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Abstract

Cannabis sativa and *Curcuma longa* have traditionally been used for the management of skin disorders; however, scientific evidence supporting their combined topical use in eczema and psoriasis remains limited. To characterize the phytochemical composition, evaluate the biological activities, investigate potential molecular mechanisms, and assess the preliminary clinical performance of a topical herbal cream containing *C. sativa* and *C. longa* extracts. Ethanolic extracts were analyzed using UHPLC and GC-MS. Antioxidant, antibacterial, cytotoxicity, and nitric oxide inhibition assays were performed. Molecular docking studies were conducted against inflammation-related protein targets. A pilot clinical study evaluated the effects of the herbal cream in patients with eczema and psoriasis over four weeks using EASI, PASI, and DLQI scores. The herbal formulation contained cannabinoids, terpenoids, and curcuminoids with measurable antioxidant activity. The extract exhibited low cytotoxicity and moderate inhibition of nitric oxide production in LPS-stimulated macrophages. Docking analyses suggested favorable interactions between selected phytochemicals and inflammation associated targets. Preliminary clinical observations indicated improvements in EASI, PASI, and DLQI scores among study completers. The herbal cream demonstrated antioxidant and anti-inflammatory properties and showed preliminary clinical potential in inflammatory skin disorders. Larger controlled clinical studies are required to confirm efficacy and establish therapeutic value.

Keywords: *Cannabis sativa*; *Curcuma longa*; herbal formulation; Eczema area and severity index (EASI); psoriasis area and severity index (PASI); dermatology life quality index (DLQI)

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1. Introduction

Eczema and psoriasis are common chronic inflammatory skin diseases that significantly impact the quality of life associated with physical, psychosocial, and mental functioning [1,2]. Eczema and psoriasis are caused by a complex combination of immune dysregulation, skin-barrier disruption, genetic factors, and environmental influences [3,4]. Eczema is characterized by T helper type 2-dominant inflammation, whereas psoriasis is associated by T helper type 1 and/or T helper type 17 immunological response [5]. Eczema tends to appear on the extensor side of extremities and face in infancy, flexure side and hands in adolescents and adults, while psoriasis lesions are most frequently found on the scalp and extensor skin [6]. The current sets of regimen for the treatment of eczema and psoriasis are not completely effective in either curing or controlling of their recurrence. Moreover, unavailability of standardized international guidelines considering the internally and topically administered hormone or immune inhibitors and antihistamines may elicit side effects. However, recent studies showed that the treatments for eczema and psoriasis using alternative medicinal plants, including traditional Thai medicine, are increasing significantly [7,8].

Thai herbal medicine provides a theoretical basis for the treatment of eczema and psoriasis with considerable benefits and biocompatibility [7,8]. Topical application of *Cannabis sativa* and *Curcuma longa* has been used traditionally for centuries for wound care and treatment of skin diseases. Major phytocannabinoids including tetrahydrocannabinol (THC) and cannabinol (CBD) derived from *C. sativa* exhibit anti-inflammatory property, immunological activity and anti-proliferative effect on keratinocytesfor treatment of eczema and psoriasis [9–13], whereas curcumin, the main active ingredient extracted from *C. longa* displayed potent anti-inflammatory effects with potential mechanisms of actions identified such as suppression of pro-inflammatory cytokines, inhibition of iNOS, cyclooxygenase-2, prostaglandin E2, and NO production, and downregulation of the MAPK pathway [14–16]. However, there is currently a lack of scientific data regarding the therapeutic effects of a traditional Thai herbal formulation of *C. sativa* and *C. longa* for the treatment of chronic skin diseases. Therefore, this study was conducted to characterize the phytochemical composition, evaluate the biological activities, investigate potential molecular mechanisms, and assess the preliminary clinical performance of a topical herbal cream containing *C. sativa* and *C. longa* extracts in participants with eczema or psoriasis.

2. Materials and Methods

2.1. Preparation of Herbal Extract

Medicinal plants including *C. sativa* (leaf) and *C. longa* (rizome) were washed and oven dried at 45 °C overnight. The plants were coarsely ground using the grinder and stored in air-tight bottles for further studies. Briefly, a sample (50 g) of both plants was added to a round-bottom flask containing 100 ml of 95% ethanol, then the extract was filtered using Whatman filter paper and the filtrate was concentrated using a rotary evaporator. The extracts were stored at 4℃ until used.

2.2. Ultra-High-Performance Liquid Chromatography (UHPLC)

The chromatography quantification of THC and CBD in herbal formulation was performed using ultra high-performance liquid chromatography system (UHPLC, Thermo, Ultimate 3000), InfinityLab Poroshell 120 EC-C18 (4.6 x 100 mm, 4 μm). Mobile phase of methanol:water (85:15 v/v) at a flow rate of 1.0 mL/min. The detector was set at 220 nm with a sample injection volume of a 10 μL for 10 min run was injected and tested. Briefly, a standard stock of THC and CBD was prepared in the concentration range of 5 to 100 μg/mL and 2.5 to 100 μg/mL by dissolving them in methanol and tested for accuracy of the method through determination of relative standard deviation (RSD) (%). Furthermore, the quantification of THC/CBD in herbal formulation was determined by

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dissolving the samples in methanol, followed by sonication for 15 min using a sonicator and centrifugation for 5 min at 4500 g. The obtained supernatant after centrifugation was filtered using a nylon membrane filter of 0.22 micron and transferred into a 1.5 mL HPLC vial and injected 10 µL in five replicates.

The curcumin was computed in herbal formulation using mobile phase of acetonitrile (50%) in water with acetic acid (2%) using column (ACE Generix 5C-18), flow rate of 1 mL/min, quantified at 425 nm with an injection volume of 10 µL as reported with slight modification [16]. Briefly, a standard curcumin of 1000 µg/mL was dissolved in the mobile phase and injected into the HPLC after passing it through a filter in five replicates with suitable dilution to check the accuracy of the method through determination of RSD (%). Furthermore, the herbal formulation was dissolved in the mobile phase at a concentration of 10 µg/mL and filtered through a 0.22 micron nylon filter. Later, the filtrate was transferred into a 1.5 mL HPLC vial and injected 10 µL in five replicates to quantify the presence of curcumin in it.

2.3. Gas Chromatography and Mass Spectroscopy (GC-MS) Analysis

The GC/GC-MS analysis was performed to identify the bioactive compounds present within the herbal extract using Agilent Technologies GC/MS. GC with a capillary column (30 m × 0.25 mm id, film thickness of 0.25 µm and HP-5 MS at a helium flow rate of 1.0 mL/min under the source temperature maintained at 230 °C, quad temperature at 150 °C, electron energy fixed at 70 (eV), and solvent delay of 5 min till 650 min at scan speed of 1562 s was operated. 1 µL of the sample was dissolved in solvent and injected using a 10 µL syringe and the obtained GC spectra were transferred to MS in electron ionization mode. The identified compound was matched with the inbuilt reference library (Agilent MassHunter Qualitative Analysis Software Ver. 10.0). Later the identified compound was reported with a percentage match.

2.4. Determination of Total Polyphenol and Flavonoid Contents

Total phenolic content and total flavonoid content of the herbal mixture were determined using the Folin-Ciocalteu method and aluminum chloride calorimetric method as previously described [17], respectively. The total phenolic content and total flavonoid content of the herbal mixture were expressed as milligrams of gallic acid equivalent (GAE) per milligram of extract and milligrams of quercetin equivalents (QEs) per milligram of extract, respectively.

2.5. Antioxidant Activity

2.5.1. DPPH (2,2-Diphenyl-1-picrylhydrazyl) Radical Scavenging Assay

Free radical scavenging capability of herbal extract solutions on DPPH radical was determined as described previously with modifications [18]. Briefly, a volume of 20 µl of each sample at different concentrations (8-1024 µg/mL) was added to 180 µL of 80 µM DPPH solution. The reaction mixtures were incubated for 30 min in the dark at room temperature and the reduction of DPPH· radical was measured at 517 nm using a microplate reader. Trolox, a standard antioxidant, was used as a positive control. Percentage inhibition of DPPH oxidation was calculated according to the following formula: DPPH scavenging effect (%) = $(A_{control} - A_{sample})/A_{control} \times 100$. The antioxidant ability of the sample was expressed as IC_{50}.

