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EVALUATION OF THE THERAPEUTIC EFFECT OF "TU VAN" GEL IN PATIENTS WITH SUBACUTE AND CHRONIC ATOPIC DERMATITIS

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ABSTRACT

Objectives: *To evaluate the therapeutic effect of "Tu Van" gel in patients with subacute and chronic atopic dermatitis.*

Subjects and methods: *A prospective, open clinical intervention study comparing before and after treatment with "Tu Van" gel on 60 patients with subacute or chronic atopic dermatitis at the Department of Five Senses, Hanoi General Hospital of Traditional Medicine, from July to November 2021. Clinical symptoms were assessed using the Scoring Atopic Dermatitis (SCORAD), Eczema Area and Severity Index (EASI) scales.*

Results: *After 30 days of treatment, itching symptoms at various levels decreased from 83.3% to 33.3% ($p < 0.05$), and insomnia decreased from 30.0% to 6.7% ($p < 0.05$); skin lesion symptoms all improved compared to before treatment ($p < 0.05$). After 30 days of treatment, the overall average SCORAD score decreased from 50.3 ± 15.8 points to 36.8 ± 17.2 points ($p < 0.05$). The average EASI score decreased from 11.7 ± 9.9 points to 7.3 ± 5.4 points ($p < 0.05$).*

Conclusions: *"Tu Van" gel has a therapeutic effect on subacute and chronic atopic dermatitis.*

Keywords: Tu Van Gel, Tu Van Cao, atopic dermatitis, subacute, chronic.

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1. INTRODUCTIONS

Atopic dermatitis (AD) is a chronic inflammatory skin condition, often progressing in flares, with clinical manifestations varying according to the stage and period of the disease. The progression of AD is characterized by itching. The disease has complex causes and pathogenesis, often occurring in patients with allergic predisposition or genetic factors [1]. Currently, AD treatment faces many difficulties, mainly symptomatic treatment with antihistamines, topical or systemic corticosteroids, and immunomodulators [2]. Among these, corticosteroids rapidly reduce symptoms but have many unwanted effects (such as skin atrophy, vasodilation, bacterial and fungal superinfections) when used for a long time. Finding remedies that treat the disease and limit the unwanted effects of drugs is extremely necessary.

From a traditional medicine remedy in the book "Chính tông Surgery" (1617), the Japanese physician Hanaoka Seishu transformed the prescription into the "Tu Van Cao" remedy and used it widely with many indications, including the treatment of AD. The remedy had the effect of moisturizing the skin, being anti-bacterial, anti-inflammatory, and specifically treating dry skin conditions [3]. This remedy had been used at the Hanoi General Hospital of Traditional Medicine, initially showing positive results. However, the paste form of the remedy still had some undesirable effects, such as a hard substance, a burnt smell, causing discomfort for patients when using the medicine, and difficulties in storage. Therefore, the research team formulated the "Tu Van Cao" remedy into "Tu Van" gel. "Tu Van" gel had been experimentally tested and did not cause acute toxicity or skin irritation.

Based on this practical situation, the research team conducted this study to evaluate the therapeutic effect of "Tu Van" gel on patients with subacute or chronic AD.

2. SUBJECTS, MATERIALS AND METHODS

2.1. Subjects, materials

- Subjects: 60 AD patients, including 30 patients in the subacute stage and 30 patients in the chronic stage, treated with "Tu Van" gel, at the Department of Five Senses, Hanoi General Hospital of Traditional Medicine from July to November, 2021.

- Exclusion criteria: patients currently having complications such as superinfection, impetiginization, erythroderma...; patients allergic to any component of the drug; pregnant or breastfeeding women; patients with chronic diseases such as tuberculosis, heart failure, liver failure, kidney failure, HIV/AIDS, mental illness... or acute diseases such as sepsis, pneumonia...; patients who discontinued treatment for more than 3 days; patients who did not agree to participate in the study.

