

Evaluation of the Antipsoriatic Activity of *Sivanar Vembu Kuzhi Thailam* in an Imiquimod-Induced Psoriasis Model: Phytochemical, Computational, and Experimental Investigations

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ABSTRACT

Psoriasis is a chronic immune-mediated inflammatory skin disorder characterized by epidermal hyperplasia and dysregulated immune responses. Long-term use of the current therapeutic agents is often limited by adverse effects, high costs, and variable efficacy. The present study evaluated the antipsoriatic potential of *Sivanar Vembu Kuzhi Thailam* (SVKT), a traditional Siddha formulation, using an imiquimod-induced psoriasis-like mouse model. The drug was subjected to physicochemical characterization, microbiological evaluation, and Gas chromatography–mass spectrometry (GC-MS) analysis to identify its major phytoconstituents. Network pharmacology was performed to explore interactions between bioactive compounds and key psoriasis-associated inflammatory targets. Female BALB/c mice were induced to develop psoriasis-like lesions. SVKT (60, 100, and 200 mg/kg, orally) was administered to test prophylactic and therapeutic efficacy. Disease progression and therapeutic response were assessed using Psoriasis Area and Severity Index (PASI) scoring, histopathological examination, and Baker's pathological scoring. GC-MS analysis identified 95 compounds. Computational analyses indicated favorable interactions of selected phytoconstituents with TNF- α , IL-17A, IL-1 β , and IFN- γ related to psoriasis. SVKT significantly reduced PASI scores, erythema, scaling, and epidermal thickening ($p < 0.05$), while histopathological evaluation demonstrated restoration of normal skin architecture and reduced inflammatory infiltration. The formulation complied with microbiological safety standards and showed no evidence of toxicity. These findings demonstrate that SVKT might possess significant antipsoriatic, anti-inflammatory, and antioxidant activities, supporting its traditional use and highlighting its potential as a safe, effective, and economical therapeutic candidate for psoriasis management.

Keywords: Psoriasis; *Sivanar Vembu Kuzhi Thailam*; Network pharmacology; Imiquimod model; Siddha

INTRODUCTION

Psoriasis is a chronic, systemic, immune-mediated disorder that encompasses a wide range of clinical manifestations from the well-recognized cutaneous plaques to psoriatic arthritis. It is frequently accompanied by dactylitis, psoriatic axial spondyloarthritis, psoriatic onychopathy, and enthesitis, which underlines the multifaceted and complex nature of the disease¹⁻³. Psoriasis can occur at any age, but it is most frequently seen in the third and fifth decades of life. Worldwide, psoriasis has an overall prevalence of approximately 1-3% of the population, with highly variable rates ranging from 0.05% to 11.9% across geographic and racial groups. In India, the prevalence ranges from 0.44% to 2.8%, depending on regional environmental and genetic differences^{4,5}. Epidemiologic investigations indicate that psoriasis is more prevalent in men during their third and fourth decades and in childhood, with an estimated prevalence of 0.71%. Environmental determinants, such as climate, sunlight exposure, and humidity, are closely linked to disease prevalence. Winter worsens, and summer improves, psoriasis, possibly because of reduced ultraviolet radiation exposure, cooler temperatures, less sunlight, and less humidity. Stress, minor injury,

infections, some medications, alcohol, tobacco, and obesity may induce or aggravate the condition^{6,7}.

Psoriasis presents several clinical subtypes, including guttate, inverse, erythrodermic, pustular, and plaque (psoriasis vulgaris), the latter occurring in approximately 90% of cases. Approximately one-third of patients develop psoriatic arthritis, characterized by pain, stiffness, swelling, and erythematous, squamous plaques on the trunk, scalp, genital area, knees, and elbows⁸. Psoriasis is increasingly being viewed as a multisystem inflammatory disease with comorbidities like inflammatory bowel disease, depression, hypertension, obesity, metabolic syndrome, type 2 diabetes, coronary artery disease, and non-alcoholic fatty liver disease. Other comorbid conditions being studied are chronic obstructive pulmonary disease, nephropathy, erectile dysfunction, dementia, and obstructive sleep apnea⁹. The pathogenesis of psoriasis is multifactorial with interactions among immune cells, keratinocytes, and skin-resident cells. Psoriasis has been recognized in the past two decades as an immune cell-mediated disorder. Activation of the inflammatory cascade is triggered by plasmacytoid dendritic cells (pDCs), followed by the maturation and generation of IL-12, IL-23, and TNF- α by myeloid dendritic cells

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(mDCs). The cytokines stimulate Th1 and Th17 cells to secrete pro-inflammatory mediators like IL-17, IL-21, IL-22, and TNF- α . In response, keratinocytes become activated, particularly by IL-17, further exacerbating the inflammatory environment and thereby amplifying the pathological process¹⁰⁻¹². The treatments available for psoriasis are categorized into three main groups: topical, phototherapy, and systemic treatments, with selection based on disease severity, comorbidities, and treatment history. Mild psoriasis is typically treated with topical therapy, which involves medications such as clobetasol, tazarotene, calcitriol, and calcipotriol¹³. Phototherapy is used when topicals are inadequate. Severe to moderate psoriasis typically requires systemic agents, such as acitretin, etretinate, methotrexate (MTX), and cyclosporine, as first-line treatment, while biologics and fumaric acid esters are considered alternatives. Biologics against IL-17, IL-23, and TNF- α have proven greatly effective, but due to their exorbitant price, the risk of side effects, safety issues, and relapses upon withdrawal limit their extensive use, and research continues into the development of safer and more effective drug variants¹⁴. Except for retinoids, all traditional therapies primarily exert anti-inflammatory effects, suppressing keratinocyte growth and promoting plaque resolution. In most areas, traditional Chinese medicine (TCM), climatotherapy, and self-administered over-the-counter (OTC) medications, are used alongside conventional therapy¹⁵.

Ayurveda and Siddha medicine are routinely employed as adjuvant therapies for psoriasis in India. Despite the availability of contemporary pharmacological options, patients are often dissatisfied with these therapies due to their high cost, limited accessibility, and potential long-term side effects, underscoring the need for complementary therapeutic approaches. Herbal medicinal preparations have garnered significant attention as potential anti-psoriatic drugs due to their ability to yield structurally diverse bioactive molecules¹⁶. These preparations are generally less expensive than contemporary medications, providing an effective alternative for treating psoriasis. In India, various herbal preparations are used in traditional medicine for treating skin conditions, with limited integration into modern medicine due to a lack of scientific evidence regarding long-term safety and effectiveness. As such, research has now shifted its focus to assessing the safety and effectiveness of herbal treatments for psoriasis¹⁷. The Siddha system of medicine, an ancient tradition prevalent among the Tamil people in India, Sri Lanka, Malaysia, and other parts of the world, offers a systematic approach to treating psoriasis. Psoriasis is called *Kalanjagapadai* in Siddha. Plaque type, the most prevalent variety, is called *Kutta karappan* or *Kanda karappan*. Psoriatic arthritis is known as *Thimir vata karappan*, and scalp psoriasis as *Manda karappan*. Of the Siddha products, *Sivanar Vembu Kuzhi Thailam* (SVKT) has been found to possess potential antipsoriatic activity¹⁸. SVKT is a polyherbal oil preparation consisting of equal proportions (1:1:1 ratio, w/w/w) of *Indigofera aspalathoides* (aerial parts), *Celastrus paniculatus* (seeds), and *Corallocarpus epigaeus* (rhizome). It is prepared using the traditional *Kuzhi Thailam* method (a destructive distillation process that does not involve external vegetable-based oils) to produce a thick, dark polyherbal bio-oil¹⁹.

The present study was designed to evaluate the antipsoriatic effects of SVKT through an integrated phytochemical, computational, and experimental approach. The phytochemical and microbiological assessments were performed to characterize the formulation and establish the basic quality standards. GC-MS profiling was used to identify the major phytochemical constituents. Network pharmacology analysis was employed to explore the potential interactions between the SVKT phytoconstituents and psoriasis-associated inflammatory targets. Finally, the pharmacological activity of an orally administered SVKT was evaluated in an imiquimod (IMQ)-induced psoriasis-like inflammation in BALB/c mice with two distinct experimental approaches; one being the preventive or prophylactic effect and another one to assess the therapeutic effects of SVKT. The IMQ model is a

well-established experimental system for inducing human psoriatic pathology and is a suitable model for screening candidate antipsoriatic drugs. Local application of IMQ to the depilated dorsal skin of mice repeatedly induces psoriasiform dermatitis, characterized by erythema, scaling, epidermal thickening, and inflammatory cell infiltration. These histopathological and clinical features mimic key features of human psoriasis (20). We hypothesized that SVKT would attenuate the IMQ-induced psoriasis-like skin inflammation and histopathological alterations, potentially through the modulation of inflammatory molecular pathways.

