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Formulation and Characterization of *Uncaria gambir* (*U. gambir*) Extract Cream as an Anti-Psoriasis Candidate: In Silico and In Vitro Studies

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Abstract

Background: Psoriasis is a chronic inflammatory skin disorder in which oxidative stress and COX-2–mediated pathways contribute to disease progression. Conventional topical therapies, particularly corticosteroids, are effective but associated with adverse effects and limited mechanistic targeting. Objective: This study investigated *Uncaria gambir* (*U. gambir*) extract as a natural anti-psoriasis candidate in a topical cream formulation through phytochemical, antioxidant, in silico, and physicochemical evaluations. Methods: The extract was screened for phenolic and flavonoid content and evaluated for DPPH radical scavenging activity (IC_{50}). Molecular docking of catechin against the COX-2 receptor was performed using quercetin as a reference. Cream formulations containing varying extract concentrations were assessed for pH, spreadability, and adhesiveness. Results: *U. gambir* extract exhibited very strong antioxidant activity (IC_{50} = 6.84 ppm), falling within the range of highly active antioxidants, although less potent than vitamin C. Catechin showed stable COX-2 binding (−4.76 kcal/mol). The 4.5% cream formulation (F2) demonstrated optimal properties, with a skin-compatible pH (~7.5) and good spreadability (~5.5 cm). Conclusion: *U. gambir* extract shows promising potential as a natural topical agent targeting oxidative stress and inflammation in psoriasis, supporting further in vivo and clinical validation.

Keywords: Psoriasis; Flavonoid; Uncaria gambir; Docking COX-2; Antioxidant

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease in which systemic inflammation and oxidative stress contribute not only to cutaneous pathology but also to metabolic disturbances, including insulin resistance. Evidence indicates that psoriasis-associated inflammation can increase the risk of progression toward type 2 diabetes, particularly at the prediabetic stage, which remains underrecognized in clinical practice (Brazzelli et al., 2021). Although metabolic screening and early intervention may help reduce long-term complications, current psoriasis management strategies rarely integrate approaches targeting oxidative stress and metabolic dysfunction. Antioxidant-based interventions have therefore been proposed as complementary strategies to improve inflammatory control while potentially mitigating metabolic risk (De Brandt & Hillary, 2022).

Conventional psoriasis therapy relies primarily on topical corticosteroids to suppress pro-inflammatory cytokines. However, prolonged use—especially at high doses—may result in local adverse effects such as skin atrophy, striae, and dermatitis, as well as systemic complications including hypothalamic–pituitary–adrenal axis suppression, osteoporosis, and metabolic disturbances (Stacey & McEleney, 2021). Notably, the use of more than 50 g/week of topical corticosteroids has been associated with an increased risk of adrenal insufficiency and osteoporosis in psoriasis patients, underscoring the need for safer long-term alternatives (Erdem, Gonul, Ozturk Unsal, & Ozdemir Sahingoz, 2024).

Natural products with antioxidant and anti-inflammatory properties have gained attention as potential adjunctive therapies (Ningsih & Rahayuningsih, 2019; Souhoka et al., 2019; Fadiyah et al., 2020; Bradic et al., 2024; Dwisari et al., 2025). *Uncaria gambir* (*U. gambir*), rich in catechin and

epicatechin (>21%), has demonstrated the ability to inhibit key inflammatory mediators such as TNF-α, IL-1, COX-2, and iNOS (Auliana et al., 2022; Ho et al., 2022). However, despite these findings, no previous studies have systematically developed and evaluated topical cream formulations of *U. gambir* for psoriasis therapy. This study addresses this gap by formulating and characterizing a *U. gambir* extract cream and assessing its bioactive potential through antioxidant testing and in silico COX-2 analysis, thereby contributing a practical formulation-based approach beyond prior phytochemical and in vitro studies.

METHODOLOGY

Research Designs

Statistical analysis was not performed in this study because the number of observations for each method was fewer than five. In general, a minimum of five independent measurements is required to meet basic assumptions for inferential statistical analysis. As this work was designed as a preliminary exploratory study, the data were evaluated descriptively to observe trends rather than statistical significance. Further studies with adequate replication are required to allow robust statistical analysis and validation of the results (Lakens, 2022).

Materials and Instrumentals

The materials and instruments used in this study were categorized into two groups: in silico and in vitro. For in silico analysis, the computational setup included a laptop equipped with 8 GB RAM, a 12th Gen Intel® Core™ i5-1235U processor (10 cores, 1.30 GHz), and the following software: ChemDraw Professional v12.0 (Informer Technologies, Inc., USA), AutoDock Vina (Molecular Graphics Laboratory, The Scripps Research Institute, USA), and BIOVIA Discovery Studio Visualizer 2021 (Dassault Systèmes, France).