2.5.2. ABTS (2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) Radical Scavenging Assay

ABTS radical-scavenging activity of the herbal mixture was assessed as previously described with modifications [19]. Briefly, ABTS solution was prepared by dissolving 2 mM ABTS and 2.45 mM potassium persulfate. After storing in the dark for 12 h at room temperature, the mixture was diluted with ethanol to an absorbance recorded at 734 nm. Subsequently, 10 µL of each sample at concentrations ranging from 8 to 1024 µg/mL was mixed with 990 µL of the ABTS radical solution

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and the absorbance was measured. Trolox, a standard antioxidant, was used as a positive control. Percentage inhibition of ABTS oxidation was calculated using the following formula: ABTS scavenging effect (%) = ($A_{control}$ - A_{sample})/$A_{control}$ ×100. The antioxidant ability of the sample was expressed as IC_{50}.

2.5.3. FRAP (Ferric Reducing Antioxidant Power) Assay

The ability of the herbal mixture to reduce ferric ions was measured using the FRAP assay as described with modifications [20]. FRAP reagent was prepared by mixing 300 mM sodium acetate buffer (pH 3.6), 10 mM ferric-tripyridyl triazine solution, and 20 mM ferric chloride solution in a ratio of 10:1:1. All samples were diluted in ethanol at a concentration of 1024 µg/mL. An aliquot of 150 µL of the sample was mixed with 1.35 mL of the FRAP reagent and then incubated at 37 °C for 30 min in the dark. The reaction was measured at an absorbance of 593 nm, and a standard curve was prepared using different concentrations of ferrous solution. The reducing capacity of each sample was expressed as micromoles of ferrous per microgram of extract.

2.6. Anti-Microbial Activity

Bacterial strains including *E. coli* ATCC 25922, *S. aureus* ATCC 25923, *S. pyogenes* DMST 17202, and *P. aeruginosa* ATCC 27853 were obtained from the Division of Biological Science, Faculty of Science, Prince of Songkla University, Thailand.

All the bacterial cultures were stored in tryptic soy broth supplemented with 40% glycerol and kept at -80 °C.

Minimum inhibitory concentrations (MICs) of herbal mixture and antibiotics (ceftazidime, erythromycin, levofloxacin, vancomycin) were determined using the standard broth microdilution method [21]. The herbal formulations (16-1024 mg/L) and antibiotics (0.0625-4 mg/L) were evaluated against bacterial strains. MIC values were defined as the lowest concentration that inhibited the visible growth of bacteria, and minimum bactericidal concentration (MBC) values as the lowest concentrations that showed no growth on tryptic soy agar plates after incubation for 24 h. Each experiment was performed at least twice.

2.7. Anti-Inflammatory Activity

2.7.1. Cell Culture and Cell Viability Assay

RAW 264.7 cells, a mouse macrophage cell line, were obtained from the Division of Biological Science, Faculty of Science, Prince of Songkla University, Thailand. Macrophages were cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% fetal bovine serum (FBS), 100 U/ml penicillin and 100 µg/ml streptomycin in a 5% CO_2 atmosphere at 37 °C.

Biocompatibility of herbal mixture against macrophage cells was evaluated by 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide (MTT) bioassay, a mitochondrial-based assay. Approximately 2 × 10^4 cells were seeded in 96-well plates (100 µL/well) and incubated at 37 °C in an incubator humidified with 5% CO_2 at 37 °C. After 24 h incubation, the culture medium was replaced with fresh DMEM medium. The herbal formulation was two-fold diluted in the plates containing DMEM to yield a final concentration of 4-2048 µg/mL. Cells without the added herbal formulation were tested as a negative control. After 24 h incubation, the cells were treated with 100 µL of fresh medium along with 50 µL of MTT solution (5 mg/mL) and further incubated at 37 °C for 4 h. The medium containing MTT was removed and 100 µL of dimethyl sulfoxide (DMSO) was added. The absorbance of the dissolved formazan dye was determined by a microplate reader at a wavelength of 570 nm using microplate reader. Percentage cell viability was calculated and compared with the negative control [22].

2.7.2. Inhibition of Nitric Oxide Production

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Nitric oxide (NO) production due to enhanced expression of inducible nitric oxide synthase (iNOS) in lipopolysaccharide (LPS)-activated macrophages was measured by a colorimetric method based on Griess reagent. Briefly, after incubation of RAW 264.7 cells with the herbal formulations or triamcinolone acetonide (TA) for 24 h, 100 µl supernatants from each well was mixed with 100 µl Griess reagent in 96-well plates. After an incubation of 15 min at room temperature, optical density was determined at 540 nm using a microplate reader [22].

2.8. Preparation of a Traditional Topical Thai Herbal Cream

The emulsion-based cream was formulated by mixing the oil phase, aqueous phase, and active components, as shown in Table 1, without incorporation of herbal extract [23]. Briefly, the oil phase ingredients were weighed in a beaker, whereas the ingredients of the aqueous phase were weighed in a separate beaker. Later, both beakers were heated to 75 ºC in a water bath. Then, the aqueous phase was slowly added to the oil phase with continued stirring. The herbal extract was weighed and incorporated into the cream bases by geometric dilution. Geometric dilution was continued until a uniform cream was obtained. The herbal cream was packaged into a plastic container and kept at room temperature for further analysis.

Table 1. Formulation of a novel topical Thai herbal cream.

Ingredients	Quantity for 100 g (%)
Active	
Herbal ethanolic extract	10
Oil Phase	
Liquid paraffin	10
White soft paraffin	10
Cetyl alcohol	10
BHT	0.1
Cotton seed oil	5
Aqueous Phase	
Propylene glycol	5
Paraben concentrate	1
Cetomacrogol 1000	3
Purified water	Up to 100%

2.8.1. Freeze–Thaw Stability

A total of 2 g of the herbal cream was weighed and filled into several vials before being subjected to the freeze-thaw cycle [24]. The herbal cream was studied under two conditions, including 4 °C for 24 h and 45 °C for another 24 h. The freeze–thaw was repeated for six cycles. Physical stability, pH and spreadability of the cream were observed initially and after the completion of each freeze–thaw cycle.

2.8.2. Physical Stability Testing

The herbal formulated cream was observed for physical appearance, color, texture, phase separation, homogeneity and odor [25]. A required quantity of cream was pressed between the thumb and index finger to determine the consistency and presence of coarse particles. Moreover, the stiffness, grittiness and greasiness of the creams upon application were evaluated [26]

2.8.3. pH Determination

The pH meter was calibrated with pH 4, 7 and 10 standard buffers before use. A total of 10% *w*/*v* of the herbal cream suspension was prepared for pH measurement at room temperature. The pH

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measurement was repeated in triplicate to obtain the representative data of the cream suspension [27,28].

2.8.4. Viscosity

Viscosity of the herbal cream formulation was determined by Brookfield Viscometer at 200 rpm, using spindle no 7.

2.9. Preliminary Clinical Evaluation of the Therapeutic Effects of a Traditional Topical Thai Herbal Cream for Eczema and Psoriasis Therapy

2.9.1. Study Design and Patient Recruitment

A pretest-posttest clinical trial was performed at the Faculty of Traditional Thai Medicine, Prince of Songkla University, Thailand. The study protocol was approved by the Ethics Committee of the Faculty of Traditional Thai Medicine, Prince of Songkla University (reference number: EC.65/TTM.01-006 and EC.65/TTM.01-007) and was also registered in Thai Clinical Trials Registry (registration ID: TCTR20240902001). The participant who agreed to participate signed a written informed consent prior to commencement of the study and was enrolled for four weeks.

The inclusion and exclusion criteria were as follows: (1) aged 18-55 years; (2) patients with a clinical diagnosis of eczema or psoriasis; (3) patients who voluntarily participated in the study and signed the informed consent form. Meanwhile the exclusion criteria were as follows: (1) patients with uncontrolled systemic illness or life-threatening infection; (2) patients who had already undergoing treatment for any chronic skin disease, substance abuse and/or dependence, pregnant or lactating women; (3) patients with psychiatric diseases and self-reported immune-compromised states; (4) patients who had allergic history to any Thai herbal medicines [7,8].

