ISSN No: 0976-5921

Research Article

Formulation and characterization of a micro-transferosomal cream incorporating *Uraria picta* extract for enhanced topical anti-inflammatory efficacy

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Received: 16-08-2025 Accepted: 25-12-2025 Published: 31-12-2025

Abstract

Uraria picta, a medicinal herb traditionally used in Ayurveda, possesses notable anti-inflammatory potential attributed to its flavonoids, terpenoids, and sterols. However, its clinical application in topical therapy is limited by poor solubility and skin permeation. This study aimed to formulate and characterize a micro-transferosomal cream incorporating *U. picta* extract to enhance dermal delivery and anti-inflammatory efficacy. Methanolic leaf extract was prepared via ultrasonic extraction, phytochemically screened, and evaluated *in silico* for Cyclooxygenase receptor (COX) inhibition. Molecular docking revealed strong binding affinities for beta amyrone and rhoifolin, surpassing diclofenac, with favorable toxicity profiles. Transferosomes were prepared using soya lecithin and Span 80, characterized microscopically, and incorporated into cream bases (F1–F6). The formulations displayed uniform vesicles (11–45 µm), stable physicochemical properties (pH 7.2–7.5), smooth consistency, and no phase separation. In vitro anti-inflammatory activity, assessed via protein denaturation inhibition, showed significant efficacy of *U. picta* extract (IC_{50} = 0.34±0.22 mg/ml) compared to diclofenac (IC_{50} = 0.47±0.29 mg/ml). Formulations with optimized vesicle size demonstrated superior spreadability and stability. The results indicate that micro-transferosomal delivery substantially enhances the topical potential of *U. picta* extract, offering a promising platform for natural anti-inflammatory therapeutics.

Keywords: *Uraria picta, Molecular docking, Transferosome, Cream, Anti-inflammatory.*

Access this article online

Website: https://ijam.co.in

DOI: https://doi.org/10.47552/ijam.v16i4.6464

Introduction

Inflammation is a complex physiological response to tissue damage or microbial invasion and plays a central role in the pathogenesis of various chronic and degenerative disorders, including arthritis, psoriasis, and eczema (1). Conventional anti-inflammatory treatments often suffer from limited dermal bioavailability, systemic adverse effects, and suboptimal patient adherence. Topical drug delivery offers a localized, non-invasive alternative; however, effective transdermal penetration remains hindered by the formidable barrier properties of the stratum corneum (2). To address this challenge, nanocarrier-based systems have garnered increasing attention, with micro-transferosomes emerging as a promising platform due to their exceptional deformability and enhanced transdermal flux (3).

Micro-transferosomes are ultra-flexible lipid vesicles composed of phospholipids and edge activators that confer membrane elasticity, facilitating deeper skin penetration without compromising vesicle integrity (4). Their dynamic architecture is particularly suited for encapsulating phytoconstituents such as polyphenols and flavonoids, which typically exhibit poor aqueous solubility and limited skin permeability. By integrating the mechanical advantages of vesicular systems with the pharmacological potential of botanical compounds, micro-transferosomes offer a compelling strategy for improving the topical efficacy of herbal therapeutics (5).

Uraria picta (Jacq.) Desv, a medicinal herb deeply embedded in Ayurvedic practice, is recognized for its robust anti-inflammatory and antioxidant activities. Its phytochemical profile—encompassing flavonoids, terpenoids, and sterols—has demonstrated modulatory effects on key inflammatory mediators, including cyclooxygenase and nitric oxide synthase, suggesting its potential in managing inflammatory dermatoses. Despite these therapeutic attributes, the topical application of *U. picta* remains inadequately explored, primarily due to formulation challenges involving solubility, stability, and dermal retention (6,7).

This investigation aims to overcome these limitations by developing and evaluating a novel micro-transferosomal cream incorporating *U. picta* extract. The formulation is designed to harness the vesicle's deformability and phytoconstituent compatibility to enhance skin permeation, therapeutic efficacy, and user acceptability. Comprehensive characterization includes assessment of vesicle size, zeta potential, encapsulation efficiency, rheological behavior, and physicochemical stability. Additionally, the anti-inflammatory potential of the cream is evaluated through in vitro assays, including protein denaturation and membrane stabilization models (8-10).