MATERIALS AND METHODS

Materials

Commercially available SVKT (Batch No.TEI18012) was from SKM Siddha and Ayurveda Company (India) Pvt. Ltd., Saminathapuram (Post), Modakkurichi, Erode District, Tamil Nadu, India, a Good Manufacturing Practice (GMP)-certified manufacturing unit. Free IMQ cream samples were obtained from Glenmark Pharmaceuticals Ltd., Goa, India. Methotrexate (MTX) was obtained from Cipla Ltd. (Mumbai, India). Hematoxylin and Eosin (H&E) staining reagents, neutral buffered formalin (10%), ethanol, xylene, and paraffin wax (56–58°C melting point) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Standard laboratory-grade chemicals and solvents used during tissue processing were procured from Merck KGaA (Darmstadt, Germany).

IAEC approval

The study was approved by the Institutional Animal Ethics Committee (IAEC), KMC, MAHE, Manipal (IAEC/KMC/78/2017, dated 28 October 2017).

Study Site

The study was conducted at the Central Animal Research Facility (CARF), KMC, MAHE, Manipal.

Experimental cohorts and animal allocation

The animal species, number of animals, sex, age, body weight and total number of animals used in the current study are outlined in below (Table 1) Each experiment used an independent cohort, and animals were not reused between experiments.

Healthy test animals (n = 81) as mentioned in table 1 were procured from the CARF of KMC, MAHE, Manipal. The animals were maintained in the animal house as per the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India, New Delhi.

The animals were continuously observed daily to monitor their health and ensure continuous access to food and water. The test animals were housed individually in polypropylene cages with paddy husk as the bedding material. They were maintained at a temperature of $27 \pm 3^\circ\text{C}$, relative humidity of $60 \pm 10\%$, and a 12-hour light/dark cycle. The bedding was changed daily, and the cages were maintained in the same location throughout the study duration. The animals were kept on a standard laboratory diet consisting of rat pellets as food and unrestricted access to water. The body weight of each animal was measured prior to the start of the experiment.

All efforts were made to ameliorate the suffering of animals. No genetic modifications or previous procedures were performed on the animals before the start of the study. Anaesthetics (ketamine 200 mg/kg and xylazine 15 mg/kg; i.p.) and the method of euthanasia (pentobarbital 200 mg/kg, i.p.) were used as per the guidelines of CPCSEA. And no procedures were carried out that would result in sustained pain.

Table 1. Experimental cohorts and animal allocations between groups

Experiment	Test Animal Species	Sex	Age (Weeks)	Body Weight (g)	Total Number of Groups	Number of Animals per Group	Total Number of Animals Used
Acute oral toxicity	Sprague-Dawley rats	Female	12 – 13	200 – 300	NA	NA	9
Prophylactic study	BALB/c	Female	8 – 10	20 – 30	6	6	36
Therapeutic study	BALB/c	Female	8 – 10	20 – 30	6	6	36

Physicochemical Evaluation of SVKT

Iodine value of SVKT²¹: The iodine value indicates the degree of unsaturation. One gram of the test drug was accurately weighed and added to a dry 300 mL iodine flask. This was dissolved with 15 mL of chloroform. Following that, a flask was sealed with a stopper, and 25 mL of iodine monobromide solution was incrementally introduced from a burette. The resulting solution was then left in the dark for 30 minutes. Then, 100 mL of distilled water and 10 mL of potassium iodide solution were added. The mixture was then titrated with a 0.1 M sodium thiosulfate solution, which was added gradually while continuously shaking until the yellow tint almost completely vanished. After adding 1.5 mL of starch indicator solution, the titration was repeated until the blue color vanished. Simultaneous blank determination was carried out.

$$\text{Iodine value} = \frac{1.269 (b - a)}{w}$$

Where w = weight in g of the sample (SVKT); a = volume of 0.1M sodium thiosulphate used in sample titration; b = volume of 0.1M sodium thiosulphate used in blank titration

Saponification Value SVKT²¹: Saponification value reflects the average molecular weight of the fatty acids present in the formulation. Two grams of the test drugs were weighed precisely and added to a 200 mL borosilicate glass flask fitted with a reflux condenser. This was mixed with 25.0 mL of 0.5 M ethanolic KOH and a small amount of pumice powder, then boiled in a water bath with reflux for 30 minutes to turn the mixture transparent. Following this, 1 mL of phenolphthalein solution was added while the mixture was still hot, and the mixture was titrated immediately with 0.5 M hydrochloric acid until the pink color disappeared. Simultaneously, a blank determination was carried out.

$$\text{Saponification value} = \frac{28.05 (b - a)}{w}$$

Where w = weight in g of the sample (SVKT); a = volume of 0.5M hydrochloric acid used in sample titration; b = volume of 0.5M hydrochloric acid used in blank titration

Acid Value of SVKT²¹: Acid value represents the amount of free fatty acids present in the formulation. 10 g of the test drug was precisely weighed and dissolved in 50 mL of a mixture of equal volumes of ether and 95% ethanol. The mixture was neutralized by adding 1 mL of a phenolphthalein solution. The substance was melted completely by gradually heating the solution in a water bath. Titered using 0.1 M KOH until the pink color persisted for 15 seconds. The volume of KOH solution used, noted as the titer value in mL, was recorded.

$$\text{Acid value} = \frac{5.61 n}{w}$$

Where n = volume of 0.1M potassium hydroxide; w = weight in g (SVKT)

Gas chromatography-mass spectrometry (GC-MS) analysis of the samples

The SVKT samples were dissolved in methanol to a final concentration of 1 mg/mL before GC-MS analysis. The analysis used a Shimadzu GC-

MS-QP2010S system with a 30 m long, 0.25 mm inner diameter, and 0.25 µm film thickness RTX-5 column. The temperature at the contact was maintained at 280°C, while the ion source was at 200°C. The carrier gas, helium, was used at a flow rate of 1 mL/min, and a 1 µL sample was injected for analysis. To ascertain and validate the identities of the chemicals, a mass spectrum obtained by MS was compared with those in the National Institute of Standards and Technology (NIST) and the WILEY collections. The analysis was conducted in Bengaluru, Karnataka, India, at Analytical Research & Metallurgical Laboratories Pvt. Ltd (ARML)²².

Determination of Microbial Contamination in SVKT

Several pathogenic microbes, including *Salmonella*, *E. Coli*, *S. aureus*, *P. aeruginosa*, molds, and yeasts, can cause contamination. Excess moisture and inadequate drying of raw materials can lead to bacterial contamination. Any raw material that is contaminated with microbes must not be processed further and must be rejected. Microbiological testing is therefore essential for standardizing herbal source materials. Both test drugs underwent microbiological testing. A sterile vial was filled with 1 mL of normal saline, and the sample was combined with saline. Bacterial contamination was examined using blood agar, while fungal contamination was checked using Sabouraud Dextrose Agar (SDA). The sample was inoculated onto both blood agar and SDA plates and incubated at 37°C for 48 hours²³.

Network Pharmacology

Genes related to psoriasis were identified using GeneCards, OMIM, and the Open Target Databases. Duplicate and false-positive targets were removed, and psoriasis-related genes were identified. The psoriasis target intersection from different databases was obtained using the Venn 2.1.0 platform. The common targets of psoriasis were identified using Venn diagrams, and a network was constructed in Cytoscape (Version 3.8.10; <https://www.cytoscape.org/>). In addition, Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) enrichment analyses were conducted on targets identified in both databases to illustrate differences between them²⁴⁻²⁷.

Acute toxicity study

A total of 9 animals were utilized to conduct the acute oral toxicity study of SVKT following guideline number 423 set by the OECD²⁸. The first three animals received 300 mg/kg dose of SVKT with the help of oral gavage and observed for the signs and symptoms of toxicity as mentioned in the OECD guideline. The dosing interval between each animal was kept at 48 hours after ensuring the previous animal's survival. As there was no mortality and moribund, the second set of animals were administered with the next dose (2000 mg/kg) and continued the observation. As there were no changes in the animal's behavior and no mortality, finally another set of three animals were administered with 2000 mg/kg of SVKT. Each set of animals was observed for 14 days for the signs and symptoms of any toxicity as per the guidelines.

