https://doi.org/10.31925/farmacia.2026.3.13 **ORIGINAL ARTICLE**

EFFECT OF RHIZOMA *SMILACIS GLABRAE* EXTRACT IN IMPROVEMENT OF SKIN LESIONS AND INFLAMMATION IN MICE WITH PSORIASIS AND HYPERURICEMIA

FANG YAO [1], HONGSHENG DING [1], BIN DU [1], JING MA [1], MENGZHU JIN [2]*

[1]*Department of Rheumatology, Jiaxing Hospital of Traditional Chinese Medicine/Jiaxing Hospital Affiliated to Zhejiang Chinese Medical University, 314001, China*
[2]*Department of Dermatology, The First Hospital of Jiaxing/Affiliated Hospital of Jiaxing University, Jiaxing, 314001, China*

**corresponding author: jmz_1001@126.com*

Manuscript received: February 2026

Abstract

This study investigated the mechanisms by which *Rhizoma Smilacis Glabrae* extract (RSGE) alleviates psoriasis associated with hyperuricemia (HUA) in a murine model. Fifty male mice were allocated to five groups: control, IMQ-induced psoriasis, HUA, HUA + IMQ, and HUA + IMQ treated with RSGE. Clinical severity (PASI score), serum biochemical parameters, histopathological changes, inflammatory cytokine expression, and MAPK signaling pathway activation were evaluated. IMQ-induced psoriasis increased PASI scores, lesion thickness, epidermal hyperplasia, inflammatory cytokine expression (IL-6, IL-17, IL-23, TNF-α), and MAPK pathway activation. HUA elevated serum uric acid (UA), creatinine (Cr), and blood urea nitrogen (BUN) levels. Coexistence of psoriasis and HUA further aggravated both cutaneous lesions and systemic biochemical abnormalities, accompanied by enhanced inflammatory responses and MAPK signaling activation ($p < 0.05$). Treatment with RSGE significantly reduced PASI scores, improved histopathological alterations, decreased UA, Cr, and BUN levels, and suppressed inflammatory cytokine expression and MAPK pathway activation compared with the HUA + IMQ group. These findings suggest that RSGE effectively attenuates psoriasis complicated by hyperuricemia, likely through modulation of inflammatory responses and inhibition of the MAPK signaling pathway.

Rezumat

Studiul a investigat mecanismele prin care extractul de *Rhizoma Smilacis Glabrae* (RSGE) ameliorează psoriazisul asociat cu hiperuricemia (HUA) într-un model experimental murin. Cincizeci de șoareci masculi au fost repartizați în cinci grupuri: martor, psoriazis indus cu imiquimod (IMQ), HUA, HUA + IMQ și HUA + IMQ tratat cu RSGE. Au fost evaluate severitatea clinică (scor PASI), parametrii biochimici serici, modificările histopatologice, expresia citokinelor proinflamatorii și activarea căii de semnalizare MAPK. Psoriazisul indus cu IMQ a determinat creșterea scorului PASI, îngroșarea leziunilor și a epidermei, precum și creșterea expresiei IL-6, IL-17, IL-23 și TNF-α. Hiperuricemia a fost asociată cu valori crescute ale acidului uric, creatininei și ureei serice. Asocierea psoriazisului cu HUA a agravat atât manifestările cutanate, cât și dezechilibrele biochimice și răspunsul inflamator, prin activarea accentuată a căii MAPK. Administrarea RSGE a redus semnificativ severitatea leziunilor, markerii inflamatori și parametrii biochimici alterați. Rezultatele sugerează că RSGE poate ameliora psoriazisul complicat cu hiperuricemie prin inhibarea inflamației și modularea căii de semnalizare MAPK.

Keywords: psoriasis, hyperuricemia, Rhizoma *Smilacis Glabrae* extract, MAPK pathway.

Introduction

Psoriasis is a chronic, recurrent, and systemic skin disease mediated by inflammation, which is incurable. Its main clinical manifestations are localized or widely distributed erythema, scales, and epidermal thickening on the skin (1). Psoriasis is closely correlated to systemic inflammatory responses associated with metabolism, including obesity, diabetes, metabolic syndromes, and hyperuricemia (HUA) (2, 3). Uric acid (UA) serves as the final product of purine metabolism in the human body, with low solubility. Excessive deposition of urate salts can cause gout attacks in the joints and uric acid kidney stones (4). HUA is positively correlated with various diseases such as obesity, diabetes, and psoriasis (5-7). Despite this, the relationship between psoriasis and HUA remains controversial.

Rhizoma Smilacis Glabrae (RSG) is the dried rhizome of *Smilax corbularia var. woodii*, a plant of the Liliaceae family. It has a sweet, light, and neutral taste, can act through the liver and stomach meridians, and plays the roles of detoxification, dampness removal, and joint relief (8). The main active components in RSG include flavonoids, flavonoid glycosides, and alkaloids, among others. Some modern pharmacological studies have confirmed that RSG has antibacterial, anti-gout, immunosuppressive, and other effects (9, 10). Wu *et al*. (11) found through network pharmacology that the formula containing RSG can mediate multiple types of inflammation-

related signaling pathways to exert therapeutic effects on periodontitis. Yang *et al*. (12) reported that different doses of RSG could lower the lipid levels of hypertensive rats. Xiao *et al*. (13) confirmed that RSGE can regulate the creatinine (Cr) and blood urea nitrogen (BUN) levels in blood in HUA mice and adjust the structure of intestinal microbiota, to participate in repairing intestinal barrier damage caused by HUA. In addition, some studies have also demonstrated that active ingredients such as astragaloside, quercetin, and resveratrol in RSGE can alleviate psoriasis-like skin lesions (14). It indicates that RSG has a therapeutic effect on psoriasis and HUA, but its potential role in treating the comorbidity of psoriasis and HUA remains to be explored.