2.9.2. Treatment Interventions

The therapeutic effects of a traditional topical Thai herbal cream including *C. sativa* and *C. longa* were assessed for the treatment of patients with eczema or psoriasis by application three times daily for four weeks.

2.9.3. Outcome Measures

Primary outcome measurements included Eczema Area and Severity Index (EASI) [29] and Psoriasis Area Severity Index (PASI) score [30]. Secondary outcome measurement was the Dermatology Life Quality Index (DLQI) score [31]. Additionally, during the study, any adverse effects were also recorded. All outcome measures were assessed at baseline and follow-up.

The EASI [29] is a scale used in clinical trials to assess the severity and extent of eczema. Clinical parameters including erythema, infiltration and/or papulation, excoriations, and lichenification were assessed for severity by the investigator on a scale of 0 (absent) to 3 (severe). The total EASI score ranges from 0 to 72 points, with the highest score indicating the worst severity of AD. It is suggested that the severity of AD based on EASI can be categorized as follows: 0 = clear; 0.1 to 1.0 = almost clear; 1.1 to 7.0 = mild; 7.1 to 21.0 = moderate; 21.1 to 50.0 = severe; 50.1 to 72.0 = very severe.

The PASI [30] is a widely used instrument in psoriasis trials that assesses and grades the severity of psoriatic lesions and the patient's response to treatment. The PASI assesses the degree of erythema, scaling, and induration of the patient's lesion. Psoriasis severity is assessed based on a combined evaluation and interpretation of PASI and DLQI. Psoriasis severity of mild, moderate, and severe is defined according to PASI and DLQI as follows: (a) mild psoriasis if PASI < 7 and DLQI < 5; (b) moderate psoriasis if PASI < 7 and DLQI ≥ 5; (c) severe psoriasis if PASI > 15 with any DLQI value.

The DLQI [31] is a widely used dermatology-specific quality-of-life instrument. The 10-item DLQI questionnaires include symptoms and feelings, daily activities, leisure, work and school performance, personal relationships, and treatment. Each of the 10 questions is scored from 0 (not at

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all) to 3 (very much) and the overall DLQI is calculated by summing the scores of each question, resulting in a numeric score between 0 and 30. The higher the score, the more the quality of life is impaired. The meaning of the DLQI scores on a patient's life is as follows: 0 to 1 = no effect; 2 to 5 = small effect; 6 to 10 = moderate effect; 11 to 20 = very large effect; 21 to 30 = extremely large effect.

2.10. Preliminary Mechanistic Evaluation of Traditional Topical Thai Herbal Cream for Eczema and Psoriasis Therapy

2.10.1. In Silico Molecular Docking

The seven phytochemicals—1,8-cineole (eucalyptol), αR-turmerone, turmerone, α-bisabolol, curcumenol, cannabidiol, and vitamin E—were selected for molecular docking based on their well-documented anti-inflammatory, antioxidant, immunomodulatory, and skin-protective properties, which are highly relevant to the treatment of psoriasis and eczema. Psoriasis and eczema are multifactorial disorders involving chronic inflammation, oxidative damage, immune dysregulation, and impaired skin barrier function; hence, compounds capable of targeting multiple pathological mechanisms were prioritized.

1,8-Cineole is known for its anti-inflammatory and soothing effects on irritated skin, making it useful in reducing erythema and pruritus. αR-Turmerone and turmerone, derived from *C. longa*, possess potent anti-inflammatory and immunomodulatory activities that help suppress pro-inflammatory cytokines involved in psoriatic lesions. α-Bisabolol exhibits strong anti-irritant, anti-inflammatory, and wound-healing properties, which are particularly beneficial in eczema management. Curcumenol demonstrates antioxidant and anti-inflammatory effects, aiding in the reduction of oxidative stress-mediated skin damage. Cannabidiol is known to regulate keratinocyte proliferation, inhibit inflammatory cytokine release, and alleviate itching, addressing key pathological features of both diseases. Vitamin E, a powerful antioxidant, plays a critical role in protecting the skin from oxidative damage, improving barrier function, and reducing inflammation.

2.10.2. Procedure for Docking

The molecular docking study was carried out using PyRx software to predict the binding affinity and interaction pattern of selected phytochemicals with target proteins relevant to inflammatory skin disorders. Initially, the ligands were selected based on their reported anti-inflammatory, antioxidant, and dermatological relevance. The three-dimensional structures of the selected ligands were downloaded from the PubChem database in SDF format. These ligand files were imported into PyRx, where they were energy-minimized using the Open Babel tool integrated within the software to obtain stable conformations. During ligand preparation, hydrogen atoms were added, torsions were assigned, and the structures were converted into PDBQT format, which is required for docking.

The target proteins involved in psoriasis and eczema–associated inflammatory pathways were downloaded from the Protein Data Bank (PDB) in PDB format using their respective PDB IDs (PDB: 5E1E or 6N7A). Protein preparation was performed using Discovery studio. This step involved removal of co-crystallized ligands, water molecules, and heteroatoms that could interfere with ligand binding. Polar hydrogen atoms were added to the protein structure, and Kollman charges were assigned to ensure accurate electrostatic interactions. The prepared protein was then saved in PDBQT format for docking analysis.

Molecular docking was performed in PyRx using the AutoDock Vina algorithm. The prepared protein was loaded as a macromolecule, and the optimized ligands were selected as docking molecules. A grid box was defined to cover the active site or binding pocket of the protein, ensuring sufficient space for ligand flexibility and interaction. Docking parameters were set to default values, and the docking simulation was executed to predict the most favorable binding poses and binding energies. The resulting docked conformations were ranked based on their binding affinity (kcal/mol), with lower energy values indicating stronger and more stable interactions. To validate the docking protocol, the co-crystallized native ligand was redocked into the active site, yielding an RMSD value

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within the acceptable range (< 2.0 Å), confirming the reliability of the docking procedure. The grid coordinates used for docking for selecting the active-site binding pocket are (X: 25.4283, Y: 44.5478, Z: 1.6584)

Post-docking analysis was performed using Discovery Studio Visualizer to examine ligand–protein interactions. The best docked complexes were analyzed for hydrogen bonds, hydrophobic interactions, π-alkyl, and other non-covalent interactions. Two-dimensional and three-dimensional interaction maps were generated to identify key amino acid residues involved in binding. These analyses provided insights into the potential interactions of selected phytochemicals with inflammatory targets associated with psoriasis and eczema.

2.11. Statistical Analysis

Data were expressed as mean ± SD. The normality of the differences between baseline and post-treatment values was assessed using the Shapiro-Wilk test. Since the data met the normality assumption ($p > 0.05$), comparisons were performed using the paired t-test. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using R software (version 4.4.3)

3. Results and Discussion

3.1. UHPLC Analysis

A consistent degree of ionization and polarity of the analytes with sensitive resolution and a short processing time were achieved by optimizing the chromatographic system utilizing a C18 column. The calibration curve in the range of 2.5 to 100 µg/mL through HPLC analysis of CBD demonstrated retention time (Rt) of 2.845 ± 0.002 min and 5.883 ± 0.001 min, correspondingly **(Supplementary data 1)**. Moreover, the RSD (%) was observed as 2.29 and 2.76 for CBD and THC, respectively. The quantification of CBD (0.15% w/w) and THC (0.99% w/w) within the herbal formulation, which appeared at Rt of 2.818 ± 0.004 min and 5.803 ± 0.01 min, respectively, confirmed the accuracy of the method. Whereas the calibration curve for curcumin in the range of 200 to 1000 µg/mL indicated a linear range with a straight line equation of y = 9E + 07x and R^2 of 0.994. The chromatogram showed retention time at 15.870 ± 0.455 min with quantification of 1.1829 ± 0.1856 mg (%) in THF **(Supplementary data 2)**.