- Materials: "Tu Van" gel, ingredients: Lithospermum root (Radix Lithospermum erythrorhizon) 200g; Angelica root (Radix Angelicae sinensis) 200g; Beeswax (Cera alba) 220g; Sesame oil (Oleum Sesami) 1,500g; excipients sufficient for 3,000g. The ingredients meet the standards of the Vietnamese Pharmacopoeia V and the Chinese Pharmacopoeia 2015. The drug was formulated as a gel (30g box), meets basic standards, produced at the Pharmacy Department, Hanoi General Hospital of Traditional Medicine, and stored in a cool, dry place, avoiding high temperatures.

2.2. Methods

- Study design: prospective, open clinical intervention comparing before and after treatment.
- Modern medicine diagnosis of AD according to Hanifin and Rajka criteria (1980) [4]:

+ Major criteria: (1) Itching; (2) Chronic and relapsing dermatitis; (3) Typical morphology and location of lesions (children: eczema localized on the face, limb extension area; older children and adults: thickened skin, lichenification in the folds); (4) Personal/family history of atopic disease (bronchial asthma, allergic rhinitis, AD).

+ Minor criteria (23 criteria): (1) Dry skin; (2) Ichthyosis; (3) Positive type 1 immediate skin reaction; (4) Increased serum IgE; (5) Early age of onset; (6) Susceptibility to skin infections; (7) Tendency towards non-specific hand/foot dermatitis; (8) Nipple eczema; (9) Cheilitis; (10) Recurrent conjunctivitis; (11) Dennie-Morgan infraorbital fold; (12) Keratoconus; (13) Anterior subcapsular cataracts; (14) Periocular darkening; (15) Facial pallor or erythema; (16) Pityriasis alba; (17) Anterior neck folds; (18) Itching when sweating; (19) Intolerance to wool or lipid soluble substances; (20) Keratosis pilaris; (21) Food allergy; (22) Dermatographism; (23) Disease progression influenced by environmental and emotional factors.

Confirmed AD diagnosis: patients must have at least three major criteria and three minor criteria.

- Traditional medicine diagnosis of AD (disease name "Nga Chuong Phong"):

+ Spleen deficiency with hidden dampness type: Dark lesions, moist skin, itching or recurrent lesions, dry or slightly thick skin, pale yellow complexion, poor appetite. Loose stools, clear and long urine. Pale, flabby tongue, white, slimy coating, slow or rapid pulse. Pale, flabby tongue, white, slimy coating, slow or rapid pulse

+ Yin deficiency with blood dryness type: Long-term illness, frequent relapses or present from childhood, dry, thick skin, gradually darkening skin pigmentation, itching with scaling. Dry mouth, poor appetite, thin body. Constipation. Pale pink tongue, little coating, thin and weak pulse.

- Diagnosis of disease stages:

+ Subacute stage: redness, swelling, scaling, crusting, secondary infection, and itching can be severe.

+ Chronic stage: thickened skin, darkening skin, clear borders, lichenification, lesions without vesicles, no secretion, severe itching.

- Sample Size: purposive sampling (60 AD patients meeting research criteria).

- Procedure: patients applied a thin layer of "Tu Van" gel, dose 0.5g per 2% skin area, 3 times/day for 30 days at the lesion site (patients performed an allergy test on the skin for the first 24 hours before using the drug). Evaluate clinical symptoms at the time before treatment (D0), after 7 days (D7), 15 days (D15), and 20 days (D20) of treatment.

- Evaluate clinical symptoms according to the SCORAD (Scoring atopic dermatitis) and EASI (Eczema area and severity index) scales:

+ Calculating total SCORAD score:

$$SCORAD = A/5 + 7B/2 + C.$$

Where a is the extent of the lesions as a percentage of body surface area (according to Wallace's rule of nines); B is the total scores of the

symptoms of erythema, papules/edema, exudation/crusting, skin excoriation, lichenification, dry skin (each symptom is on a scale of 0-3, corresponding to the level of lesions: none, mild, moderate, severe); C is the intensity of itching and insomnia in the last 3 days/nights as self-assessed by the patient on a scale of 0-10 for each symptom (mild: 0-3 points; moderate: 4-7 points: severe: 8-10 points).