The mitogen-activated protein kinase (MAPK) pathway can deliver extracellular stimuli (such as inflammatory factors, stress, and growth factors, among others) into the interior of cells, thereby regulating cell proliferation, differentiation, apoptosis, and inflammatory responses. As recognized, p38, extracellular regulated protein kinase (ERK) 1/2, and c-Jun N-terminal kinase (JNK) are important subfamily members of MAPK (15). Highly phosphorylated p38 MAPK and JNK can be detected in psoriasis lesions. Excessive activation of the MAPK pathway is a key factor driving the inflammatory response and epidermal hyperplasia in psoriasis (16). In patients with HUA, excessively high blood UA concentration can lead to the deposition of urate salts in joints and other areas, forming monosodium urate crystals. Once recognized by immune cells, these crystals can activate inflammasomes, and the activation of inflammasomes strongly depends on the MAPK pathway (17, 18). Based on this information, it is evident that both psoriasis and HUA have the activation of the MAPK inflammatory pathway, which subsequently forms a pathophysiological connection. Therefore, the MAPK pathway provides a theoretical target for developing a co-therapeutic strategy for psoriasis and HUA.

Based on this, a comorbidity model of psoriasis and HUA was prepared on mice in this work to analyze the phenotypic changes of the mice with both diseases. Subsequently, after intragastric administration of RSGE, the potential mechanism by which RSGE improves the symptoms of mice co-infected with psoriasis and HUA was explored based on the MAPK pathway. It was hoped that this could offer a reference for finding treatment plans for the comorbidity of psoriasis and HUA, as well as for controlling the condition of psoriasis patients and improving their quality of life.

Materials and Methods

Animals

Fifty SPF male Kunming (KM) mice (aged 4 to 6 weeks, with an average body weight of 20 ± 1 g; Liaoning Changsheng Biotechnology Co., Ltd., China) were enrolled for study herein. All experimental animals were raised in the experimental animal center. The average room temperature was (23 ± 2)℃, and the relative humidity was (55 ± 5) % in the center, with light and dark alternating for 12/12 hours. They were fed with conventional animal feed and could eat freely. This study has been approved by the Ethics Committee of Affiliated Hospital of Jiaxing University, and the experimental process strictly adheres to international animal research guidelines.

Grouping, model construction, and treatments

After one week of adaptive feeding of 50 KM mice, they were randomly divided into a normal control (NC) group, an Imidazolomide (IMQ) group, a HUA group, a HUA + IMQ group, and a HUA + IMQ + RSGE group, with 10 mice in each. The specific intervention methods for mice in different groups are as follows:

NC group: The mice were raised normally without any other treatments;

IMQ group: The hair on the back of the mice was removed, and then 5% IMQ cream (Sichuan MedShine Pharmaceutical Co., Ltd., China) at a dose of 62.5 mg was applied once a day for 7 consecutive days;

HUA group: Mice were fed with 10% yeast feed and received by gavage 100 mg/kg bw adenine (Shanghai Kanglang Biotechnology Co., Ltd., China) once daily for 4 consecutive weeks;

HUA + IMQ group: Mice were first fed with 10% yeast feed and received by gavage 100 mg/kg bw adenine once a day. After 4 weeks of continuous feeding, the hair on the back was removed. For 7 consecutive days, 5% IMQ cream at a dose of 62.5 mg was applied once a day.

HUA + IMQ + RSGE group: Based on modeling in the HUA + IMQ group, mice were administered by gavage 500 mg/kg bw of RAGE once a day for 7 consecutive days starting from week 4.

Except for the mice in the HUA + IMQ + RSGE group, the mice in the other groups were administered by gavage the same amount of normal saline once a day for 7 consecutive days starting from week 4. The RSGE was provided by Jiaxing Hospital of T.C.M. When in use, the RAGE was dissolved in fresh distilled water to prepare a suspension of appropriate concentration, which should be stored in a refrigerator at 4℃ for future use.

Skin lesion severity score

The Psoriasis Area and Severity Index (PASI) (19) was adopted to evaluate the severity of skin lesions on the back of mice in each group. The PASI assessment dimensions included the degree of erythema, epidermal thickening, and the degree of scales. Among them, a score of 0 (normal) indicated that there is normal skin, without erythema or desquamation; 1 point (mild) is characterized by slightly raised skin lesions, accompanied by pale red patches and a

small amount of desquamation; 2 points (moderate) indicates moderate elevation of the skin lesion, presenting as red patches with flaky desquamation; at 3 points (severe), the skin lesion is significantly raised, presenting as deep red patches accompanied by thick layered desquamation; and a score of 4 (extremely severe) indicates that the skin lesion is extremely thickened and raised, presenting as very deep red patches accompanied by thick, layered desquamation.