Observations

Upon dosage, each animal was observed individually. Initial observation was made soon after 30 min of dosage, and regular

monitoring was carried out for 24 h with special attention during the first 4 h of dosage. The animals were then monitored on a daily basis for 14 days. The observation was recorded individually for each animal, and the additional observation was made on animals if they have shown any signs of toxicity, such as changes in behaviour and changes in eyes and mucous membranes, skin and fur, somatomotor, circulatory, respiratory, autonomic, central nervous systems activity. Emphasis was placed to observe any signs of diarrhoea, salivation, tremors, sleep, lethargy, and coma for 14 days.

Induction of psoriasis

The mice were first anaesthetized intraperitoneally with a combination of ketamine (200 mg/kg) and xylazine (15 mg/kg)²⁹. Following the anaesthesia, a 3 cm x 3 cm area on their backs was carefully shaved, and any remaining hair was completely removed using a depilatory cream. To induce psoriasis in each mouse, 62.5 mg/day (3.125 mg of the active component) of imiquimod (IMQ) 5% w/w cream from Glenmark Pharmaceuticals in Goa, India was topically applied on the shaven area for 12 consecutive days^{30,31}.

Evaluation of prophylactic efficacy of SVKT in IMQ-induced psoriasis-like inflammation mouse model

Dose selection of test drugs: Three doses of SVKT were selected. 60 mg/kg was the animal-equivalent dose (AED). The AED was calculated using the formula Mouse dose (for 20 g mouse) = Human dose X 0.0026 (surface area ratio)³². The other two doses were based on the results of acute toxicity study conducted. 200 mg/kg was selected as one-tenth of the verified no-observed-adverse-effect (2000 mg/kg). The middle dose of 100 mg/kg was selected to provide an approximately graded exposure range. The drugs administered and grouping of the animals are shown in (Table 2). The mice were randomly allocated to different groups. IMQ was administered topically, and three doses of the test drugs, SVKT and MTX, were administered orally via gavage once daily for 12 consecutive days. To minimize variation, all drugs were administered at approximately the same time each day. Control of animals received only the vehicle. On the 13th day, all the animals were euthanized using intraperitoneal pentobarbital 200 mg/kg, and skin samples were taken for histological analysis.

Evaluation of therapeutic efficacy of SVKT in IMQ-induced psoriasis-like inflammation mouse model

The mice were randomly allocated to different groups. The grouping, drugs administered, and route of drug administration are mentioned in

Table 3. Following the induction of psoriasis like inflammation, the test drugs and the standard drug were orally administered from day 13 to day 18. The SVKT doses were the same as those used in the prophylactic study. All treatments were administered once a day at nearly the same time each day. On day 19, animals were euthanized by intraperitoneal injection of Pentobarbital (200 mg/kg), and skin samples were harvested for histological examination.

Evaluation Parameters of the prophylactic and antipsoriatic effect study

PASI evaluation: The severity of skin inflammation was assessed using the clinical PASI score, as outlined by Van der Fits et al. The scoring system included assessments of erythema, scales, and thickening; each was independently scored on a scale from 0 to 4 (0 = none, 1 = slight, 2 = moderate, 3 = marked, 4 = maximum), recorded every 24 hours. The total combined score was used to measure the severity of inflammation on a scale of 0 to 12³³.

Histopathological examination: Prior to processing and embedding in paraffin blocks, the skin samples were fixed for 48 hours at room temperature in 10% formalin. A rotary microtome was used to cut 5-µm-thick sections from the samples. Hematoxylin and eosin (H&E) stain was used to section the samples. The Baker's scoring system was employed to evaluate pathological changes³⁴.

Pathological/Baker's scoring: On a scale of 0 to 10, the pathological changes were scored using Baker's scoring system, and the mean score was reported. Details of skin areas, pathological alterations, and the scores are shown in Table 4.

Statistical analysis

The analysis was conducted using version 16.0 of the Statistical Package for the Social Sciences (SPSS). The data were summarized using both the mean and standard deviation (Mean ± SD). Group mean comparisons were performed using a one-way analysis of variance (ANOVA), and for detailed group comparisons, a post hoc Tukey test was conducted. Statistical significance was considered for $p < 0.05$. Two-way repeated-measures ANOVA with Bonferroni post-hoc adjustments for intra-subject correlations were used for the analysis of PASI scoring system while statistical significance was considered for $p < 0.05$ as the same animals measured repeatedly over time. The Kruskal – Wallis test followed by Dunn's post-hoc test was used to compare Baker's scores across groups, and the data are reported as medians (IQR) and statistical significance was considered for $p < 0.05$.

Table 2. Study design for the evaluation of prophylactic efficacy of SVKT in IMQ-induced psoriasis-like inflammation mouse model

Group	Drug
Group I	Normal control: Oral distilled water 10 mL/kg body weight; topical Vaseline
Group II	Psoriasis control: Topical IMQ cream 62.5 mg/day
Group III	Standard control: Topical IMQ cream 62.5 mg/day + oral MTX 1 mg/kg
Group IV	Topical IMQ cream 62.5 mg/day + oral SVKT 60 mg/kg
Group V	Topical IMQ cream 62.5 mg/day + oral SVKT 100 mg/kg
Group VI	Topical IMQ cream 62.5 mg/day + oral SVKT 200 mg/kg

Table 3. Study design for the evaluation of therapeutic efficacy of SVKT in IMQ-induced psoriasis-like inflammation mouse model

Group	Drug
Group I	Normal control: Oral distilled water 10 mL/kg body weight; topical Vaseline
Group II	Psoriasis control: Topical IMQ cream 62.5 mg daily for 12 days
Group III	Standard control: Topical IMQ cream 62.5 mg daily for 12 days, followed by oral MTX 1 mg/kg from day 13 till day 18
Group IV	Topical IMQ cream 62.5 mg daily for 12 days, followed by oral SVKT 60 mg/kg from day 13 to day 18
Group V	Topical IMQ cream 62.5 mg daily for 12 days, followed by oral SVKT 100 mg/kg from day 13 to day 18
Group VI	Topical IMQ cream 62.5 mg daily for 12 days, followed by oral SVKT 200 mg/kg from day 13 to day 18

Table 4. The Baker's scoring system

Items	Pathological alterations	Score
Keratin	1. Munro abscess	2.0
	2. Hyperkeratosis	0.5
	3. Parakeratosis	1.0
Epidermis	1. Thinning above papillae	0.5
	2. Lengthening and clubbing of rete ridges	1.5
	3. Acanthosis	0.5
	4. Lack of granular layer	1.0
Dermis	1. Lymphocytic infiltrate	0.5
	2. Mild	1.0
	3. Moderate	2.0
	4. Marked	0.5
	5. Papillary congestion	

Table 5. Physicochemical values of SVKT

Sl. No.	Physicochemical Properties	Result
1	Iodine Value	6.8
2	Saponification value	261.1
3	Acid value	10.2

Table 6. Results of microbial contamination in standard and SVKT

Microbial contamination	Standard	SVKT
Total bacterial count/g	1,00,000 cfu/mL	Absent
Yeast and mold count/g	1000 cfu/mL	Absent
<i>Salmonella</i> sp/g	Absent	Absent
<i>E. coli</i> sp/g	Absent	Absent
<i>Staphylococcus aureus</i> /g	Absent	Absent
<i>Pseudomonas aeruginosa</i> /g	Absent	Absent

RESULTS

Physicochemical Evaluation of SVKT

The physicochemical characterization of SVKT is mentioned in Table 5.

Test for specific Pathogen in SVKT

The results of microbial contamination analysis revealed that SVKT were free from any microbial load. The total bacterial count and the yeast and mould count were found to be absent in both formulations, remaining well below the permissible limits of 1,00,000 cfu/mL and 1000 cfu/mL, respectively. Furthermore, pathogenic microorganisms, including *Salmonella* spp., *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, were not detected in either formulation. These findings confirm that SVKT is microbiologically safe and complies with the standard quality requirements. The results of microbial contamination of test drugs are shown in Table 6.

GC-MS analysis of SVKT

The SVKT revealed the presence of 95 distinct compounds, as detailed in Figure 1.

The bioactive compounds present in the SVKT, along with their retention time (RT), percentage areas, molecular weights, molecular formulas, and chemical abstract service (CAS) numbers, are given in Table 7.