Calculating total EASI score:

Skin region	EASI Calculation
Head/Neck	(E+A+Ex+ L) × area score × 0.1 (× 0.2 if a child is 0-7 years old)
Upper Limbs	(E+A+Ex+ L) × area score × 0.2
Body	(E+A+Ex+ L) × area score × 0.3
Lower Limbs	(E+A+Ex+ L) × area score × 0.4 (× 0.3 if a child is 0-7 years old)
Total EASI Score	From 0-72 points
E: Erythma; L: Lichenification; Ex: Excoriation; I: liduration	

* Scoring by severity of lesion in each region: 0 points (no lesion); 1 point (mild lesion); 2 points (moderate lesion); 3 points (severe lesion).

* Scoring by the percentage of affected skin area in each region: 0 points (no eczema in this area); 1 point (1-9%); 2 points (10-29%); 3 points (30-49%); 4 points (50-69%); 5 points (70-89%); 6 points (90-100%).

- Research indicators:

+ Level of improvement in functional symptoms: itching (continuous itching, intermittent itching, no itching), insomnia (insomnia present, no insomnia).

+ Level of Improvement in skin lesions: dry skin, vesicles, papules, edema, scaling, thickened/dark skin, scratches.

+ Treatment effect of "Tu Van" gel: according to SCORAD and EASI scales [5].

+ Therapeutic effect of "Tu Van" gel: according to SCORAD and EASI scales [5]

- Ethics: the study was approved by the Scientific Council of Hanoi General Hospital of Traditional Medicine (Decision No. 451/QD-BVĐKYHCT dated April 10, 2021). Before the clinical trial, the drug was experimentally studied for acute toxicity and skin irritation according to the Ministry of Health regulations. Patients were informed about the purpose of the study and had the right to withdraw at any time.

- Data processing: u1sing SPSS 22.0 software.

3. RESULTS

3.1. Effect of improving functional symptoms

- Improvement of itching symptoms in patients at different time points (n = 60):

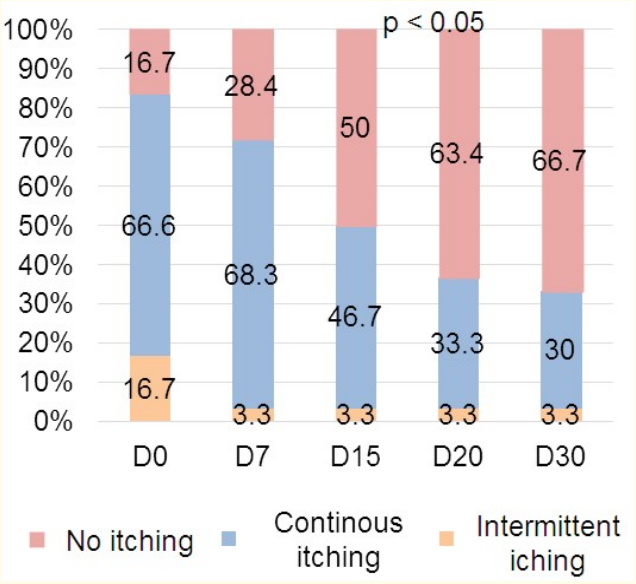

Chart 1. Improvement of itching symptoms in patients at the study time points.

After 15 and 30 days of treatment, itching symptoms decreased from 83.3% to 50.0% and 33.3%, respectively; the difference was significant with p < 0.05.

- Improvement of insomnia symptoms in patients at different time points (n = 60):

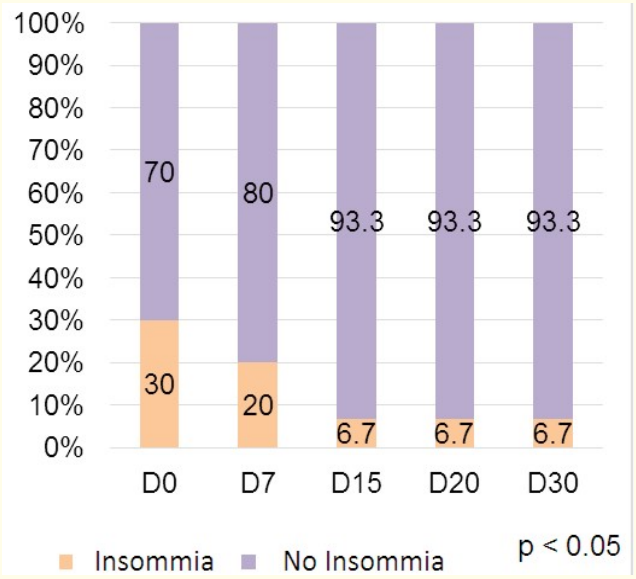

Chart 2. Improvement of patients' insomnia symptoms at the study time points.