Hematoxylin-eosin (H&E) staining

After the last intervention, the mice were fasted for 8 hours and intraperitoneally injected with 3% pentobarbital sodium (Thermo Fisher Scientific, USA) at a dose of 150 mg/kg. The mice were sacrificed by removing their necks. The skin on the back was separated, and subcutaneous tissue was removed. The skin lesion thickness was measured using a vernier caliper. Subsequently, an appropriate amount of lesion tissue was taken and fixed in formalin at room temperature for 24 hours. After gradient alcohol dehydration, xylene transparency, and paraffin embedding, paraffin sections with a thickness of 5 μm were prepared. After dewaxing and rehydration, staining was carried out using the H&E staining kit (Shanghai Beyotime Biotechnology Co., Ltd., China), followed by gradient alcohol dehydration and xylene transparency treatment, and the sheets were sealed with neutral gum. The morphological changes of the lesion tissue were observed under a 6400X optical microscope (Deli Group Co., Ltd., China), and then the epidermal layer thickness was recorded using Image Pro Plus 6.0 software (Media Cybernetics, USA).

Detection of serum biochemical indicators

When the mice were sacrificed, 6 mL of blood was collected from the eyes, centrifuged at 3,000 r/min for 10 minutes, and the supernatant was taken. The UA, Cr, and BUN levels in the serum were detected using the IDEXX Catalyst One® automatic blood biochemical analyzer (Beijing Yeeran Technology Co., Ltd., China).

Real-time fluorescence quantitative PCR detection

A portion of the lesion tissue was taken, and liquid nitrogen was added for thorough grinding. Then, Trizol reagent (Thermo Fisher Scientific, USA) was added to extract total RNA. The concentration and purity of the extracted RNA were detected using a UV5Nano ultraviolet spectrophotometer (Mettler Toledo, Switzerland). Following that, cDNA was synthesized using the AgPath-ID™One-Step RT-PCR Kit (ABI, USA). The mRNA expressions of interleukin (IL)-6, IL-17, IL-23, and tumor necrosis factor (TNF)-α were detected using AgPath-ID™One-Step RT-PCR Kit (ABI, USA). The quantitative primer information is as follows: 5'-CTGCAAGAGACTTCCATCCAG-3' and 5'-AGTGGTATAGACAGGTCTGTTGG-3' for IL-6 upstream and downstream, respectively; 5'-CTCCTGCTTCTAGGCTGGTTG-3' and 5'-CCACCTGGCACTTCGAGTTAG-3' for IL-17 upstream and downstream, respectively; 5'-TTCAGatGGGCATGAATGTTCTT-3' and 5'-CCAAATCCGAGCTGTTGTTCTT-3' for IL-23 upstream and downstream, respectively; 5'-TGTCTCAGCCTCTTCTCATT-3' and 5'-GCCATTTGGGAACTTCTCAT-3' for TNF-α upstream and downstream, respectively; 5'-TGGCCTTCCGTGTTCCTAC-3' and 5'-GAGTTGCTGTTGAAGTCGCA-3' for GAPDHIL-6 upstream and downstream, respectively. Taking GAPDH as the internal reference, the relative expressions of each target gene were calculated by the $2^{-\triangle\triangle CT}$ method.

Western blotting

A part of the lesion tissue was collected, cut into small pieces, and ground thoroughly on ice to homogenize. Then, the Radio Immunoprecipitation Assay reagent (Thermo Fisher Scientific, USA) was introduced to extract the total protein, to detect the concentration of extracted protein using the bicinchoninic acid protein quantification kit (Thermo Fisher Scientific, USA). The samples were loaded and subjected to sodium dodecyl sulfate-polyacrylamide gel electrophoresis. The proteins were transferred onto the nitrocellulose membrane (Sigma-Aldrich, USA) and sealed in a blocking solution containing 5% skimmed milk powder at room temperature for 2 hours. Subsequently, rabbit anti-ERK1/2 (Cell Signaling Technology, USA), rabbit anti-JNK (Cell Signaling Technology, USA), rabbit anti-P38 (Cell Signaling Technology, USA), and rabbit anti-GAPDH (Cell Signaling Technology, USA) primary antibodies diluted at a ratio of 1:1000 were added and incubated all night at 4°C. After membrane washing, horseradish peroxidase-labeled mouse anti-IGg (Cell Signaling Technology, USA) secondary antibody diluted at a ratio of 1:2000 was introduced for another incubation at room temperature for 1 hour. After film washing, the enhanced chemiluminescence substrate (Thermo Fisher Scientific, USA) was introduced to develop under the Chemi-Doc MP gel imaging system (Bio-Rad, USA). Next, the ImageJ software (National Institutes of Health, USA) was employed to detect the gray value of the target protein band.

Statistical analysis

Statistical analysis was conducted using Statistical Product and Service Solutions 23.0 (IBM, USA). All data underwent normality and homogeneity of variance tests and were expressed as mean ± sd. One-way analysis of variance was utilized for the comparison of differences among multiple groups, and the LSD-*t* test was employed for pairwise comparison between groups. A value of $p < 0.05$ indicated that the difference was statistically significant.

Results and Discussion

Changes in skin morphology in mice with psoriasis and hUA

The PASI score, the lesion skin thickness, and epidermal layer thickness of mice in the IMQ group and the HUA + IMQ group were obviously greater when compared to those in the NC group ($p < 0.05$). All indicators of mice in the HUA + IMQ group were much greater than those in the IMQ group ($p < 0.05$) (Figure 1).