Network Pharmacology

Initially, we investigated the potential psoriasis target using three databases: GeneCards, Open Targets, and Phenopedia. There were 960 genes from GeneCards, 231 genes from open targets, and 620 genes from phenopedia. All database targets were combined, and 79 common potential psoriasis targets were ultimately selected (Figure 2). To further identify hub genes, we imported 79 intersection genes into the Cytoscape to construct a PPI network containing 13 nodes

and 72 edges. The PPI network map was obtained and analyzed by the CytoNCA plug-in. The obtained PPI network depicts the final core targets of psoriasis: TNF- α , IL-17a, NF- κ B, and IFN- γ . To further investigate the KEGG Pathway analysis, the 79 overlapping target genes screened in the Protein-Protein Interaction (PPI) network were analyzed for enrichment and KEGG pathways. In total, there were 79 KEGG pathway enrichment results. The results indicated that the following pathways contain a higher number of genes: (hsa05321) Inflammatory bowel disease, (hsa04060) Cytokine-cytokine receptors interaction, (hsa04659) Th17 cell differentiation, (hsa04630) JAK-STAT signaling pathway, and (hsa05145) Toxoplasmosis. The first 10 representative signaling pathways in the KEGG bubble chart are shown in Figure 2. To further investigate the Gene Ontology (GO) of the 79 overlapping genes, an analysis was performed to understand the functions and biological pathways of their gene products. The results showed that GO biological processes associated with compound genes included Defense response (GO:0006952), response to other organisms (GO:0051707), response to external stimulus (GO:0009605), Immune response (GO:0006955), and immune system process (GO:0002376). Bar plot of the GO enrichment score is shown in Figure 2.

Evaluation of prophylactic efficacy of SVKT in IMQ-induced psoriasis-like inflammation mouse model

PASI scores: In the Psoriasis control group, the PASI scores, as shown in Figure 3, show a progressive increase in inflammatory symptoms after the application of IMQ from days 1 to 12. The highest intensity is observed on the twelfth day, confirming the effective development of psoriasis-like dermatitis in IMQ-treated mice. The standard drugs and all Siddha treatment groups significantly reduced PASI scores from day 2 onwards ($p < 0.05$). The psoriatic lesions induced by IMQ were effectively reversed with 100 mg/kg BW of SVKT starting from the 12th day. There were no statistically significant differences among the three test drug doses or between the test drugs and the standard drug ($p > 0.05$).

Table 7. GC-MS data of SVKT

Peak number	Retention Time	Phytochemical Name	Area %	GCMS Match Score (SI)	Chemical Formula	Molecular Weight	CAS Number
1	4.374	Phenol	0.61	95	C6H6O	94	108-95-2
2	4.651	Tricyclo[3.3.0.0(2,8)]octane-3,7-dione, 4-methyl-4-(propan-2-on-1-yl)-	0.39	73	C12H14O3	206	0-00-0
3	5.025	1,2-Cyclopentanedione, 3-methyl-	0.09	85	C6H8O2	112	765-70-8
4	5.194	2-Cyclopenten-1-one, 2,3-dimethyl-	0.08	90	C7H10O	110	1121-05-07
5	5.36	Phenol, 2-methyl-	0.29	95	C7H8O	108	95-48-7
6	5.639	Phenol, 4-methyl-	0.95	95	C7H8O	108	106-44-5
7	5.734	Caprylic acid	0.3	79	C8H16O2	144	124-07-2
8	5.886	Mequinol	0.46	84	C7H8O2	124	150-76-5
9	5.973	Benzoic acid, methyl ester	0.32	98	C8H8O2	136	93-58-3
10	6.12	Bicyclo[2.2.1]heptane, 2-(1-buten-3-yl)-	0.37	78	C11H18	150	55170-90-6
11	6.215	Bicyclo[2.2.1]heptan-2-ol, 1,5,5-trimethyl-	0.31	91	C10H18O	154	6168-62-3
12	6.544	Phenol, 2-ethyl-	0.23	81	C8H10O	122	90-00-6
13	6.727	Bicyclo[2.2.1]heptan-2-one, 1,7,7-trimethyl-, (1R)-	1.4	93	C10H16O	152	464-49-3
14	6.913	Borneol	2.66	95	C10H18O	154	10385-78-1
15	7.146	Benzenecarboxylic acid	1.4	92	C7H6O2	122	65-85-0
16	7.296	2-Hexenoic acid, 5-hydroxy-3,4,4-trimethyl-, (E)-	0.98	71	C9H16O3	172	14919-59-6
17	7.404	1-Decene, 3,4-dimethyl-	1.35	77	C12H24	168	50871-03-09
18	7.776	Phenol, 2,3,6-trimethyl-	0.62	77	C9H12O	136	2416-94-6
19	7.938	Benzene, 1-ethyl-4-methoxy-	0.28	87	C9H12O	136	1515-95-3
20	7.999	Isobomyl formate	0.45	91	C11H18O2	182	1200-67-5
21	8.278	Bicyclo[6.4.0]dodeca-9,11-diene	0.65	83	C12H18	162	0-00-0
22	8.382	Nonanoic acid	0.69	71	C9H18O2	158	112-05-0
23	8.531	Phenol, 4-ethyl-2-methoxy-	0.58	92	C9H12O2	152	2785-89-9
24	8.703	Bicyclo[2.2.1]heptan-2-ol, 1,7,7-trimethyl-, acetate, (1S-endo)-	1.88	94	C12H20O2	196	5655-61-8
25	8.791	Pentadecane	0.66	92	C15H32	212	629-62-9
26	9.051	Naphthalene, 1-methyl-	0.51	90	C11H10	142	90-12-0
27	9.475	Phenol, 2,6dimethoxy--	0.75	94	C8H10O3	154	91-10-1
28	9.677	Benzene, eicosyl-	0.54	83	C14H22	190	2189-60-8
29	10.003	9-Eicosene, (E)-	1.19	92	C20H40	280	74685-29-3
30	10.115	Tetradecane	0.88	96	C14H30	198	629-59-4
31	10.728	1,2,3-Trimethoxybenzene	0.22	76	C9H12O3	168	634-36-6
32	10.785	Phenol, 2-methoxy-4-(1-propenyl)-, (Z)-	0.57	75	C10H12O2	164	5912-86-7
33	10.946	Octadecanoic acid, 9,10-epoxy, isopropyl ester	0.29	63	C21H40O3	340	95007-80-0
34	11.008	Benzene, octyl-	0.42	83	C14H22	190	2189-60-8
35	11.283	1-Tetradecanol	1.07	93	C14H30O	214	112-72-1
36	11.383	Octadecane	1.73	94	C18H38	254	593-45-3
37	11.569	7-Heptadecene, 1-chloro-	0.28	93	C17H33Cl	272	56554-78-0
38	11.721	5-tert-Butylpyrogallol	0.27	82	C10H14O3	182	20481-17-8
39	12.145	Dodecanoic acid	0.34	83	C12H24O2	200	0143-07-07
40	12.291	Benzene, nonyl-	0.43	83	C15H24	204	1081-77-2
41	12.345	Hexane, 2-phenyl-3-propyl-	0.41	80	C15H24	204	0-00-0
42	12.412	Dichloroacetic acid, 4-hexadecyl ester	0.26	93	C18H34Cl2O2	352	0-00-0
43	12.493	1-Nonadecene	0.66	94	C19H38	266	18435-45-5
44	12.582	Octadecane	0.9	93	C18H38	254	593-45-3
45	13.182	1-(2-Aminophenyl)pyrrole	0.25	83	C10H10N2	158	16066-51-6
46	13.296	Unknown	0.26	82	C18H38	254	593-45-3
47	13.407	cis-7-Dodecen-1-yl acetate	0.31	82	C14H26O2	226	14936-65-3
48	13.488	3-Heptadecene, (Z)-	0.98	89	C17H34	238	0-00-0
49	13.55	3-Heptadecene, (Z)-	0.88	88	C17H34	238	0-00-0
50	13.635	Ergosta-5,7-dien-3-ol, (3.beta.)-	0.85	88	C28H44O	396	516-92-7
51	13.728	Heptadecane	1.29	94	C17H36	240	629-78-7
52	13.92	1-Isoleucine, N-butoxycarbonyl-, isohexyl ester	0.25	80	C17H33NO4	315	0-00-0
53	13.993	Methyl tetradecanoate	0.31	94	C15H30O2	242	0124-10-7