After 30 days of treatment, only 6.7% patients still had insomnia symptoms. The difference before and after treatment was statistically significant (p < 0.05).

3.2. Assessment of changes in skin lesion morphology

Table 1. Evaluation of changes in skin lesion morphology before and after 30 days of treatment (n = 60)

Symptom	Time point		p
	D0	D30	
Dry skin	60 (100%)	46 (76.7%)	< 0.05
Vesicles	18 (30.0%)	5 (8.3%)	< 0.05
Papules, edema	32 (53.3%)	18 (30.0%)	< 0.05
Scaling	55 (91.6%)	32 (53.3%)	< 0.05
Thickened/ dark skin	43 (72.3%)	25 (42.3%)	< 0.05
Scratches	14 (23.3%)	5 (8.3%)	< 0.05

Symptoms like dry skin, vesicles, papules/ edema, scaling, thickened skin, dark skin, and scratches were significantly improved compared to before treatment (p < 0.05).

3.3. Evaluation of the effect of "Tu Van" gel using SCORAD and EASI scales

- Assessment of symptom changes according to the SCORAD score at the time points (n = 60):

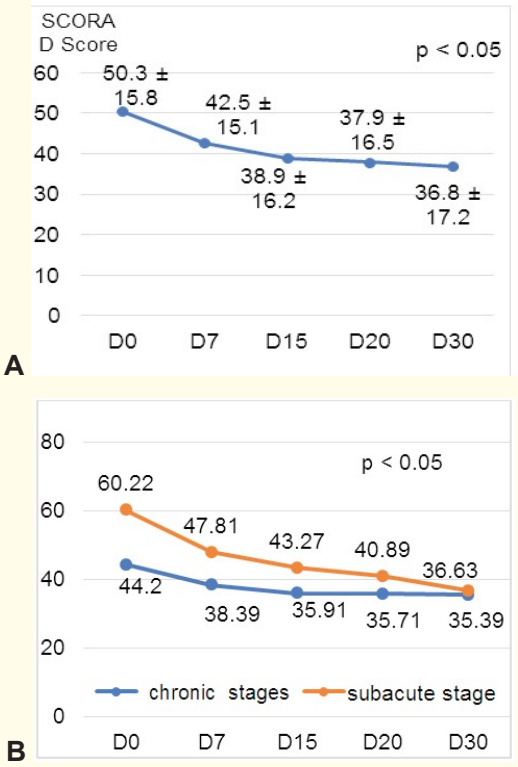

Chart 3. Changes in SCORAD scores at the study time points (A: Mean SCORAD score in 60 patients; B: Mean SCORAD score in patients with subacute and chronic stages).

After 30 days of treatment, the average SCORAD score for all 60 patients decreased from 50.3 ± 15.8 points to 36.8 ± 17.2 points. Patients with subacute AD showed better symptom improvement than patients with chronic AD (p < 0.05).

- Assessment of symptom changes according to the EASI score at the time points (Chart 4):

After 30 days of treatment, the average EASI score for all 60 patients decreased from 11.7 ±9.9 points to 7.3 ± 5.4 points. Patients with subacute AD showed better symptom improvement than patients with chronic AD (p < 0.05).