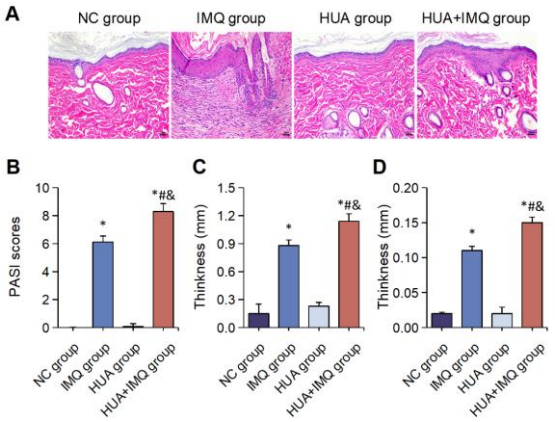

Figure 1.

Psoriasis-like skin changes in model mice. A: H&E staining results of the skin lesion, 200×; B: PASI score; C: Thickness of the affected skin; D: Epidermal layer thickness at lesion. *Compared with NC group, $p < 0.05$; #compared with IMQ group, $p < 0.05$; & compared with HUA group, $p < 0.05$

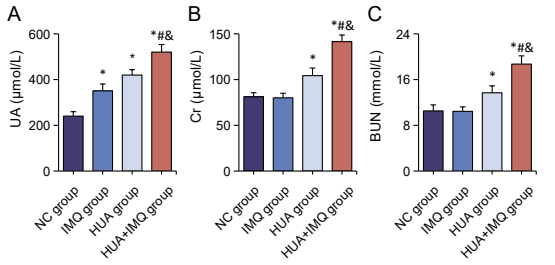

Figure 2.

Changes in serum renal function indicators of model mice. A: Serum UA level; B: Serum Cr level; C: Serum BUN level. *Compared with NC group, $p < 0.05$; #compared with IMQ group, $p < 0.05$; & compared with HUA group, $p < 0.05$

Changes in renal function of mice with psoriasis and HUA

The serum UA of mice in the IMQ group, HUA group, and HUA + IMQ group showed much higher levels in comparison to those in the NC group ($p < 0.05$). The serum Cr and BUN levels in the HUA group and the HUA + IMQ group were remarkably higher relative to those in the NC group and the IMQ group ($p < 0.05$). Among them, the serum UA, Cr, and BUN levels in the HUA + IMQ group were considerably higher when compared to those in the HUA group ($p < 0.05$) (Figure 2).

Changes in the expression of inflammatory genes at the lesion sites in mice with psoriasis and HUA

The relative expressions of IL-6, IL-17, IL-23, and TNF-α mRNA in the skin lesions of mice in the IMQ group and the HUA + IMQ group were significantly higher than those in the NC group and the HUA group ($p < 0.05$), while those at the lesion sites of mice in the HUA + IMQ group were significantly higher in contrast to those in the IMQ group ($p < 0.05$) (Figure 3).

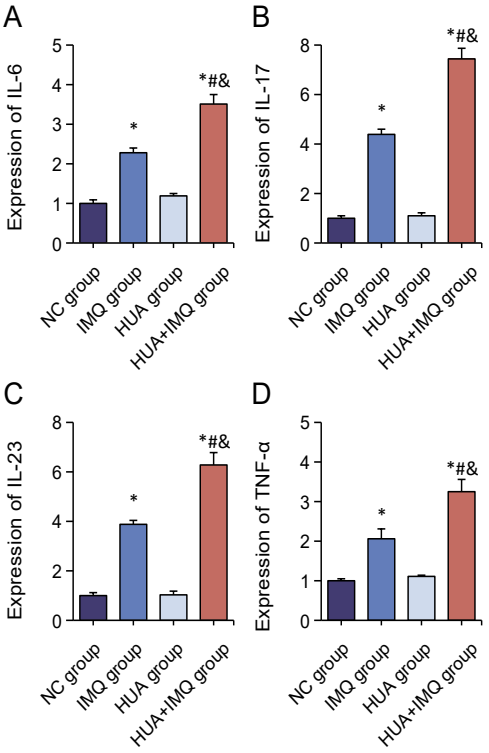

Figure 3.

Changes in the expressions of inflammatory genes at the lesion sites of model mice. A: IL-6; B: IL-17; C: IL-23; D: TNF-α.*Compared with NC group, $p < 0.05$; #compared with IMQ group, $p < 0.05$; & compared with HUA group, $p < 0.05$

Changes in MAPK pathway status at the lesion sites in mice with psoriasis and HUA

The relative expressions of p-P38, p-ERK 1/2, and p-JNK proteins in the skin lesions of mice in the IMQ group and the HUA + IMQ group were significantly higher compared to those in the NC group and the HUA group ($p < 0.05$). The relative expressions of various proteins at the lesion sites in the HUA + IMQ group of mice were significantly higher than those in the IMQ group ($p < 0.05$) (Figure 4).

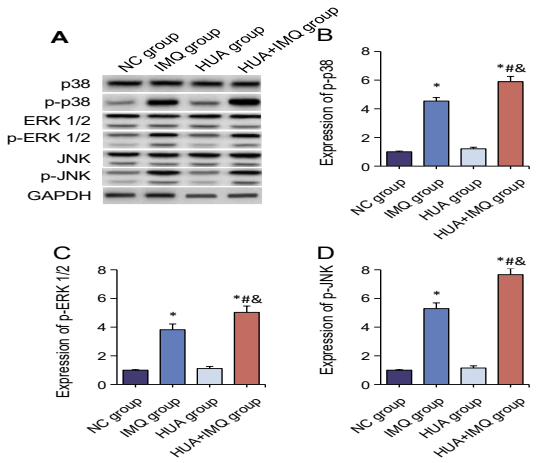

Figure 4.