54	14.413	Tetradecanoic acid	1.39	94	C14H28O2	228	544-63-8
55	14.64	5-(1-Bromo-1-methyl-ethyl)-2-methyl-cyclohexanol	1.29	82	C10H19BrO	234	111585-70-1
56	14.812	Octadecane	0.56	95	C18H38	254	593-45-3
57	15.608	(+)-trans-1-Isopropenyl-4-methyl-1,4-cyclohexanediol	0.26	78	C10H18O2	170	0-00-0
58	15.683	Cyclohexanol, 2-methyl-3-(1-methylethenyl)-, (1.alpha., 2.alpha., 3. alpha.)-	0.29	77	C10H18O	154	15934-29-9
59	15.772	Isobomyl propionate	0.44	78	C13H22O2	210	2756-56-1
60	15.882	2-Heptadecanone	2.98	94	C17H34O	254	2922-51-2
61	16.122	Hexadecanoic acid, methyl ester	3.27	96	C17H34O2	270	112-39-0
62	16.354	Ergost-25-ene-3,6-dione, 5,12-dihydroxy-, (5.alpha., 12.beta.)-	0.88	70	C28H44O4	444	560-14-5
63	16.64	n-Hexadecanoic acid	12.55	96	C16H32O2	256	57-10-3
64	16.826	Octadecan-4-one	1.49	76	C18H36O	268	94307-14-9
65	17.66	Oleanitrile	2.64	95	C18H33N	263	112-91-4
66	17.833	8-Octadecenoic acid, methyl ester	6.05	96	C19H36O2	296	2345-29-1
67	18.042	Octadecanoic acid, methyl ester	1.03	96	C19H38O2	298	112-61-8
68	18.304	Oleic acid	10.62	95	C18H34O2	282	112-80-1
69	18.445	Octadecanoic acid	2.35	96	C18H36O2	284	57-11-4
70	18.606	Hexadecanamide	1.12	93	C16H33NO	255	629-54-9
71	18.695	Tetracosane	0.32	94	C24H50	338	646-31-1
72	18.873	1,3-Dioxolane, 2-pentadecyl-	0.44	90	C18H36O2	284	61214-52-6
73	19.567	Heneicosane	0.29	94	C21H44	296	629-94-7
74	20.124	9-Octadecenamide, (Z)-	0.75	92	C18H35NO	281	301-02-0
75	20.234	Octanoic acid, 2-furanylmethyl ester	0.39	80	C13H20O3	224	39252-03-04
76	20.393	beta-d-Lyxofuranoside, O-nonyl-	0.47	73	C14H28O5	276	0-00-0
77	21.296	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	0.66	88	C19H38O4	330	23470-00-0
78	21.399	Isobornyl propionate	0.38	78	C13H22O2	210	2756-56-1
79	21.666	Bicyclo[2.2.1]heptan-2-ol, 1,3,3-trimethyl-	0.29	75	C10H18O	154	1632-73-1
80	22.084	Hexadecanoic acid, 2,3-bis(acetyloxy)propyl ester	0.31	78	C23H42O6	414	55268-70-7
81	22.594	Butanoic acid, 3-methyl-, 1,7,7-trimethylbicyclo[2.2.1]hept-2-yl ester, endo-	0.34	74	C15H26O2	238	76-50-6
82	22.715	Oleic anhydride	0.85	87	C36H66O3	546	24909-72-6
83	22.881	Naphthalene, 1-(1-decylundecyl)decahydro-	0.29	82	C31H60	432	55320-00-8
84	23.022	Isobornyl propionate	3.6	82	C13H22O2	210	2756-56-1
85	23.231	Naphthalene, 1-(1-decylundecyl)decahydro-	0.24	84	C31H60	432	55320-00-8
86	23.42	17-Pentatriacontene	0.57	86	C35H70	490	0-00-0
87	23.689	Squalene	1.06	95	C30H50	410	0111-02-04
88	24.143	Dotriacontane	0.1	94	C32H66	450	544-85-4
89	24.335	(2,6,6-Trimethylcyclohex-1-enylmethanesulfonyl)benzene	2.42	84	C16H22O2S	278	0-00-0
90	25.235	Estradiol 17-benzoate-3-p-phenylazobenzoate	0.22	60	C38H36N2O4	584	0-00-0
91	25.501	4,4,6a,6b,8a, 11,11,14b-Octamethyl-1,4,4a,5,6,6a, 6,6,7,8,8,9,10,11,12,12a, 14, 14a, 14b-oc	0.67	84	C30H48O	424	0-00-0
92	25.893	(IS,6R,9S)-5,5,9,10-Tetramethyltricyclo[7.3.0.0(1,6) dodec-10(11)-ene	0.27	78	C16H26	218	0-00-0
93	26.129	1,2,3,4-Butanetetrol, 2,3-diacetate 1,4-dibenzoate, (R*, R*)-	0.28	59	C22H22O8	414	74792-93-1
94	27.57	16-Hentriacontanone	0.24	83	C31H62O	450	502-73-8
95	33.298	Stigmasterol	0.25	61	C29H48O	412	83-48-7

Table 8. Qualitative assessment of pathological score in prophylactic efficacy experiment

Groups	Baker's score Median (IQR)
NORMAL	0 (0,0)
PSORIASIS CONTROL	7 (5.25, 8.5)
Top IMQ + oral MTX	0.5 (0, 1.125) [¶]
Top IMQ + Oral SVKT60	0.25 (0, 0.625) [¶]
Top IMQ + Oral SVKT100	0.5 (0, 1) [¶]
Top IMQ + Oral SVKT200	0.75 (0, 1.125) [¶]

[¶]p<0.05 versus psoriasis control. The Kruskal-Wallis test was used to compare Baker's scores across groups, and the data are reported as medians (IQR).

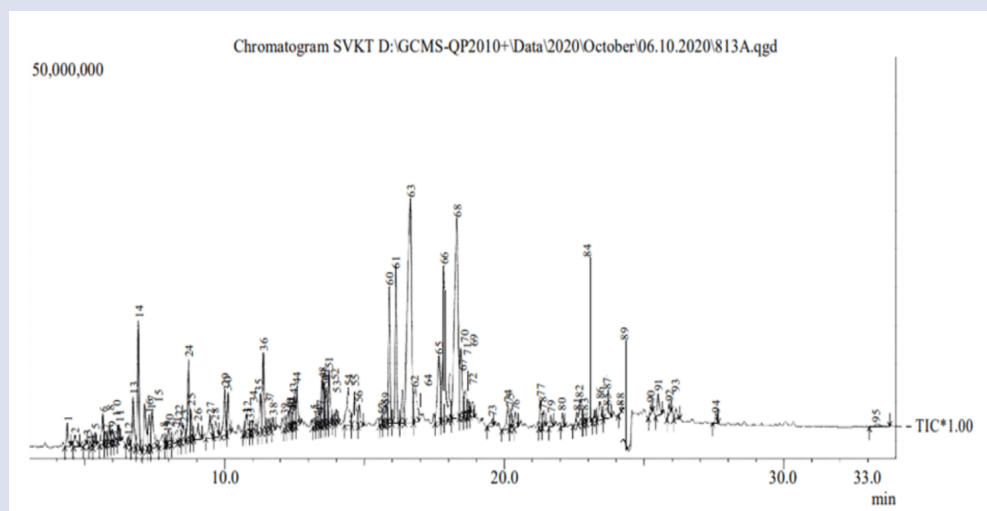


Figure 1. GC-MS chromatogram of SVKT showing distinct peaks corresponding to various bioactive compounds.

