Comparative Trial of Moisturizer Containing Spent Grain Wax, *Butyrospermum parkii* Extract, *Argania spinosa* Kernel Oil vs. 1% Hydrocortisone Cream in the Treatment of Childhood Atopic Dermatitis

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Objective: *To compare an efficacy of a moisturizer containing spent grain wax, Butyrospermum parkii extract, Argania spinosa kernel oil (S) with 1% hydrocortisone cream (HC) for the treatment of mild to moderate atopic dermatitis.*
Material and Method: *Twenty-nine patients, age between 2 and 15 years old with mild to moderate atopic dermatitis were enrolled. The body was randomly divided to left and right side. One side was applied with S cream and the other side was applied with HC cream twice daily for four weeks. Observation of recurrence rate after remission was recorded. Clinical outcomes were analyzed by using the scoring of Atopic Dermatitis (SCORAD) score. Statistical analysis was done by using descriptive statistics, pair t-test, one-way repeated ANOVA, and McNemar's test.*
Results: *It was demonstrated that both agents had improvement of SCORAD score after two weeks, with statistically significant difference ($p<0.001$). At fourth week, both agents had improvement of SCORAD score without being statistically significant different ($p>0.05$). Although the S cream side had higher remission rate than the HC cream side, there was no statistically significant difference ($p>0.05$).*
Conclusion: *S cream was as effective as HC cream in the treatment and maintenance period of mild to moderate childhood atopic dermatitis.*

Keywords: *Atopic dermatitis, Childhood, Hydrocortisone, Spent grain wax, Butyrospermum parkii (shea butter) extract, Argania spinosa kernel oils*

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Atopic dermatitis (AD) is a common chronic inflammatory skin disease. The prevalence is 10 to 20% in children and 1 to 3% in adults[1]. The predominant symptoms are intense pruritus, dry skin, and a series of exacerbations and remission of disease. AD often starts in early infancy; approximately 50% of cases begin within the first year, 30% during year one to five, and 20% after five years of age[2]. The disorder leads to a significant reduction in quality of life[3]. The pathogenesis of AD is not fully known, but it seems to be the result of genetic susceptibility, immune dysfunction, and epidermal barrier dysfunction[4,5]. Topical steroids are effective agents in managing atopic dermatitis, however, prolonged application of topical steroids results in number of adverse effects such as skin atrophy, striae, telangiectasias, and hypopigmentation[6].

Moisturizer containing non-steroidal anti-inflammatory agents has currently been recommended as an alternative treatment of mild to moderate atopic dermatitis[7]. Spent grain wax, *Butyrospermum parkii* extract, *Argania spinosa* kernel oil (STIMU-TEX AS®) composed of unsaturated and saturated fatty acid such as linoleic acid (omega 6), oleic acid, palmitic acid, and stearic acid. Linoleic acid, which has anti-inflammatory effects, is an essential fatty acid that must be obtained from food or by topical treatments[8]. Furthermore, topical linoleic acid can also repair abnormal skin barrier function[9]. Moreover, triterpene acetate and cinnamate esters found in *Butyrospermum parkii* (shea butter) extracts also possess anti-inflammatory effects[10]. The effectiveness of moisturizers containing spent grain wax, *Butyrospermum parkii* (shea butter) extract, *Argania spinosa* kernel oil (S cream) in the treatment of AD has not been studied.

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The purpose of the present study was to evaluate the comparative effectiveness of S cream vs. 1% hydrocortisone (HC) cream for the treatment and recurrence prevention of mild to moderate AD in children. The null hypothesis: the effectiveness of S cream is the same as H cream in the treatment of mild-to-moderate childhood AD. The alternative hypothesis: the effectiveness of S cream is different from H cream in the treatment of mild-to-moderate childhood AD.

Material and Method

The present study was a randomized assessment blind controlled trial that involved patients from two to 15 years of age with the diagnosis of mild or moderate AD based on the Hanifin and Rajka criteria[11]. Patients gave informed consents and the Human Research Ethics Committee of Srinakarinwirot University approved the protocol. Patients were required to meet the entrance criteria, had skin lesions on both sides of the body, and could follow concomitant therapy restrictions. A washout period of up to four weeks was required for patients taking oral medications (e.g. corticosteroids and antihistamines), and up to two weeks for patients receiving topical medications (corticosteroids, calcineurin inhibitors and moisturizers). Patients who had skin lesion other than AD in the area to be treated were also excluded.

All patients who met eligible criteria were randomized. The randomization schedule was prepared by a third party. The S cream was applied twice daily to areas affected with AD on one side of the body for eight weeks, while the opposite side was applied with the HC cream for four weeks followed by cream base for another four weeks. The cassettes of both agents were similar in shape and color, however they were labeled as 'left' or 'right'. Participants had clinical assessments at baseline, week 2 and week 4 after treatment, and final assessment at week 8 for relapse-rate evaluation. In the present study, remission meant that the SCORAD score was 0, while the relapse rate was defined as the exacerbation of the eczema after remission. Moreover, the global self-evaluation of satisfaction was done by the patients at week 4. The trial codes were opened only after data were analyzed.