For in vitro experiments, the following materials and reagents were used: *Uncaria gambir* (*U. gambir*) leaves, obtained online from local farmers in Sungai Mas, Banyuasin, West Sumatra, Indonesia; ethanol 96% and ethanol 90% (local pharmaceutical grade); lanolin (Brataco, Indonesia); stearic acid (Merck, Germany); nipagin (methylparaben) and nipasol (propylparaben) (Brataco, Indonesia); liquid paraffin (Brataco); propylene glycol (Sigma-Aldrich, USA); vaselinum album (Brataco); trichloroacetic acid (TCA – Merck KGaA, Darmstadt, Germany); thiobarbituric acid (TBA – Merck KGaA, Germany); Naphthyl ethylenediamine dihydrochloride (NED – Merck KGaA, Germany); sodium nitrate ($NaNO_3$ – Merck KGaA, Germany); 2,2-diphenyl-1-picrylhydrazyl (DPPH – Sigma-Aldrich, St. Louis, MO, USA); and hydrochloric acid (HCl – Sigma-Aldrich, USA). Additional equipment included a digital caliper, pH meter (Eutech Instruments, Singapore), light microscope (Olympus CX21, Japan), and a magnetic stirrer-heater (IKA, Germany).

Methods

In silico Study

Ligands Preparation

The ligands used in this study included catechin as the test compound, following previous studies (Dharsono et al., 2022; Kurnia et al., 2021). The three-dimensional structure of catechin was obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) with PubChem CID: 9064. Ligand preparation involved energy minimization using the MM2 method in ChemDraw Professional v12.0 (Informer Technologies, Inc., USA). Quercetin (PubChem CID: 5280343) was employed as a positive control. Both ligands were further prepared using AutoDock Tools version 1.5.6 (The Scripps Research Institute, USA) by assigning Gasteiger charges, adding nonpolar hydrogens, and setting rotatable bonds (torsions). The prepared ligand files were saved in .pdbqt format for molecular docking analysis (Khoirul Rista Abidin, Ariffialdi Nurhidayatulloh, & Nurmah, 2024; Kurnia et al., 2021; Maheswari & Salamun, 2023).

Receptors Preparation

The receptor used in this study was the COX-2 enzyme, with its crystal structure retrieved from the Protein Data Bank (https://www.rcsb.org/) under PDB ID: 6COX. The receptor was cleaned by removing water molecules and non-essential co-crystallized ligands using Discovery Studio Visualizer 2021 (Dassault Systèmes, France). Subsequent receptor preparation was performed using AutoDock Tools version 1.5.6 (The Scripps Research Institute, USA), where polar hydrogens were added, and Kollman charges were assigned. The prepared receptor was then saved in .pdbqt format for docking analysis (Abidin, Meliala, & Rini, 2023; Kurnia et al., 2021).

Docking Analysis

Molecular docking was performed using AutoDock Tools version 1.5.6 with the AutoDock Vina algorithm. The grid box was set to a size of $40 \times 40 \times 40$ points with a spacing of 0.375 Å. The center of the grid was positioned at coordinates X: 47.060, Y: 25.441, Z: 36.961, which corresponds to the active site of the COX 2 enzyme based on its crystal structure. Docking simulations were carried out using the Lamarckian Genetic Algorithm (LGA) with a run

time of 100 ns, employing default parameters from AutoDock. Binding affinity values were calculated in kilocalories per mole (kcal/mol), and molecular interactions with amino acid residues were analyzed using Discovery Studio Visualizer 2021 (Dassault Systèmes, France) in two-dimensional (2D) representation (Abidin et al., 2023).

In vitro Study

Extraction of *U. gambir*

The *U. gambir* leaf samples were taxonomically authenticated, with identification confirmed by certificate No. 172/A/LB/FMIPA/UNTAN/2025. The leaves were shade-dried in a well-ventilated area with indirect sunlight exposure, avoiding direct solar radiation, and subsequently milled into a fine powder. A total of 400 g of dried leaf powder was extracted using 2.5 L of 96% ethanol by maceration for 3 × 24 h at room temperature in a closed container. The mixture was filtered every 24 h, and the remaining residue was re-macerated using approximately 1.5 L of fresh solvent. All filtrates were combined to obtain approximately 5 L of extract solution, which was concentrated using a rotary evaporator at 40–50 °C, followed by further evaporation in a water bath to yield a viscous crude extract