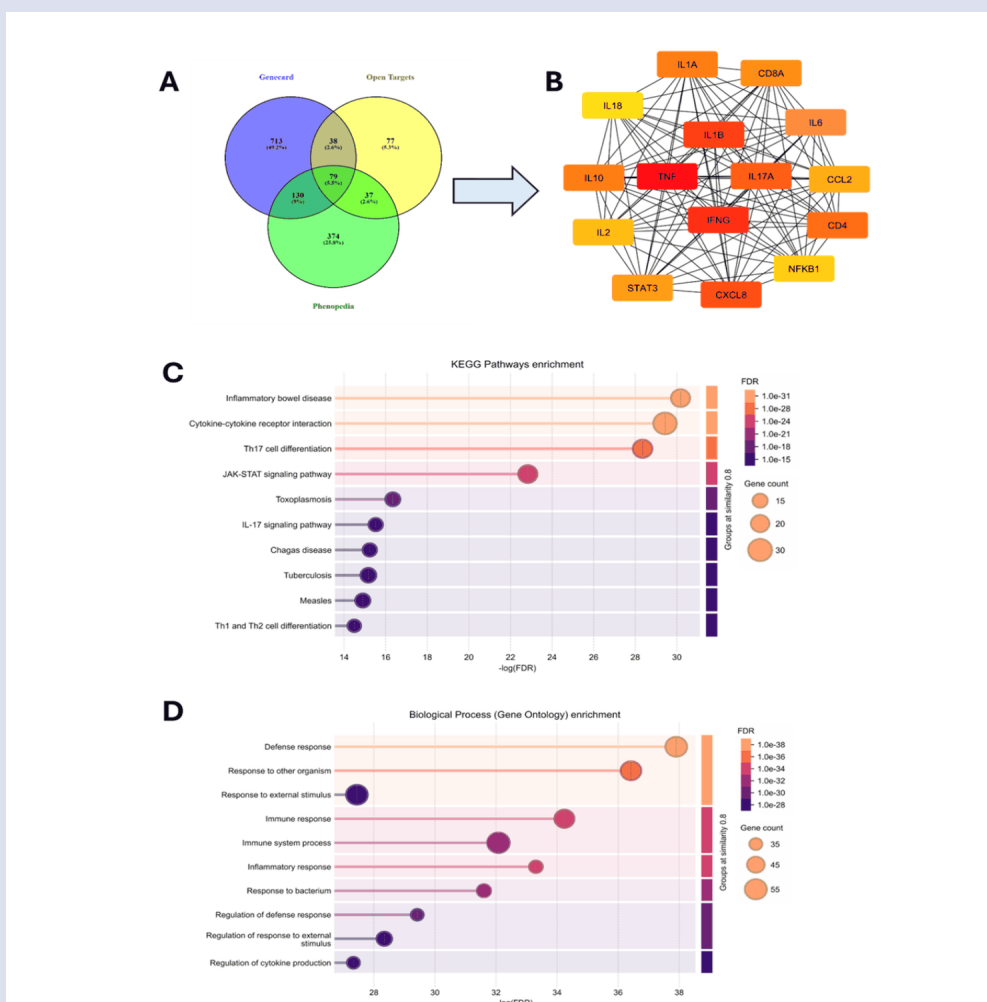


Figure 2. Identification and enrichment analysis of psoriasis-associated targets. (A) Venn diagram showing overlapping psoriasis-related genes retrieved from GeneCards, Open Targets, and Phenopedia databases. (B) Core gene network highlighting key inflammatory mediators, including TNF, IL1B, IL17A, IFNG, IL10, and STAT3, involved in psoriasis. (C) GO enrichment analysis of the common target genes reveals significant enrichment in biological processes related to cytokine signaling, immune response, and inflammation. (D) KEGG pathway analysis illustrating major pathways associated with psoriasis pathogenesis, including cytokine–cytokine receptor interaction, IL-17 signaling, and TNF signaling pathways.

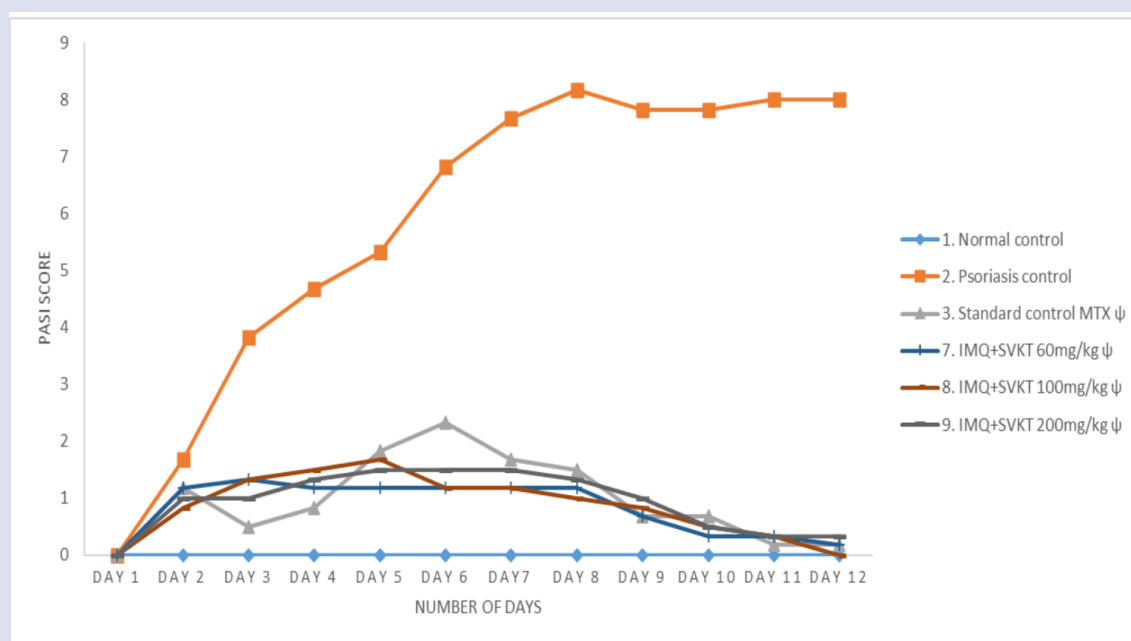


Figure 3. PASI intensity scores (erythema, thickness, and scaling) recorded during the prophylactic efficacy experiment over 12 days.

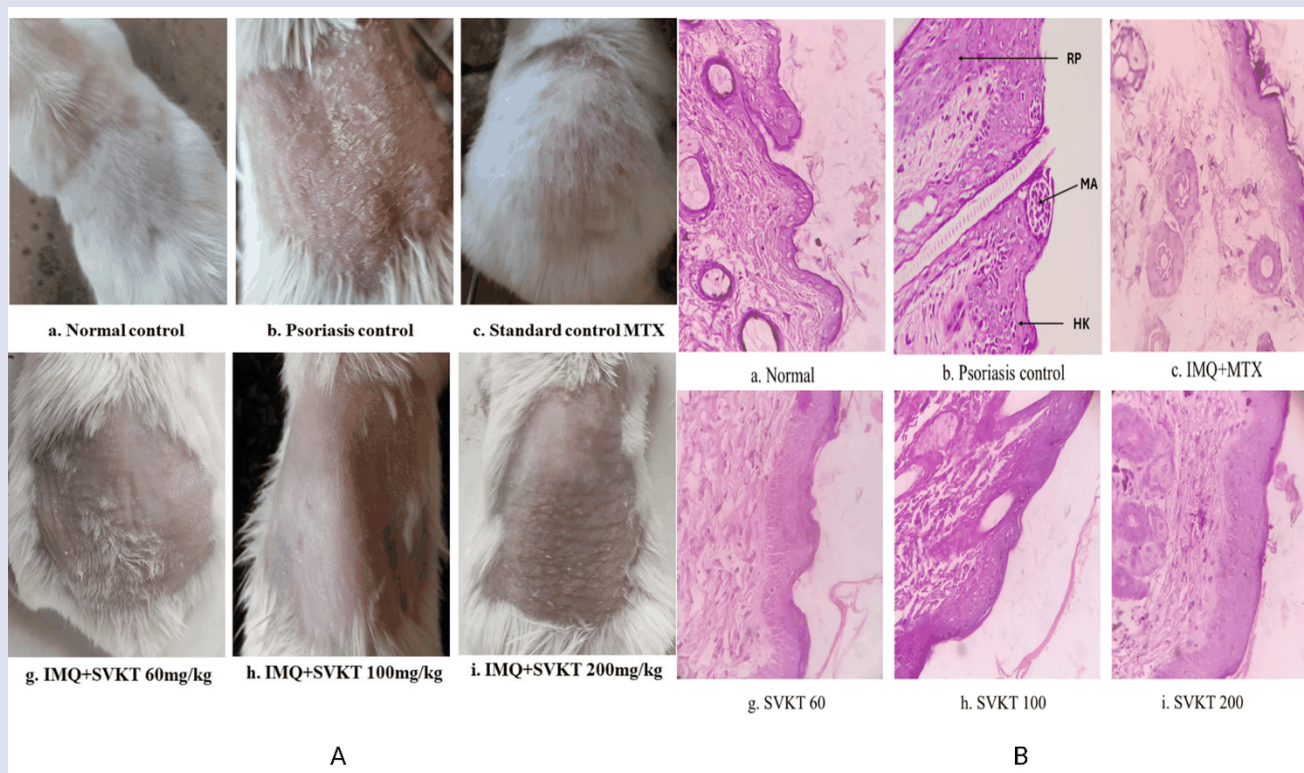


Figure 4. Evaluation of prophylactic effects in the IMQ-induced psoriasis mouse model. (A) Phenotypal presentation of dorsal skin on the 12th day showing visible differences in erythema, scaling, and thickness among normal, psoriasis control, and treatment groups. Test formulations demonstrated a marked reduction in psoriatic lesions compared to the psoriasis control group. (B) Histopathological analysis of skin sections (40× magnification) depicting normalization of epidermal thickness, reduced parakeratosis, and restoration of dermal architecture in treated groups, confirming the therapeutic efficacy of the test formulations in mitigating psoriatic inflammation.