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By integrating *U. picta* into a scientifically optimized micro-transferosomal carrier, the research aims to contribute to the advancement of phytopharmaceuticals in topical therapeutics. This approach aligns with current trends in sustainable drug delivery and natural product valorization, offering a robust platform for clinical translation of botanical agents in dermatological care.

Materials and Methods

Materials

U. picta leaves were collected from West Bengal Medicinal Plant Board and was authenticated by botanist Prof. Jha, BIT Mesra. The solvents (Methanol, Ethyl Acetate) were of AR grade. The egg albumin was obtained from Nice Chemical ltd. The water used in the experiments are all de-ionised water.

Details of the plant

U. picta, commonly referred to as *Prishniparni*, is a perennial herbaceous species belonging to the Fabaceae family, with a broad distribution across tropical regions of Asia. The plant is characterized by imparipinnate leaves, typically consisting of 5 to 9 linear-oblong leaflets that possess acute apices and entire margins. The upper leaflets often display variegation, with a glossy adaxial surface and a pubescent abaxial side—features that contribute to its distinct morphological identity. These leaves exhibit pinnate venation and are notably rich in bioactive compounds, including flavonoids, alkaloids, and saponins, which are associated with anti-inflammatory, antioxidant, and wound-healing activities (Figure 1). In traditional Ayurvedic medicine, *U. picta* leaves are employed in the treatment of respiratory and musculoskeletal ailments, highlighting their significance in ethnopharmacological practices (11).

Figure 1: *Uraria picta* plant

Solvent extraction by sonication

Fresh leaves of *U. picta* (50 g) were thoroughly cleaned, sun-dried, and subjected to methanolic extraction using an ultrasonic-assisted technique. The dried plant material was immersed in selected solvent, methanol which serves as the most abundantly used solvent for anti-inflammatory studies due to its high dielectric constant and amphiphilic properties, which facilitate the simultaneous recovery of diverse polar and non-polar bioactive metabolites like phenolics and terpenoids, yielding high concentrations of antioxidants necessary for effectively neutralizing pro-inflammatory mediators in various biological assays. The extraction was performed for 1 hour to facilitate solvent penetration, followed by sonication in an ultrasonic bath operating at 15 kHz (Labtronics Ltd., India) to enhance extraction efficiency. The resulting mixture was filtered to remove particulate matter, and the filtrate was concentrated under reduced pressure to eliminate residual solvent. The dried extract was stored in an airtight container at 4 °C until further use (12).

Chemical tests of the extract

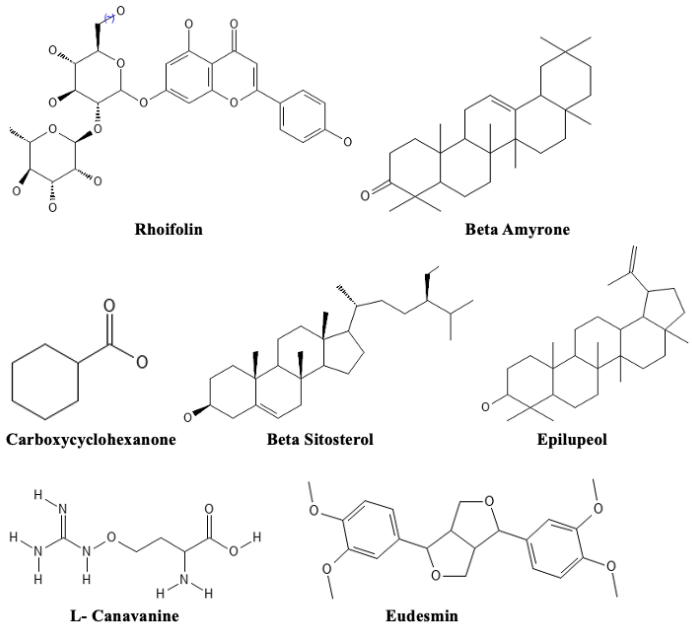
Phytochemical screening of the *U. picta* extract was conducted using a series of standard qualitative assays to identify major classes of primary and secondary metabolites. The presence of alkaloids was assessed using Wagner's and Dragendorff's reagents, while flavonoids and cardiac glycosides were evaluated via established protocols, including Baljet's test. Saponins were detected using the froth formation method, and anthraquinone glycosides were identified through Bornträger's test. Fixed and volatile oils were examined using Sudan III staining, proteins via Millon's reagent, and carbohydrates and mucilaginous substances using Molisch's test. These assays collectively confirmed the phytochemical diversity present in the methanolic extract of *U. picta* (13).