Phytochemical Analysis

A total of 2 g of leaf extract was weighed, diluted in 96% ethanol, and homogenized. For the phenolic test, 1 mL of the extract was placed in a test tube and 2 drops of 5% $FeCl_3$ solution were added. For the flavonoid test, 1 mL of extract was mixed with 0.1 g of magnesium powder and 2–3 drops of hydrochloric acid (HCl). For the tannin test, 1 mL of extract was diluted in 5 mL of hot water, cooled, then centrifuged for 5 minutes. The supernatant was separated, NaCl was added, and the mixture was filtered. Two drops of 1% $FeCl_3$ were then added to the filtrate (Hidayati & Rahmatulloh, 2022). For the saponin test, 2 mL of extract was placed in a test tube, combined with 5 mL of distilled water, vigorously shaken for 30 seconds, and observed for the formation of stable foam over 10 minutes. For the triterpenoid test, 1 mL of extract was mixed with 3 mL of chloroform, followed by the dropwise addition of Liebermann–Burchard reagent. For the alkaloid test, 5 mL of extract was mixed with 5 mL of 2M HCl, heated for 5 minutes, then 0.5 g of NaCl was added, stirred, and filtered. Three drops of 2M HCl were added to the filtrate, which was then divided into two tubes: Tube 1 received Wagner's reagent, while Tube 2 served as the control without reagent.

Antioxidant Analysis

A 0.1 mM DPPH solution was prepared in analytical-grade ethanol (p.a.) and stored in a dark bottle or wrapped in aluminum foil to prevent photodegradation. The U. gambir extract was prepared at concentrations of 5, 10, 15, 20, 40, 60, 80, and 100 ppm. Vitamin C (100 ppm) was used as a positive control. For each concentration, 2 mL of extract or control solution was mixed with 2 mL of DPPH solution. A DPPH control (without sample) and a blank (ethanol only) were included. The mixtures were protected from light, incubated at room temperature for 30 min, and the absorbance was measured at 516 nm using a UV–Vis spectrophotometer. All measurements were performed in a single run without duplicate or triplicate replication. The percentage of inhibition was calculated using the absorbance of the control (A_0) and sample (A_1), and the IC_{50} value was estimated using linear or logarithmic regression analysis (Hidayati & Rahmatulloh, 2022; Ningsih & Rahayuningsih, 2019).

Extract Cream Preparation

The cream preparation method for psoriasis was adapted from a previous protocol with several modifications to accommodate the availability of formulation ingredients (Tram & Son, 2015). The process began with the preparation of the oil phase by adding vaselin album and stearic acid into a beaker. The mixture was heated on a hotplate at approximately 70 °C until melted and homogeneous. Subsequently, *U. gambir* extract was incorporated at weights corresponding to the formulation design presented in Table 1.

Table 1. Cream Composition Formulas

Cream Compounds	F0 (0%)	F1 (2%)	F2 (4.5%)	F3 (7%)
Gambir extract (g)	0	2	4.5	7
Album vaseline (g)	8	8	8	8
Stearate Acid (g)	07.05	07.05	07.05	07.05
TEA (g)	0,052 083	0,052 083	0,0520 83	0,052 083
Glycol Propylene (g)	4	4	4	4
Nipagin (g)	0.075	0.075	0.075	0.075
Aquadest (ml)	.s 50	q.s 50	q.s 50	q.s 50

The preparation continued with the aqueous phase, in which nipagin was dissolved in distilled water heated and maintained at approximately 70 °C.

Propylene glycol and triethanolamine (TEA) were then added to the solution and stirred until homogeneous. Emulsification was carried out by slowly pouring the aqueous phase into the oil phase while continuously stirring with a magnetic stirrer at a constant temperature of approximately 70 °C for 15 minutes. After homogenization, the mixture was removed from the heat source and manually stirred until the temperature decreased to room temperature (~30 °C), allowing the cream to form completely. Following emulsification, the cream was transferred into sterile containers and subjected to further characterization tests.

Analysis of Cream Characteristics

Analysis of Organoleptic

Organoleptic evaluation was performed by observing the creams prepared in various formulations (F0–F3). To assess the stability of the creams over time, organoleptic testing was conducted by comparing their appearance on day 0 and day 14 after preparation, during storage at room temperature (Mailana, Nuryanti, & Harwoko, 2016).

Adhesion Analysis

An amount of 0.5 g of the cream preparation was weighed and placed on a glass slide, then covered with another glass slide until both surfaces adhered. The two slides were then subjected to a 1 kg load for 5 minutes, after which the load was removed and an additional 80 g weight was applied at one end of the slides. The time required for the two slides to detach was recorded as the measurement result. The procedure was repeated three times.

Homogenity Analysis

A total of 0.1 g of the cream preparation was weighed and evenly spread in a thin layer on a watch glass, after which its texture and color were observed. The preparation was considered homogeneous if it exhibited a uniform texture and color with no visible clumps. The test was repeated three times.

Spreadibility Test

An amount of 0.5 g of the cream preparation was weighed and placed in the center of a glass slide, then covered with another glass slide. After being left to stand for 1 minute, the spread diameter of the cream was measured both vertically and horizontally. Subsequently, a 150 g weight was placed on the upper slide for 1 minute, after which the diameter was measured again using a caliper. The procedure was repeated three times.

pH Measurement Test

The pH was measured by weighing 1 g of the cream and dissolving it in 10 mL of distilled water, followed by stirring until homogeneous. The measurement was then performed using a pH meter. Each measurement was repeated three times, and the average value was recorded. The procedure was carried out in triplicate.