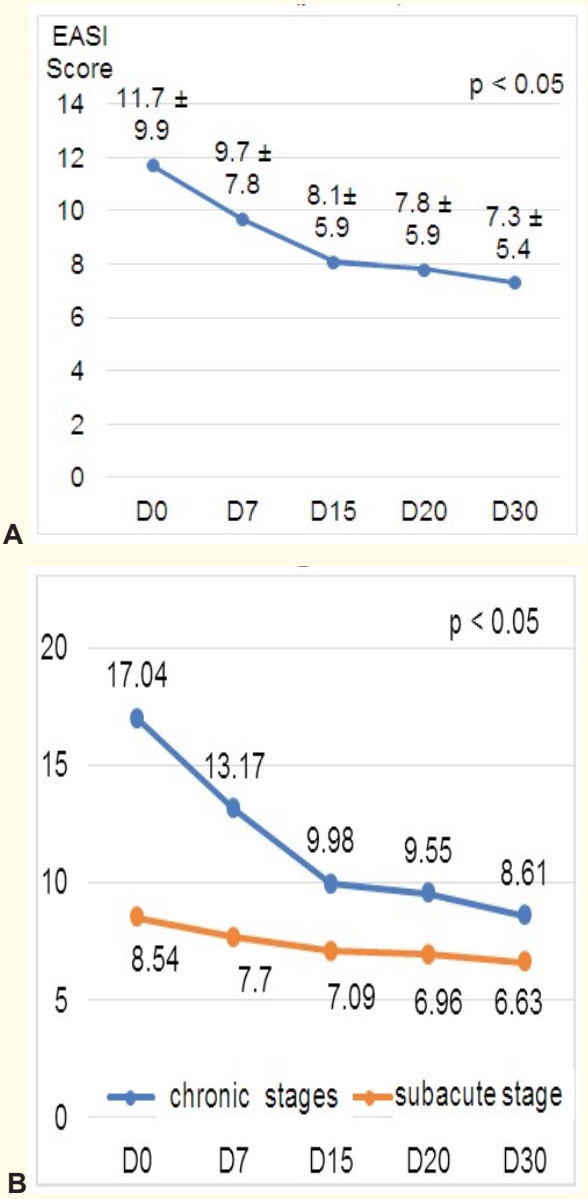

Chart 4. Changes in EASI scores at the study time points (A: Mean EASI score in all 60 patients; B: Mean EASI score in Atopic Dermatitis patients.

4. DISCUSSIONS

In this study, 83.3% of patients presented with itching. Itching is one of the main criteria for diagnosing AD [4]. It is also the cause leading to secondary lesions, such as infection, thickened skin, lichenification, hyperpigmentation, scratches, and scaling (due to patients scratching, and rubbing), making the disease's vicious cycle worse [6].

Itching is a prominent symptom of the disease and greatly affects the patient's quality of life; at the same time, it is also a valuable symptom in diagnosis, monitoring, and evaluating treatment results. Chart 1 showed that at the end of the study, 33.3% of patients still had itching symptoms (including 3.3% with continuous itching).

For patients with chronic AD, itching is mainly due to dry skin (according to traditional medicine, wind-dryness is caused by yin-blood deficiency). For patients with subacute AD (with vesicles, exudation, and thickened skin), itching is mainly caused by allergic inflammatory reactions; correspondingly, according to traditional medicine, it is caused by spleen deficiency generating dampness, leading to itching. Lithospermum root contains shikonin and its derivatives, which have anti-inflammatory effects and promote regeneration and granulation tissue formation in damaged skin. This effect is achieved through various mechanisms: inhibiting Cyclooxygenase-2, inhibiting Prostaglandin E2 synthesis, inhibiting Leukotriene B4 biosynthesis, and inhibiting mast cell degeneration [7].

Table 1 showed that after 30 days of treatment, the number of patients with vesicles and moist skin lesions significantly decreased (only 8.3% remained); the number of patients with papules, edema, and scaling decreased sharply (only 30.8% and 53.8% remained); the number of patients still having dry skin and thickened/hyperpigmented skin accounted for 76.7% and 42.3%, respectively. Dry skin and thickened/hyperpigmented lesions improved more slowly than other symptoms, as these were long-standing symptoms. Furthermore, the study was conducted during dry weather with low air humidity, significantly impacting these symptoms. Therefore, a longer follow-up was needed to evaluate the results in more detail and comprehensively.