In silico anti-inflammatory studies

Ligand preparation and optimization

Based on the findings reported by Mohan et al., all phytochemical ligands identified from *Uraria picta* leaf extract via GC-MS analysis were structurally rendered using ChemDraw Professional 15.0 (Figure 2). The corresponding three-dimensional conformations were generated using Open Babel software and exported in Structure Data File (SDF) format to facilitate subsequent molecular docking and computational analysis (14).

Figure 2. Ligands from *U. picta*



COX 2 inhibitor protein preparation and optimization

The crystallographic structure of human cyclooxygenase-2 (COX-2) complexed with Vioxx (PDB ID: 5KIR) was retrieved from the Protein Data Bank. To prepare the protein for molecular docking, all water molecules were removed, and polar hydrogen atoms were subsequently added using BIOVIA Discovery Studio 2021 Client. This step ensured proper ionization states of the amino acid residues, optimizing the protein for accurate interaction analysis (15).

Molecular docking analyses and visualization

The protein structures, obtained in PDB format, were imported into the PyRx virtual screening tool, where docking simulations were conducted using the AutoDock Vina algorithm. To identify the most reliable binding conformations, energy minimization and scoring were performed within PyRx. Subsequently, molecular interactions such as hydrogen bonds, hydrophobic contacts, and π-π stacking were analyzed and visualized using Discovery Studio 2021 Client, providing insight into the binding affinities and interaction profiles of the ligand-protein complexes(16).

Toxicity prediction

The top-scoring ligands were subjected to toxicity prediction using ProTox III software in human cells (https://tox-new.charite.de/protox_III/). The webserver takes a two-dimensional chemical structure as input and reports the possible toxicity profile of the chemical for 11 models with confidence scores (17).

ADME prediction

The top-ranked ligands were retrieved in SMILES (Simplified Molecular Input Line Entry System) format from the PubChem database. These SMILES strings were then analyzed using the SwissADME web tool to evaluate their pharmacokinetic properties. The platform provided detailed insights into key ADME parameters, including molecular weight, aqueous solubility, lipophilicity, and bioavailability score, thereby facilitating the assessment of drug-likeness and therapeutic potential (18).

Formulation of transferosome

Appropriate quantities of soya lecithin and surfactant were accurately weighed and dissolved in a chloroform–methanol mixture within a round-bottom flask, as detailed in Table 1. A thin lipid film was subsequently formed using a rotary evaporator (Dlab D125) operated at 50 °C, 600 mmHg pressure, and 100 rpm for 15 minutes. To ensure complete solvent removal, the film was subjected to vacuum drying for one hour. Separately, *Urtica picta* extract was dissolved in 10 mL of phosphate buffer (pH 7.4), preheated to 55 °C. The dried lipid film was then hydrated with the warm buffer through manual shaking for 30 minutes, followed by mechanical stirring for an additional 30 minutes using an orbital shaker (Vinayak Enterprise). The resulting transferosomal suspension was examined microscopically and subsequently stored at 4 °C for further analysis (19-21).

Table 1: formulation variables used in preparation of *U. picta* transferosomes

Sl. No	Formulation	Soya lecithin : Span 80	Chloroform : Methanol	Extract
1	F1	1:1	6:4	50mg
2	F2	1:1.5	6:4	50mg
3	F3	1:2	6:4	50mg
4	F4	1:1	6:4	100mg
5	F5	1:1.5	6:4	100mg
6	F6	1:2	6:4	100mg

Evaluation of transferosome

Organoleptic properties of the freshly prepared vesicular dispersions were assessed under ambient conditions, focusing on color, odor, and overall appearance. Vesicle morphology, size distribution, and structural integrity were examined using optical microscopy at 45× magnification. For detailed visualization, a drop of the formulation was placed on a clean glass slide, covered with a cover slip, and analyzed using phase contrast microscopy (Quasmo QMM 300). Representative photomicrographs were captured for documentation purposes. All evaluations were performed in triplicate under controlled laboratory conditions to ensure consistency and reliability of the observations (22).