RESULTS AND DISCUSSION

In silico Analysis

The docking analysis between catechin ligand and COX-2 yielded a binding energy value of −4.76 kcal/mol. Quercetin exhibited a lower binding energy of −8.05 kcal/mol, indicating a higher affinity sfor COX-2 compared to catechin. The 2D interaction visualization (Figure 1) showed that catechin interacted with several key residues in the active site of COX-2, including ASP-A:43, ASN-A:34, and ALA-A:33, through hydrogen bonding and hydrophobic interactions. In contrast, quercetin formed broader interactions with residues GLN-A:192, ARG-A:376, TYR-A:371, and GLY-A:225, thereby enhancing the stability of the protein–ligand complex.

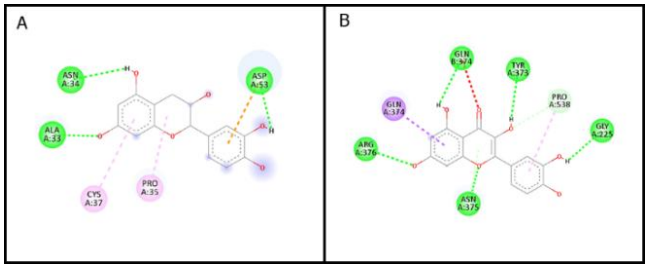

Figure 1. 2D Docking Visualization of catechin ligand with COX-2 (A) and quercetin with COX-2 (B)

The differences in ligand affinity toward COX-2 reflect variations in the structural and chemical properties of the compounds. Quercetin, with more substituted aromatic rings and a greater number of hydroxyl groups compared to catechin, allows the formation of additional hydrogen bonds and π–π stacking interactions, thereby resulting in a more stable binding.

Previous studies have indicated that the presence of hydroxyl groups at strategic positions can enhance interactions with the active residues of COX-2, thereby strengthening the anti-inflammatory effects of flavonoid compounds (Pires et al., 2021). Although catechin exhibits lower affinity, its ability to interact

with the active pocket of COX-2 still demonstrates potential as a partial inhibitor. With structural optimization or derivatization, the effectiveness of catechin could be further improved for anti-inflammatory therapeutic applications, aligning with the development of flavonoid-based COX-2 inhibitors from natural sources such as *U. gambir*.

***U. gambir* extraction**

After the extraction and evaporation processes were completed, a thick gambir extract was obtained with a final weight of approximately 26.8 g. The extract exhibited a dark brown to blackish color, a strong characteristic gambir odor, and a thick paste-like texture with slight clumping. Its form was irregular, with moderate homogeneity, although some clumps were still present. These organoleptic characteristics reflect the high concentration of active compounds resulting from the heating and solvent evaporation processes. The visual results of the organoleptic observation are presented in Figure 2, while detailed evaluations are provided in Table 2.

Figure 2. Ethanol Extract of *U. gambir* after Evaporation Process

The organoleptic test results of gambir extract in this study—characterized by a dark brown to blackish color, distinctive odor, thick paste-like texture, and moderate homogeneity with some clumps—are consistent with the findings of Liony (2014) on gambir-extract-based sunscreen cream, where increasing extract concentration intensified the color, enhanced the aroma, and reduced texture smoothness (Liony, 2014). Furthermore, a study by Jannah & Fajarini (2024) on beverages combining robusta coffee and gambir extract reported the highest organoleptic preference scores for aroma, taste, and color, with ratings approaching "like" at a 10% gambir extract formulation (Jannah & Fajarini, 2024)

These combined findings reinforce that despite its concentrated and less homogeneous form, gambir extract is generally acceptable in both food and cosmetic formulations at appropriate extract levels. This also provides a basis for further formulation development, such as improving texture smoothness or enhancing homogeneity through controlled evaporation processes or the use of stabilizing additives to optimize organoleptic acceptance without diminishing the characteristic intensity of gambir.

Table 2. The Results of Organoleptic Analysis

Parameters	Results	Score
Color	Dark brown to blackish	4
Odor	Characteristic gambir, slightly pungent	4
Texture	Thick paste, slightly clumped	3
Form	Soft solid mass, irregular shape	3
Homogeneity	Moderately homogeneous, presence of large clumps	3

The organoleptic evaluation of gambir extract in this study—characterized by its dark brown to blackish color, distinctive odor, thick paste-like texture, and moderate homogeneity with some clumping—was consistent with the findings of Liony (2014) on gambir-extract-based sunscreen cream, where higher extract concentrations resulted in deeper color, stronger aroma, and reduced texture smoothness (Liony, 2014). Similarly, Jannah & Fajarini (2024) reported that a beverage combining robusta coffee with gambir extract achieved the highest organoleptic preference for aroma, taste, and color, with scores approaching "like" at a 10% gambir extract formulation (Jannah & Fajarini, 2024).