Currently, many toolkits have been developed and applied clinically to assess the severity of AD, among which the SCORAD and EASI scales are often used in clinical trials. SCORAD combined three parts: the extent of lesions, the sum of scores for skin lesion symptoms, and the sum of scores for functional symptoms of itching and insomnia. EASI included the total score of severity symptoms (erythema, induration, crusting, excoriation, and lichenification) in each body region [8]. The scoring methods for these scales explain why the SCORAD and EASI scores for the subacute stage were higher than for the chronic stage.

Charts 3 and 4 showed that the improvement in SCORAD and EASI scores in patients with subacute AD was better than in patients with chronic AD. This result could be explained by the presence of Lithospermum root and Angelica root in "Tu Van" gel.

Lithospermum root had antibacterial effects in addition to its anti-inflammatory action. The ether extract of Lithospermum root, the petroleum ether-soluble fraction, and the acetone-soluble fraction separated from the petroleum ether fraction inhibit the growth of many types of bacteria. At a concentration of 20-30 µg/ml, shikonin had an antibacterial effect on Lactobacillus and showed significant anti-amoebic activity against Entamoeba histolytica in culture media [9].

Experimentally, Angelica root had anti-inflammatory effects. Angelica root water extract reduced the permeability of the blood vessel wall and inhibited inflammatory substances from platelets. In addition, Angelica root decoction inhibits E. coli, dysentery bacilli, and typhoid bacilli, inhibits Staphylococcus aureus, Pseudomonas aeruginosa, is anti-inflammatory, promotes regeneration, angiogenesis, and granulation tissue formation in damaged skin. Angelica, Sesame oil, and Beeswax have moisturizing properties, nourishing the skin, softening it, and strengthening the skin cell barrier... Therefore, combining these ingredients creates a preparation that is effective in treating both subacute and chronic AD [10].

5. CONCLUSIONS

"Tu Van" gel had a therapeutic effect on subacute and chronic AD. It demonstrated a better therapeutic effect in patients with subacute AD compared to patients with chronic AD.

REFERENCES

1. Jonathan I Silverberg (2017), *Public Health Burden and Epidemiology of Atopic Dermatitis*, 2017; (35 (3)): 283-289.
2. Anna B Fishbein, Jonathan I Silverberg, Eve J Wilson et al. (2020), "Update on Atopic Dermatitis: Diagnosis, Severity Assessment, and Treatment Selection", *The Journal of Allergy and Clinical Immunology*: In Practice, 2020; 8 (1): 91-101.
3. Hoang Duy Tan (2005), *Experience in Japanese Traditional Medicine, Dong Nai Publishing House.*
4. Hanifin J.M. Rajka G. (1980), "Diagnostic features of atopic dermatitis", *Acta Derm Venereol Suppl*. 1980; 92: 44-47.
5. R Chopra, P.P Vakharia, R Sacotte et al. (2017), "Severity strata for Eczema Area and Severity Index (EASI), modified EASI, Scoring Atopic Dermatitis (SCORAD), objective SCORAD, Atopic Dermatitis Severity Index and body surface area in adolescents and adults with atopic dermatitis", *British Journal of Dermatology*, 2017; 177 (5): 1316-1321, DOI 10.1111/bjd.15641.
6. Kanokvalai Kulthanan, Papapit Tuchinda et al. (2021), "Clinical practice guidelines for the diagnosis and management of atopic dermatitis", *Asian Pacific Journal of Allergy and Immunology*, 2021; 39:145-155 DOI 10.12932/AP-010221-1050.
7. Do Tat Loi (2005), *Vietnamese Medicinal Plants and Ingredients, Hanoi, Medical Publishing House.*
8. Paras P Vakharia, Jonathan I Silverberg (2019) "Adult-Onset Atopic Dermatitis: Characteristics and Management", *American Journal of Clinical Dermatology*, 2019; 20 (6): 771-779.
9. Tran Van Ki (2016), *Complete Traditional Pharmacy/Pharmacology, Da Nang Publishing House.*
10. Zhang Yafeng, Lin Zhongzi (2010), "中医治疗婴幼儿湿疹30例临床疗效观察", 中医儿科杂志, 2010; 6 (5): 18-20. ❑