Preparation of transferosome based creams

In a 100 mL beaker, the oil phase comprising beeswax (4 g) and liquid paraffin (7 mL) was combined and heated to 70°C. Simultaneously, borax (2 g) was dissolved in a sufficient quantity of distilled water in a separate 100 mL beaker and also heated to 70°C. The heated oil phase was gradually added to the aqueous phase under continuous stirring while maintaining the temperature to ensure uniform emulsification. Subsequently, varying concentrations of *Uraria picta* extract-loaded transferosomes were incorporated into the emulsion to formulate six distinct cream batches, designated as F1 through F6. The final formulations were transferred into airtight containers and stored in a cool, dry environment for further evaluation (23).

Physicochemical evaluation

The herbal cream formulations underwent a comprehensive physicochemical assessment based on parameters including color, odor, consistency, physical state, pH, washability, skin irritancy, spreadability, and phase separation. Color was evaluated using a digital Color Picker application, while odor was assessed organoleptically. Visual inspection confirmed a semi-solid consistency, and manual application revealed a smooth texture. For pH analysis, 1 g of cream was dispersed in 100 mL of distilled water and allowed to equilibrate for 2 hours. The pH was measured using a calibrated digital pH meter, with the mean value calculated from three independent readings. Washability was assessed by rinsing the cream from the skin with tap water, demonstrating easy removal across all formulations. Skin irritancy was evaluated via direct application to the forearm, followed by observation for signs of erythema or irritation; no adverse reactions were noted, confirming non-irritant properties.Spreadability was tested by placing the cream between two slides, applying a defined weight and measuring the time required for separation, with better spreadability indicated by shorter separation time; calculated using the formula Spreadability = ml/t, where m = weight of cream, l = length moved, and t = time taken. Lastly, phase separation was monitored by storing the cream in a wide-mouth container, with no visible separation observed between the oil and water phases (24).

In vitro anti-inflammatory studies of the cream

Preparation of reference drug (Positive control)

Diclofenac, a commonly used non-steroidal anti-inflammatory drug (NSAID), was employed as the reference standard. Commercial diclofenac tablets were finely pulverized using a mortar and pestle. An accurately weighed quantity of 0.2 g, equivalent to the active drug content, was measured using a calibrated digital analytical balance (Sartorius PB-10). The weighed powder was then dispersed in 20.0 mL of distilled water and homogenized thoroughly using a vortex mixer to obtain a uniform solution suitable for comparative analysis (25).

Serial dilutions

Serial dilutions of the *Uraria picta* transferosome cream and the reference drug (diclofenac) were prepared in concentrations ranging from 0.1 mg/mL to 1 mg/mL, with each sample adjusted

to a final volume of 5.0mL. For the assay, reaction mixtures were composed of 2.8 mL of phosphate-buffered saline (PBS, pH 6.4) and 0.2mL of freshly prepared egg albumin solution. Subsequently, 2.0mL of each concentration of *U. picta* extract was gently added to the respective reaction mixtures.The reference drug was processed using the same protocol and served as the positive control. Distilled water was used as the negative control to validate the baseline response. All samples were prepared in triplicate to ensure reproducibility and statistical reliability (26).

Inhibition of protein denaturation

The prepared reaction mixtures were initially incubated in a thermostatically controlled water bath at 37 ± 2 °C for 30 minutes to simulate physiological conditions. Following incubation, the mixtures were subjected to thermal denaturation by heating at 70°C for 15 minutes. After heating, the samples were allowed to cool to ambient temperature for an additional 15 minutes. Absorbance readings were recorded before and after protein denaturation using a UV-visible spectrophotometer (Shimadzu UV-1900i) at a wavelength of 680 nm. All measurements were performed in triplicate, and the mean absorbance values were calculated to ensure analytical consistency and reliability (27). The percentage of inhibition of protein was determined on a percentage basis with respect to control using the following formula.