3.2. GC-MS Analysis

Qualitative profiling using GC-MS analysis was used to identify the major phytopharmaceuticals contained in the herbal formulation exhibiting high accuracy and sensitive mass identification **(Table 2)**. The GC-MS profiling of the herbal formulation incorporated *C. sativa* and *C. longa* showed the presence of 95 compounds targeting majorly terpenoids and cannabinoids. Terpenoids, or terpenes are the most abundant and structurally varied naturally occurring bioactive compounds present in a wide range of flora. Whereas cannabinoids, originating from cannabis, known for excellent pharmacological activity, are approved in the treatment of chemotherapy-induced gastrointestinal symptoms, multiple sclerosis, and epilepsy. The GC-MS-based chemical profiling of the herbal formulation indicated presence of major twenty-seven compounds with match percentage of more than 90% such as Eucalyptol (1,8-cineole) (93.5%), α-Santalene (96.6%), cis-α-Bergamotene (94.8%), Bicyclo [2.2.1]heptane, 2-methyl-3-methylene-2-(4-methyl-3-pentenyl)-,(1S-endo) (92.0%), cis-β-Farnesene (94.4%), Benzene, 1-(1,5-dimethyl-4-hexenyl)-4-methyl (96.7%), 1,3-Cyclohexadiene, 5-(1,5-dimethyl-4-hexenyl)-2-methyl (97.9%), β-Bisabolene (97.4%), Cyclohexene, 3-(1,5-dimethyl-4-hexenyl)-6-methylene (98.0%), 7-epi-cis-Sesquisabinene hydrate (90.5%), aR-Turmerone (96.4%), Tumerone (94.0%), α-Bisabolol (94.8%), 3,7-Cyclodecadien-1-one,3,7-dimethyl-10-(1-methylethylidene) (96.8%), 2-Methyl-6-(4-methylenecyclohex-2-en-1-yl) hept-2-en-4-one (96.7%), (E)-Atlantone (97.6%), Hexadecanoic acid, ethyl ester (98.3%), Phytol (97.4%), Linoleic acid ethyl ester (96.5%), 9,12,15-Octadecatrienoic acid, ethyl ester (98.2%), δ-9-Tetrahydrocannabivarin

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(93.1%), 1H-4-Oxabenzo(f)cyclobut(cd)inden-8-ol, 1a-α,2,3,3a,8b-α,8c-α.-hexahydro-1,1,3a-trimethyl-6-pentyl (90.0%), Cannabidiol (97.9%), Cannabichromene (96.2%), Dronabinol (98.4%), Cannabinol (97.0%), and γ-Sitosterol (90.6%) **(Supplementary data 3 and Supplementary data 4)**.

Table 2. Phytochemical profiling of Thai herbal formulation using GC-MS.

Retention time (min)	Compound name	Molecular formula	Match percentage	Category and pharmacological action
7.9	Eucalyptol (1,8-cineole)	$C_{10}H_{18}O$	93.5	Monoterpenoid, anti-inflammatory, antioxidant
19.6	α-Santalene	$C_{15}H_{24}$	96.6	Sesquiterpenoids, anti-inflammatory, antioxidant, antimicrobial, antidiabetic
20.0	cis-α-Bergamotene	$C_{15}H_{24}$	94.8	Bicyclic sesquiterpenes, astringent, analgesic
20.2	Bicyclo [2.2.1]heptane, 2-methyl-3-methylene-2-(4-methyl-3-pentenyl)-, (1S-endo)-	$C_{15}H_{24}$	92	Polycyclic sesquiterpenes, antimalarial, antifungal, antibacterial, anti-inflammatory
20.5	cis-β-Farnesene	$C_{15}H_{24}$	94.4	Sesquiterpenoids, skin infections
21.1	Benzene, 1-(1,5-dimethyl-4-hexenyl)-4-methyl-	$C_{15}H_{22}$	96.7	Aromatic monoterpenoids, antioxidant
21.5	1,3-Cyclohexadiene, 5-(1,5-dimethyl-4-hexenyl)-2-methyl-, [S-(R*,S*)]-	$C_{15}H_{24}$	97.9	Sesquiterpenoids, skin infections
21.8	β-Bisabolene	$C_{15}H_{24}$	97.4	Sesquiterpenoids, anti-cancer
21.9	(Z)-1-Methyl-4-(6-methylhept-5-en-2-ylidene) cyclohex-1-ene	$C_{15}H_{24}$	83.7	Sesquiterpenes, anti-inflammatory, anti-tumor, antimicrobial
22.0	Benzenemethanol, 4-methyl-α-(1-methyl-2-propenyl)-, (R@,R@)-	$C_{12}H_{16}O$	83.6	-
22.1	Cyclohexene, 3-(1,5-dimethyl-4-hexenyl)-6-methylene-, [S-(R*,S*)]	$C_{15}H_{24}$	98	Sesquiterpenoids, skin infections
22.2	(R,Z)-2-Methyl-6-(4-methylcyclohexa-1,4-dien-1-yl)hept-2-en-1-ol	$C_{15}H_{24}O$	77.8	-
22.3	(E)-1-Methyl-4-(6-methylhept-5-en-2-ylidene) cyclohex-1-ene	$C_{15}H_{24}$	89.4	Monocyclic sesquiterpenes, anti-tumor, anti-inflammatory, antibacterial, antivirus, antiparasitic, anti-ulcer
22.6	α-Humulene	$C_{15}H_{24}$	82.6	Sesquiterpenes, anti-inflammatory, antimicrobial, antileishmanial, antiparasitic
22.9	7-epi-cis-sesquisabinene hydrate	$C_{15}H_{26}O$	90.5	Sesquiterpenes; anticancer
23.1	1,6,10-Dodecatrien-3-ol, 3,7,11-trimethyl-	$C_{15}H_{26}O$	82.6	Sesquiterpenes, anti-inflammatory
23.4	Santalol	$C_{15}H_{24}O$	75.7	Sesquiterpenes, anticancer
23.7	(E)-γ-Atlantone	$C_{15}H_{22}O$	82.7	Sesquiterpenes, antiviral

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24.0	1H-3a,7-Methanoazulene, octahydro-3,6,8,8-tetramethyl-, [3R-(3-α,3a-β,6-α,7-β,8a-α)]-	$C_{15}H_{26}$	79.4	-
24.1	7-epi-trans-sesquisabinene hydrate	$C_{15}H_{26}O$	77.2	Sesquiterpenes; anticancer
24.6	(1R,4R)-1-methyl-4-(6-Methylhept-5-en-2-yl) cyclohex-2-enol	$C_{15}H_{26}O$	87.5	Sesquiterpenes, anticancer
25.01	7-epi-cis-sesquisabinene hydrate	$C_{15}H_{26}O$	75	Sesquiterpenes, anticancer
25.4	aR-Turmerone	$C_{15}H_{20}O$	96.4	Sesquiterpenes, anti-inflammatory, antioxidant
25.5	Tumerone	$C_{15}H_{22}O$	94	Sesquiterpenes, anti-inflammatory, antioxidant
25.8	α-Bisabolol	$C_{15}H_{26}O$	94.8	Sesquiterpenoids, anti-inflammatory, analgesic
26.0	3,7-Cyclodecadien-1-one, 3,7-dimethyl-10-(1-methylethylidene)-,(E,E)-	$C_{15}H_{22}O$	96.8	Sesquiterpenoids, anti-inflammatory
26.2	2-Methyl-6-(4-methylenecyclohex-2-en-1-yl) hept-2-en-4-one	$C_{15}H_{22}O$	96.7	Sesquiterpenes, anti-inflammatory
26.4	2-Methyl-5-(2,6,6-trimethyl-cyclohex-1-enyl)-pentane-2,3-diol	$C_{15}H_{28}O_2$	73.4	-
26.5	(Z)-α-Atlantone	$C_{15}H_{22}O$	84.9	Sesquiterpenes, antiviral
26.8	Curcumenol	$C_{15}H_{22}O_2$	86.6	Sesquiterpenoids, anti-tumor, anti-inflammatory, antibacterial, antioxidant, anti-diabetic
27.1	(6R,7R)-Bisabolone	$C_{15}H_{24}O$	86.5	Sesquiterpenoids, anti-inflammatory
27.7	(E)-Atlantone	$C_{15}H_{22}O$	97.6	Sesquiterpenoids, antiviral
28.7	erythro-(cis)(1,4),(cis)(1′,4′)-4,4′-Dihydroxybicyclooctyl	$C_{16}H_{30}O_2$	76.7	-
29.1	1-(Hydroxymethyl)-2,5,5,8A-tetramethyldecahydro-2-naphthalenol	$C_{15}H_{28}O_2$	75.9	Sesquiterpenoids, anti-inflammatory
32.0	Ethyl 9-hexadecenoate	$C_{18}H_{34}O_2$	87.5	Unsaturated fatty acids, antioxidant
32.1	Hexadecanoic acid, ethyl ester	$C_{18}H_{36}O_2$	98.3	Long chain fatty acid ethyl ester, , antioxidant
34.3	Phytol	$C_{20}H_{40}O$	97.4	Acyclic diterpene alcohol, anxiolytic, antioxidant, anti-inflammatory, antimicrobial, immune modulating
35.1	Linoleic acid ethyl ester	$C_{20}H_{36}O_2$	96.5	Fatty acid esters, anti-inflammatory
35.2	9,12,15-Octadecatrienoic acid, ethyl ester	$C_{20}H_{34}O_2$	98.2	Fatty acid, anti-inflammatory
35.7	Octadecanoic acid, ethyl ester	$C_{20}H_{40}O_2$	88.4	Fatty acid, anti-inflammatory

