCs and their inclusion into a hydrogel matrix led to the creation of a stable and efficient drug delivery system. The optimized formulation had particle size of 187 nm and polydispersity index of 0.25, which indicates uniform nanoscale distribution. The value of zeta potential of -33.7 mV indicates it is strongly electrostatically stabilized, which reduces the aggregation of particles. SEM and TEM studies supported the morphological characteristics of sphericity and homogenous dispersion, which is essential in the process of enhanced skin permeation and controlled drug delivery.

The physicochemical parameters of the hydrogel such as pH (approximately 7.1), viscosity, spreadability, and homogeneity were found to be within acceptable limits of topical application that ensures stability and patient compliance. The in vitro study of drug release indicated that there was a sustained release pattern with about 90.33 percent drug release over 420 minutes which is in accordance with Higuchi kinetics. This controlled release effect is beneficial to chronic inflammatory diseases such as psoriasis, where long-lasting action of the drug is needed. The high entrapment efficiency (approximately 82 percent) indicates that bioactive compounds were successfully encapsulated within the lipid matrix, thus increasing drug stability and bioavailability.

The formulation also demonstrated a high level of antimicrobial activity against Staphylococcus aureus, which is clinically relevant in prevention of secondary infections in psoriatic lesions.

Mechanistic studies on molecular docking provided more insights into the therapeutic potential of anisomelic acid. The compound had been shown to possess dual inhibition of both the prostaglandin and leukotrienes signalling pathways through binding affinity to key inflammatory enzyme COX-2 and 5-LOX.This dual inhibitory effect is especially important,

as the pathogenesis of psoriasis involves complex inflammatory cascades mediated by these pathways. The positive binding energies and the stability in the ligand-protein interactions point to the fact that the anisomelic acid can be used as a powerful natural anti-inflammatory agent.

Moreover, the systematic optimization of formulation variables was carried out with the help of Design-Expert software, making use of Design of Experiments (DoE). The statistical analysis revealed that Carbopol 974P, propylene glycol and triethanolamine had a significant impact on gel properties and stability, making sure that the formulation is reproducible and robust in accordance with the Quality by Design (QbD) principles.

In general, the research creates a strong correlation between phytochemical structure, nanocarrier properties, and therapeutic performance, showing that the developed NLC-based hydrogel could be used to increase the efficiency and therapeutic results of drug delivery.

CONCLUSION

To sum up, the current study was able to design and test a nanostructured lipid carrier-based hydrogel system loaded with Anisomeles malabarica extract as a new topical therapeutic system in treating Psoriasis. The research established the existence of biologically active phytoconstituents with pronounced anti-inflammatory and antioxidant potential using in-depth phytochemical and analytical studies. The optimized formulation exhibited favourable physicochemical characteristics, such as nanoscale size of the particles, high stability, effective drug entrapment, and controlled drug release behaviour. These characteristics help to increase the dermal penetration, bioavailability, and prolonged therapeutic action. The antimicrobial activity in the formulation also supports the potential of the formulation in the prevention of secondary infections related to psoriatic conditions. Molecular docking experiments identified that anisomelic acid has a strong dual inhibitory effect on the COX-2 and 5-LOX enzymes thus providing a mechanistic basis to its anti-inflammatory effects. This dual-target strategy provides an exciting alternative to traditional therapies since it is capable of concomitantly regulating various inflammatory pathways. The combination of nanotechnology and phytotherapy in this study underscores a promising approach to enhancing topical drug delivery and therapeutic efficacy. The NLC-based hydrogel developed has a strong potential of being a safe, effective and innovative treatment option of psoriasis. Nevertheless, additional in vivo experimentation, clinical testing, and long-term stability testing are required to confirm the safety, efficacy and scalability of the formulation to commercial and clinical applications.

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