Statistical analysis

All the data reported are an average of triplicate observations. The data were expressed as means ± standard deviation

Results

Extract yield

The solvent was removed from the extracts using a rotary evaporator (Dlab D125) under vacuum. The resulting solid extract had a mean yield of 8.89% ± 0.73%. The dried extract was stored in an airtight container for subsequent analysis (28).

Chemical Tests

Various chemical tests were performed, revealing the presence of various phytoconstituents in the methanolic extract of *U.picta* depicted in Table 2.

Table 2: Presence of phytoconstituents in the extract

Chemical tests	Phytoconstituents
Alkaloid	Present
Volatile oil	Absent
Fixed Oil	Present
Protein	Absent
Carbohydrate	Absent
Flavonoids	Present
Glycoside a. Anthraquinone b. Saponin c. Cardiac	 Absent Present Absent
Gums and Mucilage	Present

Based on this table an alkaloids and flavonoid rich extract was observed which can have major effect as anti inflammatory formulation (29).

In silico studies of *U. picta*

Molecular docking studies were performed using PyRx to evaluate the binding affinities and interactions between phytochemical ligands derived from *Uraria picta* leaves and the crystallographic structures of human COX-1 (PDB ID: 6Y3C) with active pockets of Asn112, Asp116 and Gln78 in a grid pocket of 43.25 Å x 47.73 Å x 63.12 Å and COX-2 (PDB ID: 5KIR) having active pockets containing Val523 with a side pocket around Arg513 grided in 61.77 Å x 71.33 Å x 63.12 Å, with Vioxx-bound conformations serving as reference models. The binding energies of the ligands ranged from –9.6 to –4.1 kcal/mol, with β-amyrone and rhoifolin exhibiting the strongest affinities against both COX isoforms (–9.6 and –9.4 kcal/mol for COX-1; –9.2 and –8.8 kcal/mol for COX-2, respectively), surpassing the standard anti-inflammatory drug diclofenac (–7.4 and –6.0 kcal/mol) (Table 3). Visualization using Discovery Studio 2021 confirmed key interactions between active ligands and amino acid residues within the catalytic domains of COX-1 and COX-2 (Figure 3), suggesting strong antagonistic potential. Drug target prediction further validated COX inhibition as a shared mechanism among β-amyrone, rhoifolin, and β-sitosterol. Toxicity profiling via ProTox III classified these compounds within classes 4 to 6, with LD_{50} values ranging from 890 to 29,700 mg/kg, indicating low toxicity and favorable safety margins (Table 4). ADME analysis using SwissADME revealed molecular weights between 142.15 g/mol and 578.12 g/mol, with Lipinski rule violations ranging from 0 to 3 (Table 5). Although β-amyrone and rhoifolin demonstrated potent binding, their low predicted bioavailability underscores the need for advanced delivery systems—such as vesicular formulations—to enhance therapeutic efficacy. These findings support the potential of *U. picta*-derived compounds as safe and effective COX inhibitors, warranting further investigation for anti-inflammatory applications (30,31).

Table 3: Binding affinity of ligands in 5KIR & 6Y3C

Ligands	Binding Affinity (cΔG in kcal/mol)	
	5KIR	6Y3C
Beta Amyrone	-9.2	-9.6
Rhoifoline	-8.8	-9.4
Carboxycyclohexanone	-6	-6.1
Diclofenac	-7.4	-6
Beta Sitosterol	-8.4	-7.8
Lupeol	-8	-8.8
Eudesmin	-8.4	-6.8
L-canavanine	-5.6	-5.7
Epilupeol	-8.1	-8.8
Mannofuranose	-7.3	-6.2
Stigmastenone	-7.3	-7.7
Octadecanoic acid	-4.4	-4.1

Figure 3. Interaction diagram of A. 5KIR_Beta amyrone B. 5KIR_Rhoifolin C. 6y3c_Beta amyrone D. 6y3c_Rhoifolin