Changes in the expressions of MAPK pathway-related proteins at the skin lesions of model mice. A: Western blot result; B: p-p38; C: p-ERK 1/2; D: p-JNK. *Compared with NC group, $p < 0.05$; #compared with IMQ group, $p < 0.05$; & compared with HUA group, $p < 0.05$

The effect of RSGE on the skin morphology of mice with psoriasis and HUA

The PASI score, lesion skin thickness, and epidermal layer thickness of mice in the HUA + IMQ + RSGE group were significantly decreased compared to those in the HUA + IMQ group ($p < 0.05$) (Figure 5).

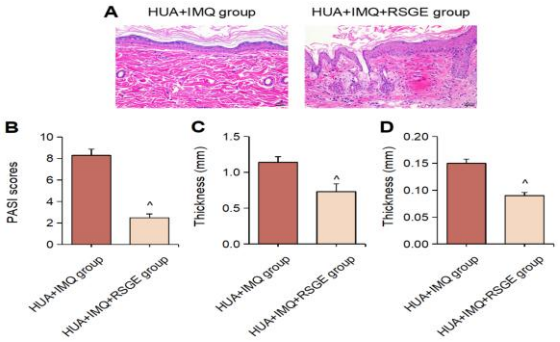

Figure 5.

Psoriasis-like skin changes in mice with psoriasis and HUA after intervention with RSGE. A: H&E staining results of skin lesions, 200×; B: PASI score; C: Lesion skin thickness; D: Epidermal layer thickness. ^Compared with HUA + IMQ group, $p < 0.05$

The effect of RSGE on renal function in mice with psoriasis and HUA

The serum UA level of mice in the HUA + IMQ + RSGE group was significantly higher relative to that in the HUA + IMQ group, while the Cr and BUN levels were much lower ($p < 0.05$) (Figure 6).

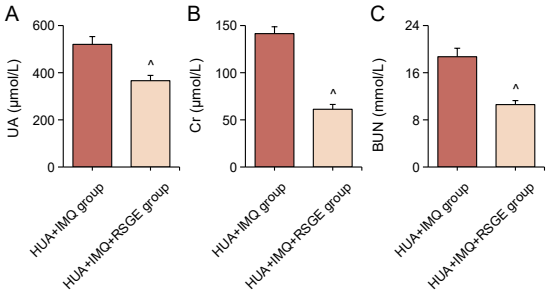

Figure 6.

Changes in serum renal function indicators of mice with psoriasis and HUA after intervention with RSGE. A: UA in serum; B: Cr in serum; C: BUN in serum. ^ Compared with HUA + IMQ group, $p < 0.05$

The effect of RSGE on the expression of inflammatory genes in the skin lesions of mice with psoriasis and HUA

The relative expressions of IL-6, IL-17, IL-23, and TNF-α mRNA in the serum skin lesions of mice in the HUA + IMQ + RSGE group were significantly lower in comparison to those in the HUA + IMQ group ($p < 0.05$) (Figure 7).

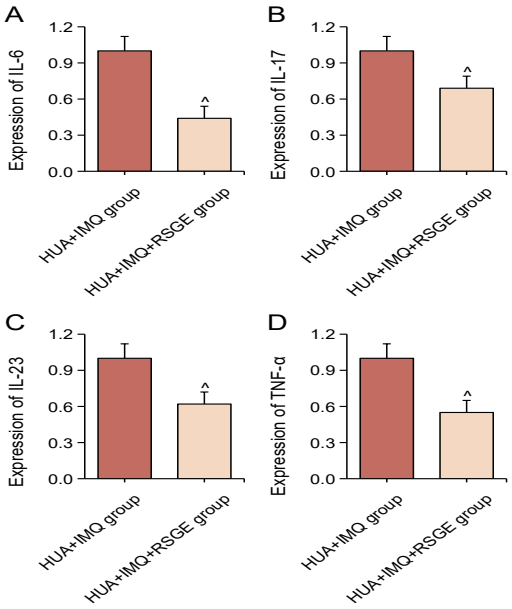

Figure 7.

Changes in expressions of inflammatory genes in the skin lesions of mice with psoriasis and HUA after intervention with RSGE. A: IL-6; B: IL-17; C: IL-23; D: TNF-α. ^ Compared with HUA + IMQ group, $p < 0.05$

The effect of RSGE on the MAPK pathway status at the lesion sites of mice with psoriasis and HUA

The p-P38, p-ERK 1/2, and p-JNK in serum at the lesion site in the HUA + IMQ + RSGE group of mice

exhibited significantly lower expression relative to those in the HUA + IMQ group ($p < 0.05$) (Figure 8).