Collectively, these findings suggest that despite its concentrated and less homogeneous characteristics, gambir extract is generally acceptable in both food and cosmetic formulations at appropriate levels. This also provides a foundation for further formulation improvements, such as enhancing texture smoothness or increasing homogeneity through controlled evaporation processes or the incorporation of stabilizing additives, thereby improving organoleptic acceptance without diminishing the distinctive attributes of gambir.

Phytochemical Analysis

Phytochemical screening of *U. gambir* extract revealed the presence of phenols, flavonoids, saponins,

and alkaloids, as indicated by positive results in the respective specific tests (Table 3). In contrast, tests for tannins and triterpenoids yielded negative results, indicating the absence of these metabolite groups in the sample. The presence of phenols and flavonoids suggests potential antioxidant activity, whereas saponins and alkaloids may contribute to other biological effects such as antibacterial and anti-inflammatory properties.

Table 3. Phytochemical Analysis of *U. gambir* Extract

Test Parameter	Result
Phenol test	Positive (+)
Flavonoid test	Positive (+)
Tannin test	Negative (−)
Saponin test	Positive (+)
Alkaloid test	Positive (+)
Triterpenoid test	Negative (−)

Phytochemical screening of *U. gambir* extract confirmed the presence of phenols, flavonoids, saponins, and alkaloids, while tannins and triterpenoids were not detected (Table 3). The presence of phenols and flavonoids is consistent with the report of Auliana et al. (2022), which stated that *U. gambir* extract is rich in polyphenols, particularly catechins, contributing to its antioxidant and anti-inflammatory activities (Auliana et al., 2022). Another study by Pradana et al. (2022) reported that phenolic compounds in gambir exhibit strong free radical scavenging capacity (IC_{50} DPPH = 9.71 µg/mL) (Hidayati & Rahmatulloh, 2022). The presence of alkaloids and saponins has also been reported by Farhana et al. (2019), who associated these compounds with antibacterial effects against Streptococcus mutans (Hidayati & Rahmatulloh, 2022). These findings are consistent with the study of Abdurrahman et al. (2019), which demonstrated that saponins in medicinal plants play a role in anti-inflammatory activity (Ningsih & Rahayuningsih, 2019).

Antioxidant Analysis

The antioxidant activity assay using the DPPH method (Table 4) showed an increase in percentage inhibition with rising extract concentrations from 5 to 40 ppm, with mean inhibition values of 30.90% at 5 ppm, 51.65% at 10 ppm, and a maximum of 87.66% at 40 ppm. At higher concentrations (60–100 ppm), the inhibition values fluctuated and slightly decreased (80.41–82.06%), indicating saturation of radical scavenging activity. This saturation effect resulted in a non-linear response across the tested concentration range, which explains the relatively low coefficient of determination obtained from linear regression analysis (R^2 = 0.381). Therefore, the relationship between concentration and inhibition percentage was not adequately described by a simple linear model. Accordingly, IC_{50} determination was performed using a log-linear (ln) regression approach (Figure 3), yielding an IC_{50} value of 6.84 ppm for U. gambir extract.

Table 4. DPPH Test of *U. gambir* Extract

Conc. (ppm)	Replication 1		Replication 2		Replication 3		Mean Inhibition (%)
	Abs	% Inhibition	Abs	% Inhibition	Abs	% Inhibition	
0	0.37	–	0.37	–	0.4	–	0
5	0.25	1.36	0.26	1.24	0.25	38.86	30.90
10	0.18	2.18	0.18	2.13	0.1	74.61	51.65
15	0.11	70.97	0.08	3.21	0.11	3.04	3.08
20	0.09	81.65	0.07	3.34	0.08	84.63	80.86
40	0.07	86.89	0.06	3.7	0.073	3.65	87.66
60	0.08	3.26	0.09	82.73	0.09	82.90	3.36
80	0.07	86.89	0.08	3.22	0.08	84.80	3.42
100	0.08	3.29	0.08	84.82	0.1	74.96	81.92

Note: Abs (Absorbance), Conc. (Concentration)