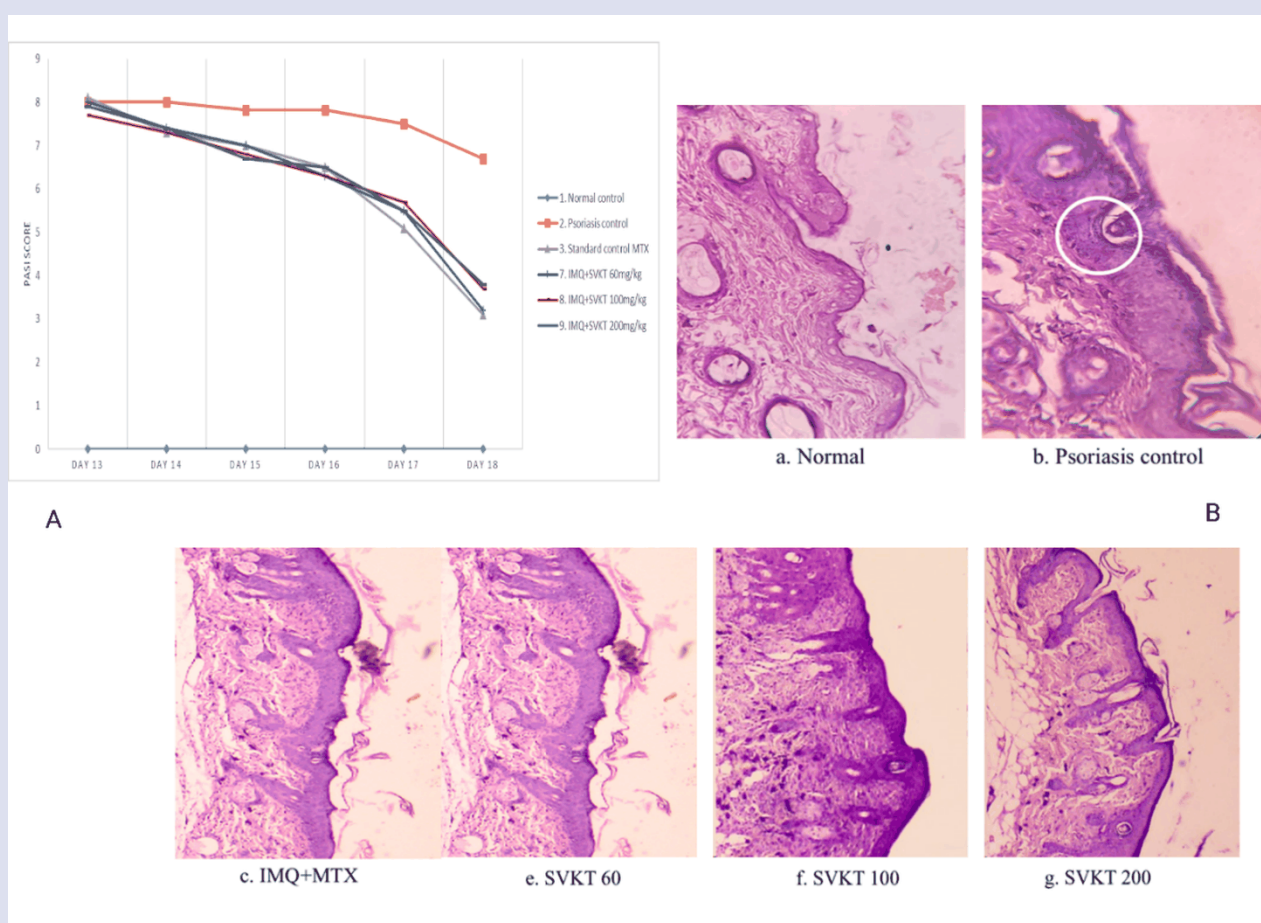


Figure 5. Evaluation of the therapeutic efficacy of test formulations in the psoriasis mouse model. (A) Change in mean PASI intensity scores (erythema, thickness, and scales) recorded in the therapeutic efficacy experiment. (B) Histopathological findings of skin sections from normal, psoriasis control, and test drug-treated groups in the therapeutic efficacy experiment (40× magnification).

Phenotypic observation: In the psoriasis control group (b), the examination of the mice's dorsal skin surface revealed progressively increasing redness, swelling, and scaling from day 1 to day 12. The inflammation reached its peak level on day 12. Treatment with both the standard drug (c) and the test drugs (d-i) caused a substantial recovery from psoriasis. This was evident from the gradual reduction in skin thickness and scaling, as well as lower PASI scores in the treated groups (Figure 4A). Figure 4B illustrates the histopathological findings of dorsal skin sections from the normal group, the psoriasis control group, and those treated with the test drugs.

Pathological scoring: The pathological score is represented as Baker's score in Table 8. The disease control group showed the highest score. The scores of the groups treated with standard and test drugs were significantly lower than those of the disease control group ($p < 0.05$). There were no statistically significant differences among the three test drug doses or between the test drugs and the standard drug ($p > 0.05$).

Evaluation of the therapeutic efficacy of SVKT in IMQ-induced psoriasis-like inflammation mouse model

PASI scores: In the data presented in Figure 5A, PASI intensity scores following psoriasis induction in mice were observed across all groups. The psoriasis control group exhibited disease characteristics on day 18, as evidenced by a high PASI score. Whereas PASI scores of all Siddha treatment groups and the standard treatment group were significantly low when compared to the psoriasis control group ($p < 0.05$) on day 18.

There were no statistically significant differences among the three test drug doses or between the test drugs and the standard drug ($p > 0.05$). Figure 5B depicts the histopathological findings of dorsal skin sections from the normal group, the psoriasis control group, and those treated with test drugs.

Pathological scoring: The pathological score is represented as Baker's score in Table 9. The disease control group showed the highest score. The scores of the groups treated with standard and test drugs were significantly lower than those of the disease control group.

DISCUSSION

The goal of this research was to analyze the prophylactic and therapeutic effect of the Siddha formulation SVKT on psoriasis development using the IMQ-induced psoriasis mouse model. In the present research, after 12 daily IMQ applications, mice developed typical psoriatic plaques, indicating that the model was successfully induced.

IMQ via Toll-like receptors 7 and 8 (TLR7/8) on dendritic cells (DCs) results in the induction of the IL-23/IL-17 axis, a key psoriasis pathogenic pathway. Activated DCs secrete IL-23, which stimulates the proliferation and activation of Th17 and $\gamma\delta$ T cells, leading to the production of pro-inflammatory cytokines, including IL-17A, IL-22, and TNF- α ³⁵⁻³⁷. In parallel, IMQ-stimulated plasmacytoid DCs (pDCs) produce IFN- α , IL-6, and IL-23, which further enhanced inflammatory cascades.

Psoriasis is associated with a multifaceted interaction among immune cells and cytokines. Of these, IL-6 is highly upregulated in psoriatic lesions, inducing keratinocyte proliferation and differentiation of IL-17-producing T lymphocytes³⁸. Activated neutrophils mediate psoriatic inflammation by delivering neutrophil extracellular traps (NETs), which stimulate epidermal TLR4/IL-36R crosstalk and perpetuate chronic inflammation³⁹. Furthermore, nuclear factor- κ B (NF- κ B) is critical, and its activation by keratinocytes as well as immunocytes leads to epidermal hyperplasia and inflammatory infiltration⁴⁰.