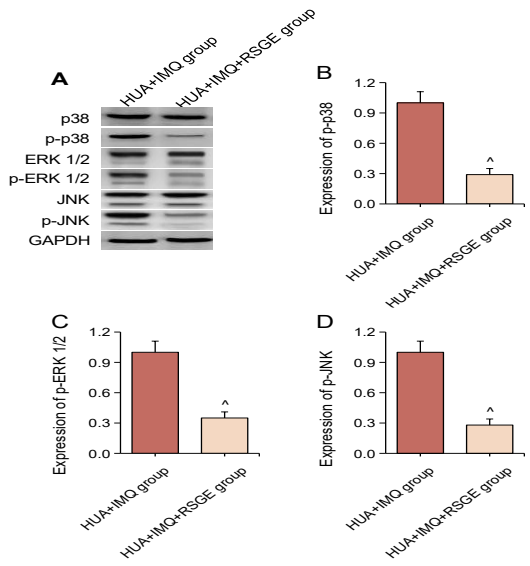

Figure 8.
Changes in expressions of MAPK pathway-related proteins in the skin lesions of mice with psoriasis and HUA after intervention with RSGE. A: Western blot result; B: p-p38; C: p-ERK 1/2; D: p-JNK. ^Compared with HUA + IMQ group, $p < 0.05$

This work revealed that compared with mice with psoriasis and HUA monopathy, mice with psoriasis and HUA had greatly higher PASI score, increased epidermal layer thickness at the lesion site, upregulated expressions of inflammatory genes (*i.e.*, IL-6, IL-17, IL-23, and TNF-α), and elevated blood UA, Cr, and BUN levels. These observations are similar to the result found by Tamer *et al.* (20) that patients with severe psoriasis have higher blood UA levels. Psoriasis is a chronic systemic inflammatory disorder mediated by genetic, environmental, and immune factors. After the onset of the disease, activated dendritic cells initiate and amplify the Th1/Th17 immune response by secreting factors such as IL-23, while activated T cells produce core effector factors such as IL-17A, TNF-α, and IFN-γ (21, 22). Ultimately, these factors directly act on keratinocytes, inducing their abnormal proliferation and feedback the release of chemokines, thereby forming self-sustaining chronic inflammation (23). A high UA level can elevate the expressions of various indicators like IL-1β, IL-6, and TNF-α, and neutralizing IL-17 can alleviate UA-induced kidney injury (24). This work unveiled sharply upregulated expressions of various inflammatory genes in mice co-infected with psoriasis and HUA. The rise in blood UA was accompanied by an intensification of renal dysfunction, suggesting that high UA levels not only aggravate the skin symptoms and inflammatory responses of psoriasis but also further affect kidney function.

Secondly, it was observed in this work that after intragastric administration of RSGE, the mice co-infected with psoriasis and HUA exhibited a sharply lowered PASI score, reduced epidermic layer thickness at the lesion site, downregulated expressions of IL-6, IL-17, IL-23, and TNF-α decreased significantly, and decreased levels of blood UA, Cr, and BUN. These observations align with the result reported by Wang *et al.* (25) that RSGE can improve renal inflammation and oxidative stress responses in rats with UA nephropathy by promoting UA excretion. This finding is consistent with the results reported by Xu *et al.* (26), whose study showed that astragaloside IV in RSGE alleviated skin inflammation in IMQ-induced psoriatic mice, reduced the accumulation of IL-17-producing T cells in skin lesions, and inhibited the expression of pro-inflammatory cytokines, thereby exerting a therapeutic effect. Psoriasis is a systemic inflammatory disease closely related to metabolic disorders, and HUA is one of the most common complications (27). The RSGE contains a variety of bioactive components and has multiple pharmacological effects. Tang *et al.* (28) pointed out that RSGE could greatly improve the skin symptoms of IMQ-induced psoriasis in mice by regulating the Th17/Treg balance of skin lesions. Similarly, Zhao *et al.* (29) reported that RSGE could inhibit the inflammatory response induced by lipopolysaccharide in RAW264.7 cells and subsequently secrete inflammatory factors such as IL-1β and IL-6. Some scholars have confirmed that RSG can improve the renal pathological changes in mice with acute kidney injury and exert therapeutic effects (30). Our findings suggested that RSGE can improve the psoriasis-like skin symptoms of mice co-infected with psoriasis and HUA by inhibiting inflammatory genes at the lesion site while enhancing the kidney function.

To further explore the potential mechanism of the extract of RSGE in treating mice with both psoriasis and HUA, we detected the changes in the protein expressions of p38, JNK, and ERK1/2, members of the MAPK pathway subfamily, at the skin lesions of mice. The MAPK pathway is involved in regulating the immune-inflammatory response, abnormal cell proliferation, and differentiation in psoriasis (31). Research has demonstrated that the expressions of ERK, JNK, and p38 in psoriasis lesions are all abnormally elevated (32). This supports the result that the expressions of p-38, p-ERK 1/2, and p-JNK in the skin lesions of IMQ mice were considerably higher relative to those in the NC group in this work. Affected by psoriasis, IL-17 and TNF-α can further stimulate and activate the MAPK pathway. For instance, Han *et al.* (33) demonstrated that the p38/ERK MAPK pathway was abnormally activated in the kidneys of HUA mice, which subsequently affected the kidney function and UA excretion. Subsequently, this work revealed that expressions of p-38,

p-ERK 1/2, and p-JNK proteins in the skin lesions of mice co-infected with psoriasis and HUA were greatly elevated in comparison to those of mice with IMQ and HUA. This implies that high UA levels will enhance the activation of the MAPK pathway at the lesion sites in mice with psoriasis. Additionally, sharply decreased expressions of various proteins in the skin lesions of co-infected mice with psoriasis and HUA were observed after intragastric administration of RSGE in this work. This observation is supported by the findings of Guo *et al.* (34) that RSGE can improve T cell differentiation and immune function in a mouse model of psoriasis and regulate the ERK pathway to alleviate psoriasis-like skin symptoms. For this reason, RSGE shows high potential in treating the comorbidity of psoriasis and HUA by mediating the MAPK pathway.