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37.0	δ-8-Tetrahydrocannabinol	$C_{21}H_{30}O_2$	87.1	Cannabinoids, appetizer, reflective mood, management of chronic pain, chemotherapy
37.7	δ-9-Tetrahydrocannabivarin	$C_{19}H_{26}O_2$	93.1	Cannabinoids, appetizer, reflective mood, management of chronic pain, chemotherapy
38.6	1H-4-Oxabenzo(f)cyclobut(cd)indeen-8-ol, 1a-α,2,3,3a,8b-α,8c-α.-hexahydro-1,1,3a-trimethyl-6-pentyl	$C_{21}H_{30}O_2$	90	Cannabinoids, chemotherapy
39.5	Cannabidiol	$C_{21}H_{30}O_2$	97.9	Cannabinoids, management of chronic pain, chemotherapy
39.7	Cannabichromene	$C_{21}H_{30}O_2$	96.2	Cannabinoids, management of chronic pain, chemotherapy
40.1	Cannabicoumaronone	$C_{21}H_{28}O_3$	75.1	Cannabinoids, management of pain, skin burn, asthma, epilepsy
41.0 1	Dronabinol	$C_{21}H_{30}O_2$	98.4	Cannabinoids, management of pain, skin burn, asthma, epilepsy
42.0	Cannabinol	$C_{21}H_{26}O_2$	97	Cannabinoids, management of pain, skin burn, asthma, epilepsy
42.4	Pregna-5,7-diene, 3-(methoxymethoxy)-20-formyl-	$C_{24}H_{36}O_3$	75.2	Cannabinoids, management of pain
45.4	Squalene	$C_{30}H_{50}$	89.7	Triterpenoid hydrocarbon, anticancer, antioxidant, emollient
49.3	Vitamin E	$C_{29}H_{50}O_2$	91.1	Antioxidant
50.4	(3methyl,24R)-ergost-5-en-3-ol	$C_{28}H_{48}O$	76.8	Triterpenoid, anticancer, anti-inflammatory, antibacterial, antiviral
51.5	γ-Sitosterol	$C_{29}H_{50}O$	90.6	Phytosterol, management of hypercholesterolemia
53.0	Olean-12-en-3-ol, acetate, (3β)-	$C_{32}H_{52}O_2$	75.9	Triterpenoid, anticancer, anti-inflammatory, antibacterial, antiviral
53.4	9,19-Cycloergost-24(28)-en-3-ol, 4,14-dimethyl-, acetate, (3β,4α,5α)-	$C_{32}H_{52}O_2$	79.6	Triterpenoid, anticancer, anti-inflammatory, antibacterial, antiviral

The results showed the presence of several bioactive compounds that belong to major categories of terpenoids and cannabinoids with fractions of minute quantities of fatty acids. These classes of phytopharmaceuticals exhibited a wide range of highly significant pharmacological activity, as validated by numerous in vitro, preclinical, and clinical studies [32–37].

3.3. Total Phenolic and Flavonoid Contents and Antioxidant Activities

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The total phenolic content, total flavonoid content, and antioxidant activities of the herbal formulation are presented in **Table 3**. Total phenolic and flavonoid contents were shown in the herbal formulation with values of 93.59 ± 2.69 mg GAE/g extract and 1.06 ± 0.05 mg QE/g extract, respectively. The herbal formulation displayed DPPH and ABTS free radical scavenging activities with the IC_{50} values of 125.68 ± 1.26 and 34.53 ± 1.09 μg/mL, respectively. In addition, the herbal formulation also had the capability to reduce Fe^{3+} to Fe^{2+} with the FRAP value of 34.67 ± 1.04 mg Fe_2SO_4/g extract.

Table 3. The total phenolic content, total flavonoid content, and antioxidant activities of Thai herbal formulation.

Sample	Total phenolic content (mg GAE/g extract)	Total flavonoid content (mg QE/g extract)	DPPH IC_{50} (μg/ml)	ABTS IC_{50} (μg/ml)	FRAP (mg Fe_2SO_4/g extract)
THF	93.59 ± 2.69	1.06 ± 0.05	125.68 ± 1.26	34.53 ± 1.09	34.67 ± 1.04
Ascorbic acid	NA	NA	6.61 ± 0.01	2.83 ± 0.02	NA

Values are means ± SDs of three separate experiments. Thai herbal formulation, THF. DPPH, 2,2-diphenyl-1-picrylhydrazyl; ABTS, 2,2′-azino-bis (3-ethylbenzthiazo-line-6-sulphonic acid); FRAP, ferric reducing antioxidant power; GAE, garlic acid equivalent; QE, quercetin equivalents. IC_{50}, 50% inhibitory concentration NA, not applicable.

Oxidative stress is one of the major phenomena associated with eczema and psoriasis pathogenesis [38]. Some studies demonstrated that bioactive compounds with anti-oxidant effects have been extensively used to combat skin oxidative stress for the management of inflammatory skin diseases [39,40]. Therefore, treatment based on plant-derived antioxidants may be a beneficial strategy for eczema and psoriasis management [40,41].

3.4. Antibacterial Effects

Intrinsic antibacterial activities of herbal formulation were evaluated against *E. coli* ATCC 25922, *S. aureus* ATCC 25923, *S. pyogenes* DMST 17202, and *P. aeruginosa* ATCC 27853. The herbal formulation possessed mild intrinsic antibacterial activities against all tested bacterial strains, with MIC and MBC more than 512 μg/ml.

Medicinal plant extracts have been harnessed for their antibacterial and anti-inflammatory activity, contributing to skin healing [42]. Previous studies documented that most medicinal plant extracts exhibited weak antibacterial activities in comparison with antibiotics, however, some medicinal plant extracts could act as resistance modifying agents to reverse the resistance to antimicrobial agents in the bacterial cell [43,44]. Various antibacterial mechanisms of medicinal plants were the inhibition of DNA, proteins, and cell envelope biosynthesis, and the damage to the cell membrane, depending on the spectrum and the content of compounds present in herbal medicines [43,44]. Moreover, the effectiveness of medicinal plant extracts to inhibit bacterial growth was related to the synergistic effect between the active compounds of the extracts.

3.5. Cytotoxic Effects in RAW 264.7 Macrophages and Effects of Herbal Formulation on Nitric Oxide Levels in Lipopolysaccharide-Stimulated Macrophages

Prior to in vitro assessment of anti-inflammatory activity, the potential cytotoxicity of the herbal formulation towards the macrophage cell line RAW 264.7 was evaluated by mitochondrial-MTT reduction assay. The results indicated that all studied concentrations (0.0001 - 0.1 mg/ml) of the herbal formulation did not affect the viability of RAW 264.7 cells, compared to the positive control (TA) **(Table 4)**.

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Table 4. Viability of RAW 264.7 macrophages treated with Thai herbal formulation (THF) and triamcinolone acetonide (TA).

Sample	% Cell viability at various concentrations (mg/ml)			
	0.0001	0.001	0.01	0.1
THF	100.54 ± 1.29	97.67 ± 1.28	95.72 ± 1.55	94.47 ± 1.79
TA	101.82 ± 2.74	102.25 ± 2.75	104.10 ± 1.95	105.80 ± 2.41

Values are means ± SDs of three separate experiments.