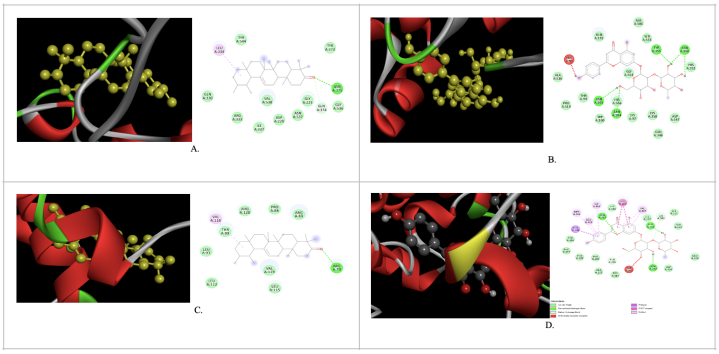


Table 4: **Toxicity prediction of Ligands**

Ligands	Level of Toxicity(1=highly	Predicted LD50(mg/kg)
Beta Amyrone	5	5000
Rhoifoline	5	5000
Carboxycyclohexanone	6	5200
Beta Sitosterol	4	890
Lupeol	4	2000
Eudesmin	4	1500
L-canavanine	4	923
Epilupeol	4	2000
Mannofuranose	6	29700
Stigmastenone	5	2300
Octadecanoic acid	4	900

Table 5: **ADME prediction of Ligands**

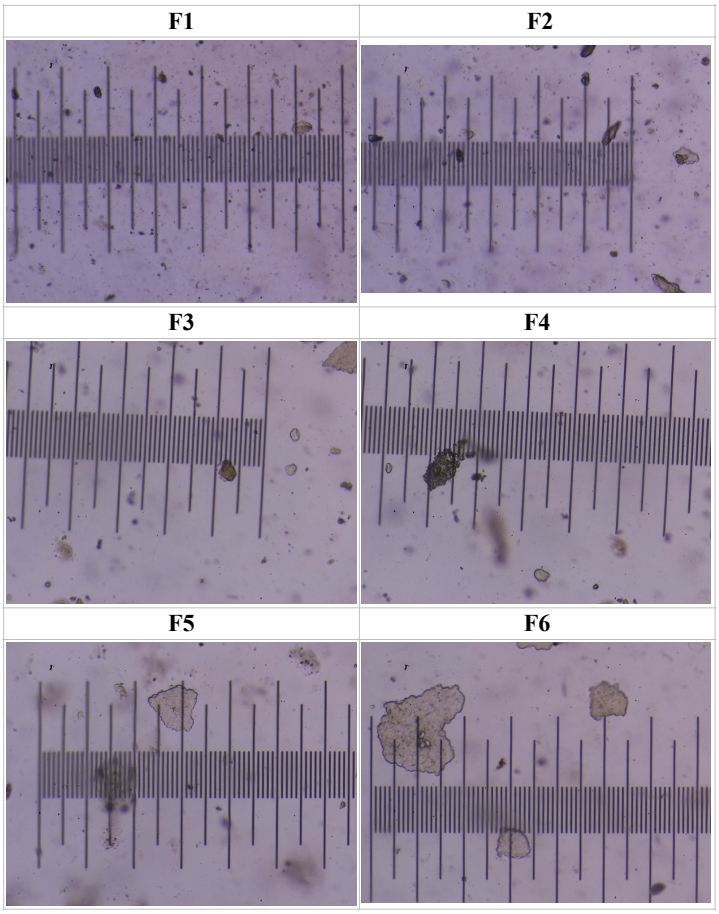
Molecule	MW	Lipinski #violations	Ali Class	Bioavailability Score
Rhoifolin	578.52	3	Moderately soluble	0.17
L Canavanine	176.17	0	Highly soluble	0.55
Eudesmin	386.44	0	Soluble	0.55
Beta Sitosterol	414.71	1	Poorly soluble	0.55
Carboxycyclo-hexanone	142.15	0	Soluble	0.85
Beta amyrone	424.7	1	Poorly soluble	0.45
Mannofuranoside	194.18	0	Highly soluble	0.55
Octadecanoic acid	284.48	1	Poorly soluble	0.85
Stigmastenone	412.69	1	Poorly soluble	0.55

Evaluation of transferosome

The organoleptic evaluation of the prepared suspension revealed a moss green color with a slimy texture and a characteristic odor. Subsequent microscopic analysis of the six transferosomal formulations (F1-F6) confirmed the presence of well-dispersed vesicular structures. Particle sizes across the formulations ranged from a mean of 11±0.9 µm to 45±1.2 µm.