On the other hand, several limitations of this work have to be pointed out herein. (1) It initially clarified the aggravating effect of HUA on psoriasis and the intervention effect of RSGE, but the specific molecular mechanism, especially the detailed links of how RSGE regulates UA levels and affects the MAPK pathway, has not been fully elucidated. (2) The results are only verified in animal models, lacking clinical data support for patients with psoriasis complicated with HUA. Therefore, the transformation of the research conclusions into clinical applications still needs further evaluation. For this reason, future research will delve into the specific molecular targets of RSGE in regulating UA metabolism and interfering with the MAPK/Th17 inflammatory axis and conduct clinical studies to verify its translational value in treating psoriasis complicated with HUA.

Conclusions

This study demonstrates that HUA can significantly exacerbate psoriatic skin lesions by excessively activating the MAPK signaling pathway and intensifying Th17-related inflammatory responses. However, RSGE could effectively reverse this deteriorating effect and simultaneously improve the renal function indicators related to HUA. This discovery revealed that HUA not only functions as an important aggravating factor for psoriasis, but also provides a highly promising natural drug candidate strategy for the clinical treatment of psoriasis, especially for patients with psoriasis complicated with HUA.

Acknowledgement

Not applicable.

Funding

This work was supported by the Special Research Project of Affiliated Hospitals of Zhejiang Chinese Medical University in 2023 (2023FSYYZQ16), Second Batch of Jiaxing Traditional Chinese Medicine Key Discipline Support - Traditional Chinese Medicine Internal Medicine (Jiawei [2023] No. 65-3), and Jiaxing Key Discipline of Medicine (2023-FC-006).

Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Ethics approval and consent to participate

All experimental procedures were approved by the Ethics Committee of Affiliated Hospital of Jiaxing University (No. JUMC 2023-212).

AI use disclosure

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

References

1. Sugumaran D, Yong ACH, Stanslas J. Advances in psoriasis research: from pathogenesis to therapeutics. Life Sci. 2024;355:122991.
2. Yan L, Wang W, Dong M, Wang R, Li C. Skin metabolic signatures of psoriasis and psoriasis concurrent with metabolic syndrome. J Inflamm Res. 2025;18:505-517.
3. Oancea C, Banu C, Ciobanu LP, Nedelescu M, Aurelian J, Gîță CD, et al. Serum liver markers associated with features of metabolic syndrome in the working-age population. Farmacia. 2025;73(3):628-636.
4. Kuwabara M, Hisatome I, Ae R, Kosami K, Aoki Y, Andres-Hernando A, et al. Hyperuricemia, a new cardiovascular risk. Nutr Metab Cardiovasc Dis. 2025;35(3):103796.
5. Taner S, Gezici E, Unal A, Tolunay O. The association of obesity and hyperuricemia with ambulatory blood pressure in children. Pediatr Nephrol. 2025;40(3):787-796.
6. Serban D, Dascalu AM, Arsene AL, Tribus LC, Vancea G, Pantea Stoian A, et al. Gut microbiota dysbiosis in diabetic retinopathy-current knowledge and future therapeutic targets. Life. 2023;13(4):968.
7. Zhao D, Zhao JR, Wang S, Sun JH. Evaluating causal influence of serum uric acid on psoriasis via observational study and transethnic Mendelian randomization analyses. Sci Rep. 2024;14(1):26332.
8. Zhan XZ, Wei TH, Yin YQ, Xu JQ, Yu H, Chen XL, et al. Determination and mechanism of Xiao-Ai Jie-Du decoction against diffuse large B-cell lymphoma: in silico and in vitro studies. J Ethnopharmacol. 2024;319(Pt 2):117271.
9. Tang Y, Yang F, Wen X, Zhou Y, Tang R, He X, et al. Component characterization of *Smilax glabra* Roxb., and its inhibitory activity against *Helicobacter pylori* through targeted suppression of its secreted urease. Front Cell Infect Microbiol. 2025;15:1617330.