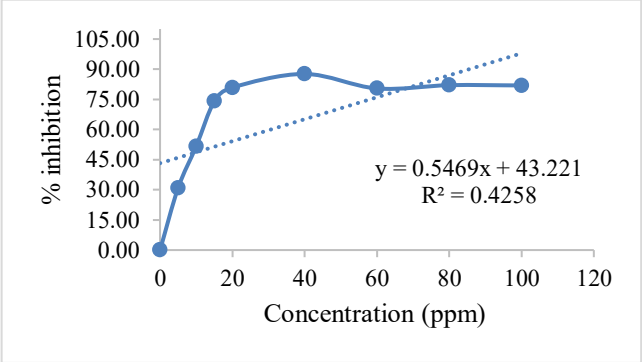

Figure 3. The Curve of DPPH Test of *U. gambir* Extract

The antioxidant activity test of vitamin C showed that the percentage of inhibition increased with rising concentrations from 0 to 12 ppm. As presented in Table 5, vitamin C at a concentration of 2 ppm already exhibited an inhibition effect of 0.71%, which continued to increase to 0.98% at 12 ppm. The curve in the figure displayed a positive trend with a linear regression equation of y = 0.0669x + 0.3769 and an R^2 value of 0.5992, indicating a moderate relationship between concentration and DPPH inhibition. However, the relationship was not entirely linear, particularly at lower concentrations where the inhibition response rose sharply. Therefore, calculation of the IC_{50} value is more accurately performed using a log-linear regression model (Figure 4).

Table 5. DPPH Test of Vitamin C

Concentration (ppm)	Absorbance	% Inhibition
0	0.04	0
2	0.11	0.05
4	0.07	0.06
6	0.033	0.07
8	0.024	0.07
12	0.011	0.07

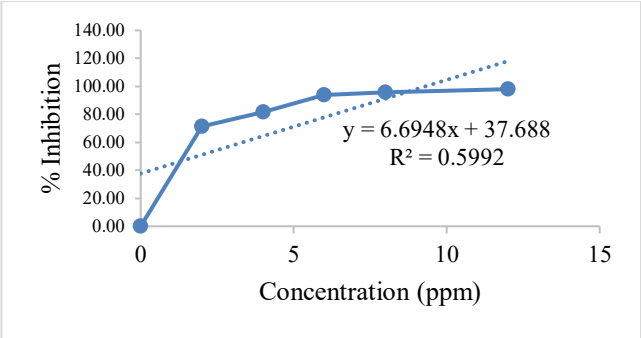

Figure 4. The Curve of DPPH Test of Vitamin C

The results of this study are consistent with the typical behavior of the DPPH assay, where antioxidant activity increases proportionally at lower concentrations and reaches a plateau at higher concentrations. Accordingly, IC_{50} determination was performed using a log-linear (In) regression model rather than simple linear regression, as this approach more accurately describes the non-linear concentration–inhibition relationship (Srinivasan & Lloyd, 2024; Xiao, Kai, & Yamamoto, 2020). The IC_{50} value of *U. gambir* extract (6.84 ppm) indicates very strong antioxidant activity. This finding aligns with previous reports showing that methanolic *U. gambir* extract exhibited a DPPH IC_{50} of 9.71 µg/mL and strong ABTS activity (IC_{50} = 6.63 µg/mL) (Hidayati & Rahmatulloh, 2022). Compared with standard antioxidants, vitamin C and vitamin E have also demonstrated strong activity, although vitamin C is generally more potent (Laksono et al., 2023; Hamrun, Djamaluddin, & Dahri, 2022).

Comparable studies have demonstrated that antioxidants within this IC_{50} range effectively suppress inflammatory signaling pathways. Specifically, strong polyphenolic antioxidants have been shown to downregulate interleukin-6 (IL-6) expression by inhibiting oxidative stress–mediated NF-κB activation, a key mechanism implicated in psoriasis pathogenesis (Dobrică, Cozma, Găman, Voiculescu, & Găman, 2022). Catechin-rich extracts with IC_{50} values below 10 ppm have also been reported to significantly reduce IL-6 and TNF-α production in keratinocyte and macrophage models (Pires et al., 2021).

Thus, the strong antioxidant capacity of *U. gambir* provides a plausible mechanistic basis for its potential anti-inflammatory effects in psoriasis. Nevertheless, this study is limited to in vitro and in silico evaluations. No in vivo or clinical studies were conducted to directly confirm IL-6 suppression or therapeutic efficacy. Therefore, further investigations using psoriasis animal models and clinical trials are required to validate these preliminary findings and establish translational relevance.

Cream Preparation

Organoleptic Analysis

The gambir extract cream was successfully formulated in three concentration variations: F0 (without extract), F1 (2%), F2 (4.5%), and F3 (7%). Visually, F0 exhibited a homogeneous white color, neutral odor, and soft texture. The addition of gambir extract in F1 produced a light brown color, a mild characteristic gambir aroma, and a thick texture with good homogeneity. F2 showed a medium brown color with a stronger gambir aroma, whereas F3 displayed a dark brown color with the most intense aroma. The cream formulations are presented in Figure 5, and the organoleptic evaluation results are shown in Table 6.