The inhibitory activity of the herbal formulation and the positive control on NO production in LPS-stimulated macrophages, compared to the controls, are shown in **Table 5**. The final concentration of herbal formulation at 0.01 and 0.1 mg/mL showed effective inhibition of NO production at 15.68 ± 5.64% and 15.79 ± 2.81%, respectively. Meanwhile, the corresponding concentration of the positive control (TA) showed 25.81 ± 3.18% and 26.88 ± 3.10% inhibition, respectively.

Table 5. Inhibitory activity of Thai herbal formulation (THF) and triamcinolone acetonide (TA) of nitric oxide (NO) production in lipopolysaccharide (LPS)-stimulated RAW 264.7 macrophages.

Sample	% Nitric oxide inhibition at various concentrations (mg/ml)			
	0.0001	0.001	0.01	0.1
THF	11.25 ± 3.51	5.33 ± 3.69	15.68 ± 5.64	15.79 ± 2.81
TA	21.86 ± 3.41	23.66 ± 1.80	25.81 ± 3.18	26.88 ± 3.10

Values are means ± SDs of three separate experiments.

According to eczema and psoriasis diseases, inflammation causes the weakness of the skin barrier structure and increased cell permeability, stimulating serious problems in skin moisturizing [45]. Scientific evidence has revealed that medicinal plants or natural compounds could reinforce the skin barrier due to their anti-inflammatory activity [45–47].

3.6. Physical Stability, Viscosity, and pH of a Traditional Topical Thai Herbal Cream Before and After Freeze-Thaw Stability

The characteristics of a novel topical Thai herbal cream were demonstrated in **Table 6**. The physical appearance of a topical Thai herbal cream appeared greenish, smooth, and homogenous before freeze-thaw stability. After freeze-thaw stability, their characteristics were similar in terms of texture, homogeneity, and pH.

Table 6. Physical stability, viscosity, and pH of cream before and after freeze-thaw stability.

Characteristics	Before freeze-thaw stability	After freeze-thaw stability
Physical appearance	 Greenish, smooth, homogenous	 Dark green, smooth, homogenous
Viscosity (cP)	2,100	1,700
pH value	pH 6.2	pH 6.2

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Centipoise, cP.

The semi-solid formulation, cream, is designed for topical application to the skin. The formulation offers skin protection and hydration while serving as a vehicle for phage delivery. Moreover, cream is simple to use, slightly irritating to the skin, and often readily removable with water [48]. According to the physicochemical properties, an oil-in-water cream (o/w) was selected as a dosage form for this study. Additionally, an o/w cream supported the barrier function of the baby's skin without occlusion, provided a good longer-lasting hydration effect and had adequate consistency, easy spreading, a pleasant skin feeling, proper pH, and good microbiological stability [49].

3.7. Preliminary Clinical Evaluation of the Therapeutic Effects of a Traditional Topical Thai Herbal Cream for Eczema and Psoriasis Therapy

Four female patients, aged 21 to 45 years with a mean age of 33.25 years, diagnosed with eczema, completed treatment for four weeks. All patients alleviated their symptoms by applying the topical herbal cream three times daily for four weeks. The EASI and DLQI scores after four weeks of treatment were compared with the scores at baseline **(Table 7)**. A significant reduction in EASI scores was observed at the end of 2 weeks onwards, indicating that the topical herbal cream required a certain amount of time to elicit therapeutic effects [95% CI: 1.15 (0.31 to 1.99)]. At the end of the study, the mean of EASI and DLQI scores greatly reduced from 4.11±3.14 to 1.28±1.46 [95% CI: 2.83 (-0.14 to 5.80)] and 6.25±5.25 to 1.00±0.82 [95% CI: 5.25 (-2.03 to 12.53)], respectively. The condition of topical herbal cream-treated patients markedly improved after treatment, with a decrease in erythema, oedema, scaling, itching and lichenification **(Figure 1)**. Regarding psoriasis therapy, a 44-year-old male patient with psoriasis was treated with topical herbal cream three times daily for four weeks. At the end of the study, the patient responded effectively to the treatment, as indicated by the PASI score decreased from 39 to 16.2. In addition, the DLQI score also decreased from 7 (moderate effect on patients' lives) to 2 (small effect on patients' lives). The condition of topical herbal cream-treated psoriasis patients remarkably improved after treatment, with a decrease in erythema, scaling, itching and induration **(Figure 2)**.

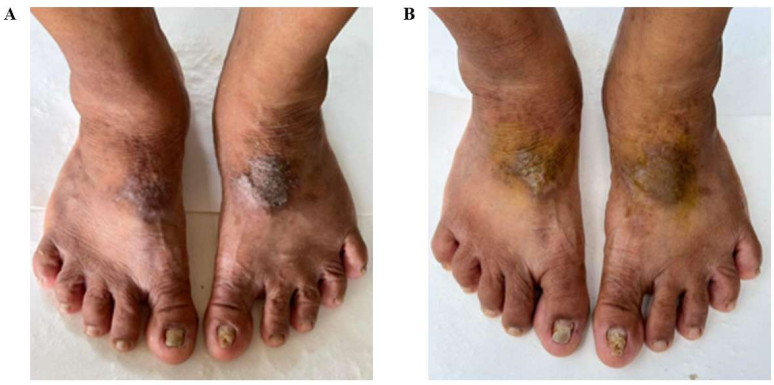

Figure 1. Clinical photos of a representative eczema patient prior to Thai herbal cream at week 0 (A) and after treatment at week 4 (B).

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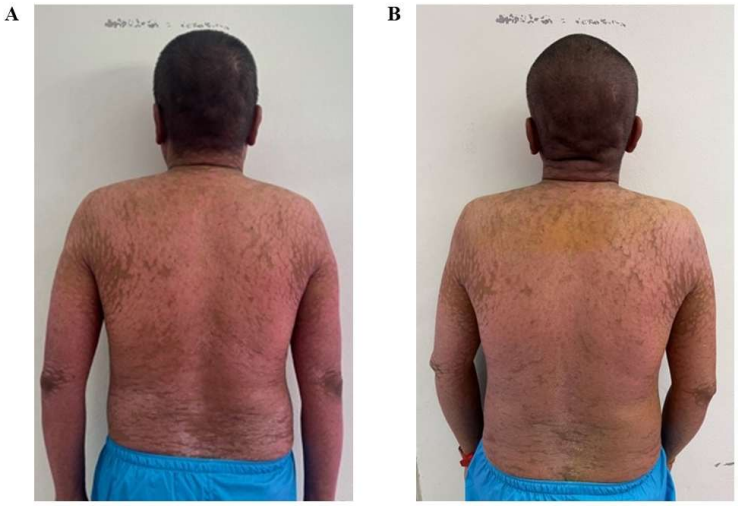

Figure 2. Clinical photos of a psoriasis patient prior to Thai herbal cream at week 0 (A) and after treatment at week 4 (B).

Table 7. Improvements in the Eczema Area and Severity Index (EASI) score and Dermatology Life Quality Index (DLQI) score over the four-week intervention for four participants with eczema.

Variable	Before therapy (n = 4)	After therapy (n = 4)	Mean difference (95% CI)	*P* value
EASI				
Week 2	4.11 ± 3.14	2.96 ± 2.62	1.15 (0.31 to 1.99)	0.022*
Week 4	4.11 ± 3.14	1.28 ± 1.46	2.83 (-0.14 to 5.80)	0.056
DLQI				
Week 4	6.25 ± 5.25	1.00 ± 0.82	5.25 (-2.03 to 12.53)	0.105

Values are presented as mean ± SD. Statistical comparisons were performed using the paired t-test. All hypothesis tests were two-sided, and a *P* value < 0.05 was considered statistically significant.

A preliminary uncontrolled clinical evaluation revealed reductions in EASI and DLQI scores among four people with eczema. An enhancement in PASI score was noted in a patient with psoriasis. However, interpretation is limited by the small sample size, lack of controls, and participant attrition.