A notable size gradient was observed, indicating a concentration-dependent impact of the plant extract on vesicle morphology. Formulations F1, F2, and F3, which utilized the lowest extract concentration (100 µg), exhibited the smallest particle sizes and a more homogenous size distribution. This suggests that a lower concentration of the active compound favors the formation of compact and stable vesicles, effectively preventing aggregation and fusion. Conversely, formulations F4–F6, which incorporated higher extract concentrations, resulted in larger and more heterogeneous vesicles. This phenomenon is likely due to increased internal osmotic pressure and potential membrane instability induced by the higher solute load.These findings underscore that the 100 µg extract concentration (F1–F3) is optimal for maintaining vesicular integrity and achieving a uniform size distribution (Figure 4). This precise control over particle size is critical, as it directly correlates with the potential for enhanced bioavailability and therapeutic efficacy through effective transdermal delivery (32,33).

Figure 4: Transferosome formulations (F1-F6) under microscope (45X)



Evaluation of transferosome based cream

The prepared formulation was subjected to a thorough physical evaluation to assess its quality and consistency. The organoleptic properties, including color, odor, and texture, were visually and manually inspected. The cream presented as a semisolid, white formulation with a pleasant odor. Manual application to the skin revealed a smooth and uniform consistency. These results, along with a detailed summary of the evaluation, are compiled in a tabular format (Table 6) (34).

Table 6: Physicochemical properties of transferosome based cream

Parameter	F1	F2	F3	F4	F5	F6
Color	B3B9AD (White)	B2B0A3 (White)	BABFB9 (White)	B1B7A9 (White)	BDC4B4 (White)	B0B6A8 (White)
Odor	Characteristic smell	Characteristic smell	Characteristic smell	Characteristic smell	Characteristic smell	Characteristic smell
State	Semisolid	Semisolid	Semisolid	Semisolid	Semisolid	Semisolid
Consistency	Smooth	Smooth	Smooth	Smooth	Smooth	Smooth
pH	7.2	7.2	7.4	7.3	7.3	7.5
Spreadability	0.5g.cm/s	0.3g.cm/s	0.4g.cm/s	0.3g.cm/s	0.5g.cm/s	0.4g.cm/s
Phase separation	No Phase	No Phase	No Phase	No Phase	No Phase	No Phase Separation

***In vitro* anti-inflammatory assay**

The anti-inflammatory potential of the *U. picta*-based transferosome cream was evaluated using the egg albumin denaturation method. The highest inhibition of protein denaturation was observed with the *U. picta* extract at concentrations ranging from 0.1 mg/ml to 1 mg/ml. A detailed summary of these inhibition rates is presented in Table 2. Comparing the inhibition rates, the reference drug (0.47±0.29 mg/ml) demonstrated a higher effect than the *U. picta* extract at a concentration of 0.34±0.22 mg/ml. However, these findings still indicate that the *U. picta* extract possesses promising anti-inflammatory properties, suggesting its potential for therapeutic application (Table 7) (35).

Table 7A: *In vitro* anti inflammatory activity of standard (Diclofenac)

Concentration(mg/	% inhibition	IC50 value
0.1	0.12±0.03	0.47±0.29 mg/ml
0.25	23.37±0.11	
0.5	56.14±0.09	
1	83.92±0.22	

Table 7B: *In vitro* anti inflammatory activity of transferosomal cream

Concentration(mg/	% inhibition	IC50 value
0.1	0.16±0.06	0.34±0.22 mg/ml
0.25	61.03±0.22	
0.5	60.71±0.18	
1	63.14±0.13	