The pro-inflammatory cytokine TNF- α also exacerbates psoriasis by promoting the differentiation of T-cells into pathogenic Th1 and Th17 subsets, which secrete IFN- γ and IL-17, respectively. TNF- α also promotes the expression of endothelial adhesion molecules, enabling leukocyte invasion into psoriatic skin, thereby promoting keratinocyte hyperproliferation and plaque formation⁴¹. Most of today's biologics for psoriasis, such as TNF- α inhibitors, IL-17 inhibitors, and IL-23 blockers, target these specific cytokine pathways, thereby establishing their central role in disease pathogenesis.

All the constituents together confer anti-inflammatory, antioxidant, immunomodulatory, and wound-healing attributes on SVKT, which are pertinent to the management of psoriasis. Each constituent has shown considerable biological activity related to psoriasis pathogenesis.

I. aspalathoides have been found to possess significant antioxidant and anti-inflammatory activity. Ethanolic and methanolic extracts have potent DPPH and ABTS radical scavenging activities, as well as strong ferric ion-reducing abilities⁴²⁻⁴³. In vivo experiments demonstrate improved wound healing, decreased lipid peroxidation, and increased activity levels of superoxide dismutase (SOD) and ascorbic acid, indicating a robust antioxidative defence⁴⁴. The plant also exhibits antiproliferative activity against keratinocytes and reduces pro-inflammatory cytokine levels, making it an excellent candidate for an antipsoriatic drug.

C. paniculatus seed oil extract has demonstrated intense anti-inflammatory and antioxidant activities in different experimental models. In IMQ-induced psoriasis, topical treatment with *C. paniculatus* seed oil significantly reduced PASI scores, attenuated epidermal thickness, and suppressed the production of inflammatory cytokines, including TNF- α , IL-23, IL-17A, and IL-1 β ⁴⁵. Moreover, this plant contains extracts that inhibit lipoxygenase, an enzyme in eicosanoid formation and inflammation. The chloroform extract of the plant has been shown to possess excellent antioxidant activity in DPPH, FRAP, and TEAC assays, which underscores its antioxidant and anti-inflammatory properties⁴⁶.

Rhizome extracts of *C. epigaeus* demonstrate DPPH radical scavenging activity that is concentration-dependent, indicating strong antioxidant potential⁴⁷. The herb has traditionally been employed in Siddha medicine to treat inflammatory and dermatological disorders, as revealed by its inclusion in SVKT. These antioxidant activities can help counteract oxidative stress in psoriatic skin, thereby reducing inflammation and tissue injury. Psoriasis pathogenesis encompasses several overlapping mechanisms, including immune dysregulation, oxidative stress, and deranged keratinocyte proliferation. The therapeutic action of SVKT lies in its capacity to modulate all these processes in concert.

Bioactive substances identified in SVKT using GC-MS include palmitic acid, myristic acid, oleic acid, borneol, squalene, and stigmasterol, all of which contribute to its anti-inflammatory activity. Palmitic acid (Hexadecanoic acid) suppresses PLA2, the principal enzyme that produces inflammatory lipid mediators, and thus decreases inflammation⁴⁸. Myristic acid (Tetradecanoic acid) enhances IL-10 synthesis, an anti-inflammatory cytokine that suppresses nitric oxide production and attenuates pro-inflammatory signals⁴⁹. Caprylic acid

analogs have been found to suppress NF- κ B and TNF- α expression while enhancing IL-10 expression, thereby supporting evidence of the anti-inflammatory activity of SVKT⁵⁰. Borneol has demonstrated strong anti-inflammatory activity by inhibiting the infiltration of lymphocytes and macrophages and reducing the levels of TNF- α , IL-8, and IL-6 in inflammatory models⁵¹. Squalene and stigmasterol also inhibit NF- κ B activation, reduce TNF- α expression, and block neutrophil infiltration, thereby decreasing tissue inflammation^{52,53}. Collectively, these molecules modulate various inflammatory pathways involved in psoriasis, similar to the mechanisms targeted by TNF- α and IL-17 blockers in contemporary treatments.

Many signaling pathways interact to contribute to the development of this disease, thereby warranting polypharmacological strategies for treatment. In this study, a network pharmacology approach, coupled with molecular docking, was used to elucidate the molecular mechanisms underlying SVKT's therapeutic role in psoriasis⁵⁴. PPI network analyses suggested that TNF- α , IL17A, IFNG, and NFKB1 are the main hub genes associated with the mechanism of action of SVKT. This finding aligns with current knowledge of psoriasis pathogenesis, in which activation of the TNF- α /IL-23/IL-17 signaling axis plays a pivotal role in its development. Tumor necrosis factor- α (TNF- α) is one of the main cytokines involved in psoriasis and has been a promising therapeutic target for several drugs. TNF- α induces dendritic cell activation and keratinocyte proliferation, and enhances the expression of various cytokines, such as IL-6, IL-17, and IFN- γ ⁵⁵. Similarly, IL-17A has been identified as an essential mediator of inflammatory responses in the epidermis and of keratinocyte activation⁵⁶. It is therefore clear that the hub genes' involvement in these pathways is biologically relevant in explaining SVKT's therapeutic potential. In addition, Gene Ontology analysis revealed strong enrichment in immune response, inflammatory response, defense response, regulation of cytokine production, and response to external stimuli. This finding supports our hypothesis that SVKT can interfere with multiple immune mechanisms in disease pathogenesis⁵⁷. Lastly, KEGG pathway analysis also showed significant enrichment in the following pathways: cytokine-cytokine receptor interaction, Th17 cell differentiation, IL-17 signaling pathway, and JAK-STAT signaling pathway.

While most synthetic medicines are targeted against a single protein, herbs often contain multiple active ingredients that can target multiple interrelated signaling pathways simultaneously. This feature seems to perfectly suit the complex nature of psoriasis and may explain why traditional herbal formulations are effective despite containing many phytochemicals.

The measured iodine value, saponification value, and acid value are reported as batch-characterization data. Because no validated compendial specification for SVKT was identified, these results were not classified as compliant/noncompliant and should be considered only preliminary values. The absence of microbial load also confirms microbiological safety and product integrity⁵⁸.

Histopathological examination of skin sections from IMQ-treated mice revealed characteristic changes of psoriasis, including hyperkeratosis, acanthosis, rete ridge elongation, Munro's microabscesses, and dilated dermal capillaries. These pathological features closely resemble human psoriatic plaques, validating the translational validity of the IMQ model for assessing therapeutic interventions^{30,59}. Whereas, the skin tissues of SVKT-treated mice revealed significant recovery as compared to the psoriasis control. There was considerable diminishment in epidermal thickness, reconstitution of rete ridges to normal, reduced infiltration of inflammatory cells, and alleviation of vascular congestion. These observations document the strong anti-inflammatory and antiproliferative actions of SVKT. The noted improvements correlate with the molecular mechanisms outlined, including the inhibition

of pro-inflammatory cytokines, reduction of oxidative stress, and inhibition of keratinocyte hyperproliferation. The concomitant reduction in PASI and Baker's scores further supports the clinical importance of these histopathological changes. The multifactorial efficacy of SVKT, encompassing anti-inflammatory, antioxidant, immunomodulatory, and antiproliferative activities, parallels the pharmacological approaches employed by contemporary biologics and small-molecule inhibitors. SVKT might have provided modulation of pathways through its natural bioactive compounds, offering a comprehensive and potentially safer solution than synthetic agents.

LIMITATIONS OF THE CURRENT STUDY

- The present study was not designed to understand the molecular mechanism of individual phytoconstituents of SVKT.
- The immunohistochemical analysis of inflammatory markers in the skin tissue could have provided additional insights into the potential mechanism by which SVKT could have reduced the inflammatory process in psoriasis.

CONCLUSION

The study provides significant evidence that SVKT exhibits antipsoriatic, antioxidant, and anti-inflammatory activities with the potential to counteract the pathologic changes induced by IMQ in a psoriasis model. Phytoconstituents of SVKT, might have acted synergistically to restore epidermal architecture, normalize keratinocyte proliferation, and suppress key pro-inflammatory mediators. Histopathological examination supported this evidence through reduced acanthosis, parakeratosis, and inflammatory cell infiltration. The cumulative data on pharmacological, histological, and network pharmacological findings clearly establish SVKT as a promising polyherbal formulation with multifaceted mechanisms that counter the immune dysregulation hallmarks of psoriatic pathology. As a scientifically validated Siddha remedy, SVKT thus may serve as a safer, cost-effective, and likely impactful alternative or adjunct to conventional therapies for antipsoriatics. However, clinical validation and formulation standardization beyond this pilot study are required for translating these findings into evidence-based clinical practice.

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