3.8. Preliminary Mechanistic Evaluation of Traditional Topical Thai Herbal Cream for Eczema and Psoriasis Therapy

Psoriasis and eczema are chronic inflammatory skin disorders characterized by dysregulated immune responses, oxidative stress, epidermal barrier dysfunction, and sustained activation of pro-inflammatory signalling pathways. Molecular docking was employed to elucidate the binding affinity and interaction profiles of selected phytochemicals with two relevant protein targets (PDB IDs: 5E1E and 6N7A), which are involved in inflammatory pathways, keratinocyte proliferation, and immune modulation **(Table 8 and Figure 3)**. The docking outcomes provide mechanistic insight into the potential of these phytoconstituents as multi-target anti-inflammatory and skin-protective agents. The protein targets 5E1E and 6N7A were selected because they represent key components of the Janus kinase (JAK)-mediated inflammatory signaling pathway, which plays a central role in the pathogenesis of psoriasis and eczema. Aberrant activation of JAK-dependent cytokine signaling contributes to immune dysregulation, chronic inflammation, and excessive keratinocyte proliferation observed in these skin disorders. Since JAK inhibitors have demonstrated significant clinical efficacy

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in the treatment of inflammatory dermatological diseases, these proteins were considered suitable molecular targets for evaluating the potential anti-inflammatory activity of the selected phytochemicals through molecular docking studies.

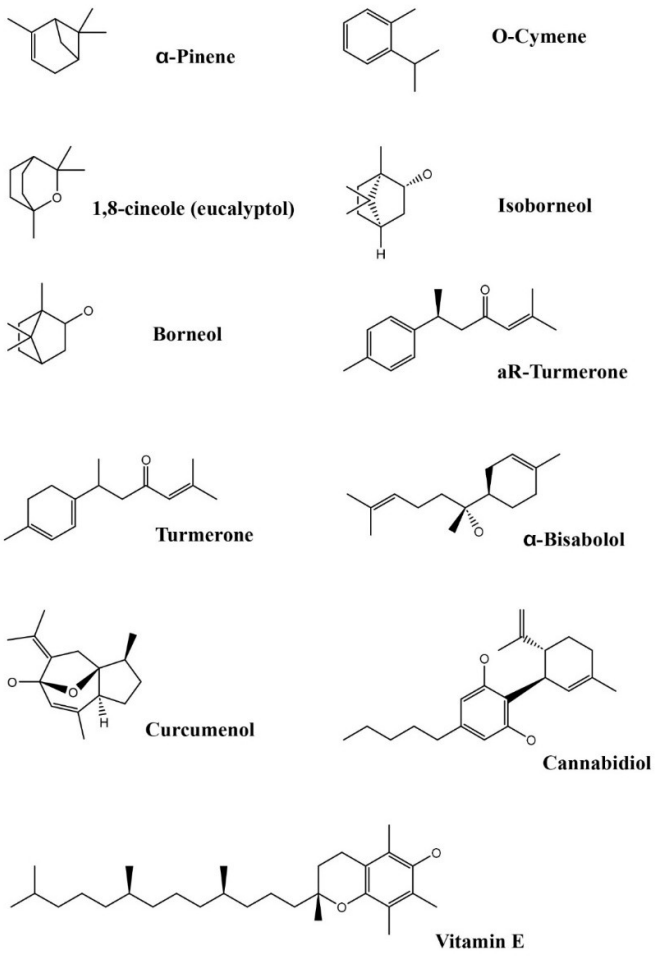

Figure 3. Chemical structures of selected phytochemicals of the plant based on LC-MS data.

Table 8. Binding affinities and protein interactions of selected phytoconstituents in psoriasis and eczema.

Compound	IUPAC	Binding energy		Compound interaction
		5E1E	6N7A	
1,8-cineole (eucalyptol)	1,3,3-trimethyl-2-oxabicyclo [2.2.2]octane	-5.2	-5.6	Pi-Alkyl/Alkyl – LEU A:881, VAL A:889, LEU A:1010 Conventional H-bond – LYS B:908 Carbon H-bond – GLY B:1023 Pi-Sigma – LEU B:881
aR-Turmerone	(6S)-2-methyl-6-(4-methylphenyl)hept-2-en-4-one	-7.3		Pi-Alkyl/Alkyl – LEU B:881, VAL B:889, LEU B:1010 Pi-Sigma – LEU A:881
Tumerone		-6.8	-6.9	Pi-Alkyl/Alkyl – LEU A:881, LEU A:1010 Conventional H-bond – LEU B:959

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◎-Bisabolol	2-methyl-6-(4-methylcyclohexa-1,3-dien-1-yl)hept-2-en-4-one (2R)-6-methyl-2-[(1R)-4-methylcyclohex-3-en-1-yl]hept-5-en-2-ol	-6.4	-5.6	Pi-Alkyl/Alkyl – LEU B:881, VAL B:889, LEU B:1010 Pi-Alkyl/Alkyl – LEU A:881, VAL A:889, ALA A:906, PHE A:958, LEU A:959, LEU A:1010 Pi-Alkyl/Alkyl – LEU A:881, ALA A:906, PHE A:958, LEU A:959, LEU A:1010 Carbon H-bond – GLY A:884 Pi-Alkyl/Alkyl – HIS A:885, PHE A:886, LEU A:910, HIS A:918, ARG A:1041
Curcumenol	(1S,2S,5S,8R)-2,6-dimethyl-9-propan-2-ylidene-11-oxatricyclo [6.2.1.01,5]undec-6-en-8-ol	-7.4	-7.4	Pi-Alkyl/Alkyl – LEU B:881, VAL B:889, ALA B:906, LEU B:1010 Carbon H-bond – SER B:963 Pi-Alkyl/Alkyl – LEU B:881, VAL B:889, ALA B:906, LEU B:1010
Cannabidiol	2-[(1R,6R)-3-methyl-6-prop-1-en-2-ylcyclohex-2-en-1-yl]-5-pentylbenzene-1,3-diol	-6.8	-6.4	Conventional H-bond – LEU B:881, LEU B:959 Pi-Sigma – LEU B:881 Pi-Alkyl/Alkyl – VAL B:889, LEU B:891, ALA B:906, MET B:956, PHE B:958, LEU B:1010 Conventional H-bond – ILE A:1060, ALA A:1061 Pi-Sigma – ILE A:1060 Pi-Alkyl/Alkyl – ILE A:1028, ILE A:1060, ALA A:1061, VAL A:1064 Pi-Anion – GLU A:1033
Vitamin E	(2R)-2,5,7,8-tetramethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-3,4-dihydrochromen-6-ol	-7.3	-5.8	Pi-Sigma – LEU B:1010 Pi-Alkyl/Alkyl – LEU B:881, VAL B:889, ALA B:906, ALA B:1005, LEU B:1010, TRPP B:1047 Pi-Alkyl/Alkyl – VAL A:865, PRO A:896 Pi-donor H-bond – TYR A:894
Tofacitinib (Standard)	(3R,4R)-4-methyl-3-[methyl(7H-pyrrolo [2,3-d]pyrimidin-4-yl)amino]piperidine	-8.9	-8.2	Pi-Alkyl/Alkyl Gly A 884 and Leu A959

Among the evaluated compounds, curcumenol, αR-turmerone, and vitamin E exhibited the strongest binding affinities (−7.3 to −7.4 kcal/mol), indicating stable ligand–protein complexes **(Figure 4 and Figure 5**) when compared with Tofacitinib as reference standard a JAK inhibitor. Curcumenol demonstrated consistent binding energies against both targets (−7.4 kcal/mol) and formed hydrophobic interactions with key residues such as LEU, VAL, and ALA, along with a stabilizing carbon hydrogen bond with SER B:963. These interactions suggest effective accommodation within the active site, supporting its reported anti-inflammatory and antioxidant properties, which are highly relevant in attenuating cytokine-mediated inflammation and oxidative damage in psoriatic and eczematous skin. αR-Turmerone showed favorable binding (−7.3 kcal/mol) dominated by π-sigma and π-alkyl interactions with hydrophobic residues (LEU and VAL) across both chains. Such interactions indicate strong hydrophobic complementarity, which is often associated with effective inhibition of inflammatory mediators. Given its known immunomodulatory and anti-inflammatory