Discussion

This study demonstrates the significant potential of micro-transferosomal systems to enhance the topical delivery and anti-inflammatory efficacy of *U. picta* extract. Phytochemical profiling revealed that the methanolic extract is enriched with flavonoids and saponins—bioactive classes well recognized for their ability to modulate key inflammatory mediators, including cyclooxygenases (COX) and inducible nitric oxide synthase. *In silico* molecular docking analyses provided mechanistic validation, revealing strong binding affinities of major constituents, notably β-amyrone and rhoifolin, toward the active sites of both COX-1 and COX-2 (36). Remarkably, these interactions surpassed those of the standard non-steroidal anti-inflammatory drug diclofenac, a well-established COX inhibitor, thereby substantiating the superior inhibitory potential of *U. picta* phytoconstituents at the molecular level (16). Formulation optimization indicated that micro-transferosomal vesicles prepared with 50 mg extract (F1–F3) exhibited a narrow and favorable size distribution (11–45 µm), a critical determinant for enhanced deformability and transdermal permeation. Conversely, formulations containing higher extract loads (F4–F6) produced larger and heterogeneous vesicles, likely attributable to osmotic stress and phospholipid bilayer destabilization, resulting in compromised vesicular integrity (32).

The optimized micro-transferosomal creams displayed desirable physicochemical attributes, including near-neutral pH (7.2–7.5), smooth texture, satisfactory spreadability, and excellent physical stability, supporting their suitability for topical application. Notably, in vitro anti-inflammatory evaluation demonstrated significantly greater inhibition of protein denaturation compared to diclofenac, reinforcing the enhanced therapeutic potential of the *U. picta*-loaded formulations (23,34).Collectively, the convergence of phytochemical richness, strong in silico target engagement, optimized vesicular architecture, and superior in vitro anti-inflammatory performance underscores the promise of micro-transferosomal *U. picta* cream as a novel phytopharmaceutical candidate for the management of inflammatory dermatoses. This work further highlights the strategic integration of natural bioactives with nanocarrier-based delivery platforms as an effective approach to overcome solubility and permeability constraints inherent to plant-derived therapeutics. Nevertheless, comprehensive in vivo efficacy studies, long-term stability assessments, and well-designed clinical investigations are warranted to establish translational relevance and ensure clinical safety.

Conclusion

This study demonstrates the enhanced topical delivery and anti-inflammatory efficacy of a micro-transferosomal cream formulated with *Uraria picta* extract. The methanolic extract, enriched with flavonoids and saponins, exhibited strong in silico inhibition of cyclooxygenase, with β-amyrone and rhoifolin showing higher binding affinities than diclofenac and favorable toxicity profiles. Optimized formulations containing lower extract concentrations produced vesicles ranging from 11 and 45 µm, promoting uniformity, deformability, and transdermal penetration. The creams maintained desirable physicochemical attributes, including smooth texture, neutral pH, pleasant odor, and physical stability, ensuring user acceptability and product integrity. *In vitro* protein denaturation assays revealed superior inhibition compared to diclofenac, confirming the extract's therapeutic potential. The integration of potent phytoconstituents with micro-transferosomal delivery effectively addressed challenges related to solubility, permeability, and formulation stability, positioning this system as a promising natural and safe topical intervention for inflammatory skin disorders. Further in vivo and clinical validation is recommended to support its translational applicability.

Acknowledgement

The authors would like to acknowledge Central Instrumentation Facility and Corwin Hansch Memorial CADD centre, Brainware University for providing us with all necessary instrumentation facilities to carry out the researches.

Abbreviations

mL: Millilitre; mg: Milligram; µm: Micrometre; °C: Degree Celsius; rpm: Revolutions per minute; kHz: Kilohertz; nm: Nanometre; IC_{50}: Half maximal inhibitory concentration; UV: Ultraviolet; PDB: Protein Data Bank; LD_{50}: Median lethal dose; MW: Molecular Weight; ADME: Absorption, Distribution, Metabolism, and Excretion; NSAID: Non-Steroidal Anti-Inflammatory Drug; SDF: Structure Data File; COX: Cyclooxygenase; GCMS: Gas Chromatography-Mass Spectrometry; AR: Analytical Reagent; q.s.: Quantum satis (as much as needed); g: Gram; µL: Microlitre; Å: Angstrom; pH: Potential of Hydrogen.

Funding

NA

Conflict of Interest

NA

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