10. Bao C, Luo J, Meng Y, Gao Z. Effects of Paeoniflorin extract-mediated miRNA-140 targeting of WNT/β-catenin signaling pathway on proliferation and apoptosis of chondrocytes in osteoarthritis. Farmacia. 2025;73(6):1605-1625.
11. Wu Y, Liu M, He X, Zhou H, Wei J, Li H, et al. A breakthrough in periodontitis treatment: revealing the pharmacodynamic substances and mechanisms of Kouqiangjie formula. J Ethnopharmacol. 2024;323:117738.
12. Yang X, Qian H, Yang C, Zhang Z. Investigation of the molecular mechanism of Smilax glabra Roxb. in treating hypertension based on proteomics and bioinformatics. Front Pharmacol. 2024;15:1360829.
13. Xiao J, He W, Fang X, Zhou R, Huang A, Wang Y, et al. Smilax glabra Roxb. ameliorates hyperuricemia via regulating renal urate transporter and remodulating intestinal microbiota in mice. Cell Biochem Funct. 2025;43(7):e70100.
14. Wu X, Zhou H, Cheng G, Wang Y, Fu Y, Li S, et al. Smilax glabra Roxb. extract alleviates psoriasis-like lesions in mice by the synergistic effects of TOP2A inhibition and AhR activation. Int Immunopharmacol. 2025;164:115408.
15. Yehia Abdelzaher W, A Abdel-Gaber S, Atef Fawzy M, Hamid Sayed Abo Bakr Ali A, Ezzat Attya M, Geddawy A. Atorvastatin protects against cyclophosphamide-induced thyroid injury in rats via modulation of JNK/ERK/p38 MAPK signaling pathway. Int Immunopharmacol. 2023;124(Pt B):111061.
16. Negrei C, Arsene AL, Teodorescu CD, Boda D, Ilie M. Acitretin treatment in psoriasis may influence the cell membrane fluidity. Farmacia. 2012;60(6):767-772.
17. Rodríguez-Iturbe B, Johnson RJ, Sánchez-Lozada LG. Relationship between hyperuricemia, HSP70 and NLRP3 inflammasome in arterial hypertension. Arch Cardiol Mex. 2023;93(4):458-463.
18. Jiang X, Zhu Z, Liu Q, Jiang X, Liu Z, Li S, et al. Shenling Baizhu San attenuates testicular spermatogenic dysfunction in hyperuricemic mice via dual modulation of MAPK/NF-κB and NLRP3 inflammasome pathways. Hereditas. 2025;162(1):195.
19. Lebwohl M, Gooderham MJ, Warren RB, Thaçi D, Foley P, Gottlieb AB, et al. Outcomes of psoriasis area and severity index (PASI) and PASI components in two phase III trials of deucravacitinib in patients with moderate to severe plaque psoriasis. Clin Exp Dermatol. 2025;50(10):2030-2036.
20. Tamer F, Edek YC, Aksakal AB. Does biological agent treatment have an impact on serum uric acid levels in patients with psoriasis? Curr Med Res Opin. 2023;39(10):1297-1302.
21. Svedbom A, Mallbris L, González-Cantero Á, Playford M, Wu C, Mehta NN, et al. Skin inflammation, systemic inflammation, and cardiovascular disease in psoriasis. JAMA Dermatol. 2025;161(1):81-86.
22. Kim J, Lee J, Lee J, Kim K, Li X, Zhou W, et al. Psoriasis harbors multiple pathogenic type 17 T-cell subsets: selective modulation by risankizumab. J Allergy Clin Immunol. 2025;155(6):1898-1912.
23. Shen X, Qiao W, Yan W, Xie H, Zhang C, Sun Y, et al. Keratinocyte-specific H4K12 lactylation drives a non-canonical IL-17-dependent signaling in psoriasis progression in mice. Nat Commun. 2025;16(1):8639.
24. Yang L, He T, Yu Y. Uric acid promotes interleukin-17 expression to cause kidney injury. J Biochem Mol Toxicol. 2024;38(1):e23550.
25. Wang S, Fang Y, Yu X, Guo L, Zhang X, Xia D. The flavonoid-rich fraction from rhizomes of Smilax glabra Roxb. ameliorates renal oxidative stress and inflammation in uric acid nephropathy rats through promoting uric acid excretion. Biomed Pharmacother. 2019;111:162-168.
26. Xu Q, Liu Z, Cao Z, Shi Y, Yang N, Cao G, et al. Topical astilbin ameliorates imiquimod-induced psoriasis-like skin lesions in SKH-1 mice via suppression dendritic cell-Th17 inflammation axis. J Cell Mol Med. 2022;26(4):1281-1292.
27. Liu Z, Ma X, Chang T, Yao C, Song M, Biyue S, et al. Associations between psoriasis, psoriatic arthritis and gout or hyperuricemia: a systematic review and meta-analysis. Am J Med Sci. 2025;369(6):671-678.
28. Tang Y, Yu J, Zhao W, Liu J, Peng H, Zhang H, et al. Total glucosides of Rhizoma Smilacis Glabrae: a therapeutic approach for psoriasis by regulating Th17/Treg balance. Chin J Nat Med. 2023;21(8):589-598.
29. Zhao X, Chen R, Shi Y, Zhang X, Tian C, Xia D. Antioxidant and anti-inflammatory activities of six flavonoids from Smilax glabra Roxb. Molecules. 2020;25(22):5295.
30. Zhao L, Yue Z, Wang G, Qin J, Ma H, Tang D, et al. Smilax glabra Roxb. alleviates cisplatin-induced acute kidney injury in mice by activating the Nrf2/HO-1 signaling pathway. Phytomedicine. 2025;139:156550.
31. Selvakumar B, Rah B, Jagal J, Sekar P, Moustafa R, Ramakrishnan RK, et al. Modulation of Plet1 expression by N-acetylglucosamine through the IL-17 A-MAPK pathway in an imiquimod-induced psoriasis mouse model. Inflamm Res. 2024;73(12):2217-2230.
32. Xu Q, Sheng L, Zhu X, Liu Z, Wei G, Zhang T, et al. Jingfang granules exert anti-psoriasis effect by targeting MAPK-mediated dendritic cell maturation and PPARγ-mediated keratinocytes cell cycle progression in vitro and in vivo. Phytomedicine. 2023;117:154925.
33. Han Q, Chen N, Peng K, Wang M, Chen M, Mamadalieva NZ, et al. Urolithin C ameliorates hyperuricemia by mitigating renal dysfunction through ROS-p38/ERK MAPK axis suppression. J Agric Food Chem. 2025;73(36):22485-22501.
34. Guo Y, Mao W, Bai N, Jin L, Tang S, Lin X, et al. Integrated network pharmacological analysis revealed that Smilax glabra Roxb. alleviates IMQ-induced psoriatic skin inflammation through regulating T cell immune response. J Ethnopharmacol. 2024;325:117836.