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activity, αR-turmerone may contribute to reducing erythema, scaling, and immune cell infiltration observed in psoriasis and eczema. Vitamin E, a well-established antioxidant in dermatological therapy, displayed good binding affinity (−7.3 kcal/mol for 5E1E) and formed π-alkyl and π-donor hydrogen bond interactions with residues such as TYR A:894 and LEU B:1010. These interactions reinforce its role in stabilizing the target protein and mitigating oxidative stress–driven inflammation. The docking results complement its clinical utility in improving skin barrier function and reducing pruritus and inflammation in eczematous conditions. Cannabidiol (CBD) exhibited moderate to strong binding (−6.8 to −6.4 kcal/mol) and formed multiple conventional hydrogen bonds, π-sigma, and π-anion interactions, notably with GLU A:1033. This diverse interaction profile indicates robust target engagement and supports CBD's reported ability to suppress inflammatory cytokines, regulate keratinocyte proliferation, and alleviate itching—key pathological features of both psoriasis and eczema. Turmerone, α-bisabolol, and 1,8-cineole demonstrated moderate binding affinities (−5.2 to −6.9 kcal/mol) with predominantly hydrophobic and occasional hydrogen-bonding interactions. α-Bisabolol and 1,8-cineole, known for their soothing, anti-irritant, and anti-inflammatory properties, showed stable interactions with residues involved in the binding pocket, suggesting their supportive role in reducing skin inflammation and irritation, particularly in eczema. Therefore, the predominance of hydrophobic interactions (π-alkyl, π-sigma) across most ligands reflects the lipophilic nature of the binding cavity, favoring phytochemicals with terpenoid and phenolic scaffolds. The presence of conventional and carbon hydrogen bonds further enhances complex stability, indicating potential inhibitory effects on inflammation-related targets.

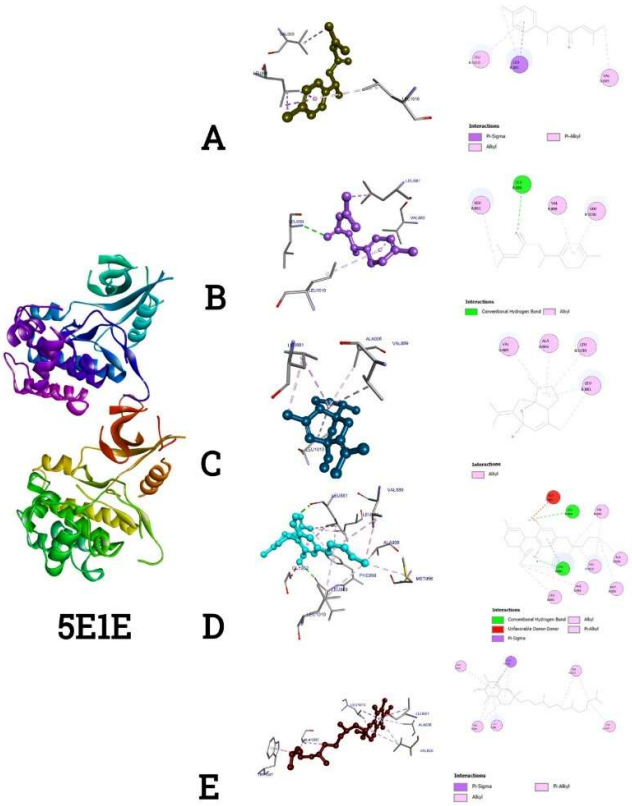

Figure 4. 2D and 3D structures of ligands and proteins in molecular docking against 5E1E.

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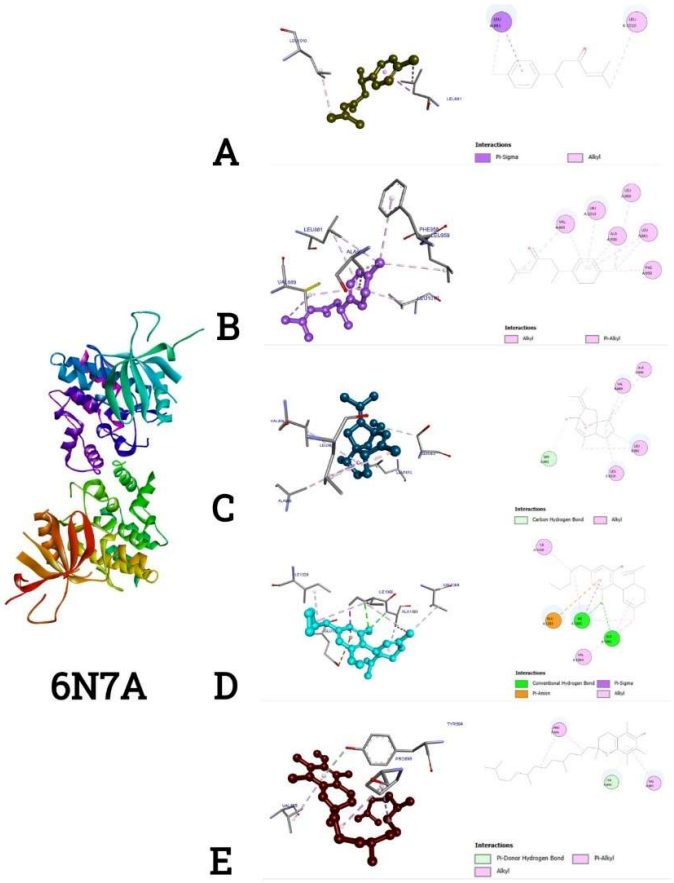

Figure 5. 2D and 3D structures of ligands and proteins in molecular docking against 6N7A.

Traditional Thai herbal medicine provides a theoretical basis for the treatment of eczema and psoriasis. The findings indicated that successful treatment of eczema and psoriasis with the topical herbal cream involved in their antioxidant and anti-inflammatory activities, promoting healing and protecting the skin's barrier function. These results were in accordance with a previous study that the combination of antioxidant and anti-inflammatory molecules was a therapeutic strategy to ameliorate the clinical symptoms of eczema and psoriasis patients [50,51]. Thai herbal formulation, including *C.* sativa and *C. longa* are important source for the research on novel eczema and psoriasis treatments due to their wide diversity of biological compounds and actions **(Table 2)**. Cannabinoids, the active constituents of *C.* sativa, and their derivatives are known to have anti-inflammatory property, immunological activity and anti-proliferative effects on keratinocytes for eczema and psoriasis treatment [9,10]. Two major phytocannabinoids including THC and CBD are derived from *C.* sativa. The bioactive compounds THC and CBD interact with the human endocannabinoid system in the skin, helping to reduce inflammation and alleviate symptoms of eczema and psoriasis [11–13]. Curcumin, the main active ingredient extracted from *C. longa*, has been proposed as a treatment for eczema and psoriasis. Curcumin has been claimed to have potent anti-inflammatory effects with potential mechanisms of actions identified such as suppression of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, and IL-17), inhibition of iNOS, cyclooxygenase-2 (COX-2), prostaglandin E2 (PGE2), and NO production, and downregulation of the MAPK (P38, JNK, ERK) pathway [14,15]. Increasing evidence has shown that herbal products' structural diversity and multidirectional mechanisms of action have revealed the synergistic activity to treat eczema and psoriasis [52,53]. The combined regulations of cannabinoid receptor inhibition, pro-inflammatory cytokine production, NO reduction, and MAPK pathway inhibition by the topical herbal cream are considered therapeutic strategies to treat eczema and psoriasis.

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4. Conclusions

The present findings suggest that a topical herbal cream containing *C. sativa* and *C. longa* possesses antioxidant and anti-inflammatory properties and may provide symptomatic benefits in eczema and psoriasis. However, the clinical observations were derived from a very limited sample size and should be interpreted cautiously. Further mechanistic investigations and adequately powered randomized controlled trials are required to validate efficacy, safety, and therapeutic mechanisms.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: We encourage all authors of articles published in MDPI journals to share their research data. In this section, please provide details regarding where data supporting reported results can be found, including links to publicly archived datasets analyzed or generated during the study. Where no new data were created, or where data is unavailable due to privacy or ethical restrictions, a statement is still required. Suggested Data Availability Statements are available in section "MDPI Research Data Policies" at https://www.mdpi.com/ethics.

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