Figure 5. Organoleptic Test of *U. gambir* Cream

Table 6. Organoleptic Comparison of *U. gambir* Cream

Parameter	Day 0			
	F0	F1	F2	F3
Color	White	Greenish brown	Yellowish brown	Greenish brown
Odor	None	Characteristic gambir	Characteristic gambir	Characteristic gambir
Consistency	Thick	Thick	Thick	Thick
Parameter	Day 14			
	F0	F1	F2	F3
Color	White	Dark brown	Light brown	Medium brown
Odor	None	Mild gambir odor	Moderate gambir odor	Strong gambir odor
Consistency	Soft, easily spread	Thick, slightly dense, homogeneous	Thick, homogeneous, slightly soft	Very thick, slightly sticky, homogeneous

An increase in gambir extract concentration in the cream formulation demonstrated a positive correlation with color and odor intensity. The higher the concentration, the darker the cream color and the more dominant the gambir aroma, which is most likely due to the accumulation of pigments and volatile compounds in the suspended phase. This also affected the texture properties; concentrated extract tended to increase viscosity and compactness of the emulsion matrix, making the cream feel thicker and less smooth during organoleptic testing. These findings are consistent with reports on the effects of plant extracts on the rheological and organoleptic properties of emulsions, where extract addition can modify the consistency index and viscoelasticity of semi-solid products (Bradic et al., 2024; Morávková & Stern, 2019).

Moreover, several formulation studies have shown that the presence of active plant constituents influences the parameters of color, odor, and viscosity of the final product, requiring adjustments in the formulation base (e.g., type of emulsifier or addition of stabilizing gums/polymers) to maintain the desired sensory characteristics without reducing the functional extract content (Ziarno, Kozłowska, Ratusz, & Hasalliu, 2023). Overall, all three formulations (F0, F1, F2, and F3) met the basic organoleptic criteria for creams; however, recommended improvements include optimizing extract concentration and selecting texture-conditioning agents to enhance smoothness and homogeneity while preserving the desired color and aroma profile (Karsheva & Georgieva, 2010).

Adhesion Test

Based on Table 7, the adhesion test results showed that formulations F0 (0%), F1 (2%), and F3 (7%) exhibited adhesion times of more than 1 minute in all repetitions, indicating good adhesive properties of the creams. In contrast, formulation F2 (4.5%) demonstrated variable adhesion times, namely 55 seconds in the first repetition, 33 seconds in the second repetition, and more than 1 minute in the third repetition.

Table 7. Adhesion Test of *U. gambir* Extract Cream

Formulation	Replication 1	Replication 2	Replication 3
F0	> 1 minute	> 1 minute	> 1 minute
F1	> 1 minute	> 1 minute	> 1 minute
F2	55 seconds	33 seconds	> 1 minute
F3	> 1 minute	> 1 minute	> 1 minute

The adhesion test of *U. gambir* extract cream showed that formulations F0 (0%), F1 (2%), and F3 (7%) exhibited adhesion times of more than 1 minute in each repetition, indicating good and stable adhesive properties. In contrast, formulation F2 (4%) demonstrated variability in adhesion time, ranging from 33 to 55 seconds, which may be attributed to differences in the homogeneity of extract distribution within the cream matrix or localized changes in viscosity. According to Pratasik et al. (2019), adhesive strength is an important indicator of the resistance of topical preparations to detachment or loss of contact with the skin, which directly affects their therapeutic effectiveness (Suhesti, Antari, Nasrina, & Putra, 2025).

Furthermore, in topical emulsions, rheological properties such as adhesiveness and cohesiveness are strongly associated with user sensory experience and the physical stability of the formulation (Stabrauskiene et al., 2025). The lower adhesion performance observed in F2 suggests a potential reduction in surface contact during application, indicating the need for optimization of the cream base, such as adjusting emulsifier concentration or adding viscosity enhancers to strengthen adhesion, particularly at intermediate extract concentrations.

Homogeneity test

Based on Table 8, homogeneity testing was conducted to ensure uniform distribution of components within the gambir extract cream formulations, without the presence of coarse particles

or phase separation. Observations revealed that all formulations—F0 (control), F1, F2, and F3—exhibited consistent characteristics with smooth texture and uniform color. No clumps, solid particles, or phase separation were detected in any of the tested preparations. These findings indicate that the mixing and stirring processes during formulation were optimal, resulting in homogeneous creams across all formulations.

Table 8. Homogeneity Test of *U. gambir* Extract Cream

Formulation	Homogeneous
F0	Yes
F1	Yes
F2	Yes
F3	Yes

These findings are consistent with the study by Singh et al., which reported that the homogeneity of herbal creams is influenced by stirring speed and duration, the type of emulsifier, and the viscosity of the cream base. Furthermore, good homogeneity also supports physical stability during storage, thereby preventing changes in color, odor, and texture (Singh et al., 2015).

Spreadability Test

Based on the measurements presented in Table 9, the base cream (F0) demonstrated a relatively wider spreadability compared to the formulations containing *U. gambir* extract, both before and after the application of load. Formulation F2 (4.5%) exhibited fairly good spreadability (4.8/4.6 cm before load and 5.5/5.2 cm after load), closely approaching that of the F0 control. In contrast, F1 (2%) showed the smallest spreadability before load (2.2–2.7 cm), although an increase was observed after load was applied. Meanwhile, F3 (7%) displayed lower spreadability than F2, both before and after the load application.

Table 9. Spreadibility Test of *U. gambir* Extract Cream

Replication	F0 (0%) H/V	F1 (2%) H/V	F2 (4.5%) H/V	F3 (7%) H/V
Before Load				
1	4.4 / 4.4	2.3 / 2.7	4.8 / 4.6	3.1 / 2.7
2	3.1 / 3.6	2.2 / 2.7	2.8 / 2.9	2.7 / 2.8
3	2.3 / 2.7	2.4 / 2.4	3.3 / 3.4	2.6 / 2.7
After Load				
1	5.1 / 5.2	2.9 / 3.3	5.5 / 5.2	3.7 / 3.4
2	3.9 / 4.2	3.3 / 3.6	4.5 / 4.3	2.8 / 3.9
3	3.4 / 3.6	4.2 / 4.1	3.3 / 3.4	3.9 / 3.6

Note: H = Horizontal, V = Vertical.

The spreadability test results presented in Table 9 indicate that the base cream (F0) exhibited a wider spreading ability compared to formulations containing *U. gambir* extract. This may be attributed to the increased viscosity of the cream caused by the addition of the extract, which reduced its ability to spread evenly (Indriatmoko, Suryani, Rudiana, & Kurniah, 2021). Formulation F2 (4.5%) exhibited spreadability values most comparable to the base formulation (F0) both before and after load application, indicating that this concentration achieved an optimal balance between extract incorporation and cream viscosity. At this level, the extract concentration was sufficient to deliver bioactive compounds without excessively increasing internal resistance or structural rigidity of the semisolid matrix, which commonly reduces spreadability at higher concentrations. Such behavior is consistent with semisolid formulation principles, where moderate increases in active content can maintain favorable rheological properties, while excessive loading leads to decreased flow and application performance (Mishra, Singh, Gupta, & Bansal, 2010).

In contrast, F1 (2%) demonstrated the lowest spreadability before load, although an improvement was observed after load application. This phenomenon may be related to a denser internal structure of the cream at lower concentrations, which became easier to spread under pressure. Formulation F3 (7%) exhibited reduced spreadability, indicating that increasing extract concentration beyond the optimum point increases viscosity and decreases spreading characteristics (Manian, Jain, Vora, & Banga, 2022). These findings confirm that the 4.5% extract formulation (F2) is the most suitable choice for the development of *U. gambir* extract cream.

pH Level Test

The pH test results (Table 10) of the creams showed that the base formulation without extract (F0) had the highest average pH value (8.03), whereas formulations with the addition of *U. gambir* extract demonstrated a decrease in pH with increasing extract concentration—F1 (2%) at 7.88, F2 (4%) at 7.54, and F3 (7%) with the lowest value at 6.86. This pattern

indicates that *U. gambir* extract possesses relatively acidic chemical properties, such that higher extract concentrations directly reduced the pH of the system.

Table 10. pH Level Test of *U. gambir* Extract Cream

Replication (x)	F0	F1 (2%)	F2 (4.5%)	F3 (7%)
1	7.98	7.82	7.77	6.86
2	8.14	7.98	7.35	6.86
3	7.98	7.84	7.49	6.86
Average	8.03	7.88	7.54	6.86

Although mildly acidic formulations (pH 4–6) are generally considered optimal for maintaining epidermal function and skin microbiome balance (Lukić, Pantelić, & Savić, 2021), all formulations in the present study exhibited near-neutral to slightly alkaline pH values (6.86–8.03). While these values deviate from the ideal physiological skin pH, they remain within the acceptable safety range for topical preparations and are commonly observed in preliminary cream formulations prior to pH optimization.

Slightly lower pH values observed in formulations F2 and F3 indicate a concentration-dependent effect of the extract, suggesting potential for adjustment toward a more skin-compatible range. Previous studies have shown that acidic formulations (pH ≈ 4.5) can enhance skin barrier function and hydration (Blaak et al., 2020). However, achieving such conditions often requires further formulation refinement. From a formulation perspective, extract concentrations of 2–4% (F1 and F2) provided a balance between maintaining acceptable pH and delivering bioactive content, indicating their suitability as candidate formulations for subsequent optimization.

CONCLUSION

This study is the first to develop and evaluate a topical cream formulation of *U. gambir* extract as a potential anti-psoriasis agent. The extract exhibited very strong antioxidant activity (IC_{50} = 6.84 ppm), and in silico analysis showed that catechin can interact with the COX-2 receptor, supporting its anti-inflammatory potential. The F2 formulation (4.5%) demonstrated the most favorable physical characteristics. However, the findings are limited to in vitro and in silico analyses, and in vivo and clinical studies are required to confirm efficacy and safety. These results provide a basis for further pharmaceutical development of natural topical alternatives to long-term corticosteroid therapy.

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