The S cream consisted of linoleic acid (omega6) and oleic acid. Other ingredients were palmitic acid, stearic acid, polyphenols, tocopherols, phenolic acid, and squalene.

Cream base was comprised of butylene glycol, mineral oil, ethylhexyl stearate, tocopheryl acetate, sodium polyacrylate. The HC cream comprised of 1% hydrocortisone acetate in the cream base that composed of cetostearyl, propylene glycol, glycerin, stearic acid, EDTA Na_2.

The main outcome measure was SCORAD index (Severity Scoring of Atopic Dermatitis index) with some modification. The SCORAD index includes the assessment by a physician of objective signs (extent and intensity) and of subjective symptoms (pruritus and sleep disturbance) complied on a visual analogue scale by the patients. Extent was calculated using the "rule of nine" on the skin surface area involved. The intensity was evaluated by erythema, edema/papulation, oozing/crusts, excoriations, lichenification, and dryness of the involved skin (from 0 to 3 points for each item). Then the final score was calculated by the following equation: A/5 + 7B/2 + C (A = extent; B = intensity; C = subjective symptoms). As we designed with each drug on either side of the body, the scores must be multiplied by 2. The global self-evaluation of satisfaction was graded as excellent, good, fair, and uncharged outcome. Adverse events were recorded at each visit.

Statistical analysis

Comparison of SCORAD index between S cream side and HC cream/Cream base side and the reduction of the SCORAD score from baseline were tested by paired t-test. The improvement of the SCORAD score in each group was analyzed using one-way repeated ANOVA. McNemar's test was used for testing the difference between S cream and HC cream/Cream base sides in the SCORAD improvement, the presentation of signs, and patients' satisfaction. Pruritus score was compared between groups using Wilcoxon signed rank test. The recurrent rate was described by using descriptive statistics. The *p*-value of <0.05 was considered statistical significance.

Results

After exclusions, 31 patients were enrolled in the present study. However, only 29 patients completed the trial, 18 male and 11 female with a mean age was 4.24±2.46 years (range from 2 years to 12 years). Two patients were lost to follow-up before completing the protocol. The mean value of baseline SCORAD score of the S cream side and the HC cream side was 25.6 (SD = 7.9) and 25.7 (SD = 7.5) respectively without statistically significant difference ($p = 0.703$).

The SCORAD score decreased significantly in week 2 and week 4 compared to baseline in both the

Table 1. Number of patients with improvement in the SCORAD score after treatment

Time	Treatment	SCORAD score, n (%)			*p*-value*
		No	Mild	Moderate	
Baseline	HC-cream	0 (0.0%)	4 (13.8%)	25 (86.2%)	1.000
	S-cream	0 (0.0%)	3 (10.3%)	26 (89.7%)	
Week 2	HC-cream	0 (0.0%)	14 (48.3%)	15 (51.7%)	1.000
	S-cream	0 (0.0%)	13 (44.8%)	16 (55.2%)	
Week 4	HC-cream	4 (13.8%)	24 (82.8%)	1 (3.4%)	0.317
	S-cream	5 (17.2%)	23 (79.3%)	1 (3.4%)	

* McNemar's test

S cream side and the HC cream side ($p<0.001$). However, there was no statistically significant in the reduction of the SCORAD score between groups as shown in Fig. 1 and 2. The results showed significant improvement in the SCORAD score with 17.2% and 13.8% of patients assessed as clear after four weeks in the S cream side and the HC cream side respectively as illustrated in Table 1. There was a non-significant ($p>0.05$) reduction in the SCORAD score in both groups during the four weeks of treatment.

When both agents were compared, analyzing based on each signs and symptoms including erythema, edema, excoriation, lichenification, dryness, and pruritus, it was discovered that there were decreased in erythema, edema, excoriation, lichenification, and pruritus present on both sides without statistically significant difference ($p>0.05$). However, as for the dryness present, it was found that in week 4, the side treated with S cream had more decreased in the dryness present than that of HC cream with statistical significance ($p = 0.016$). This was shown in Fig. 3. As for the relapse rates, it was 17.2% on the HC cream side, and 10.3% on the S cream side ($p = 0.500$).

Regarding recurrent rate, it was discovered that none suffered from recurring rashes (0%) for both the S cream side and the HC cream base side treatments.

Table 2. Patients' self assessed satisfaction

Treatment	Grading, n (%)			*p*-value*
	Excellent	Good	Fair	
S-cream	8 (27.6)	18 (62.1)	3 (10.3)	0.160
HC-cream	12 (41.4)	15 (51.7)	2 (6.9)	

* McNemar's test

The patients' satisfaction with good to excellent outcome was 89.7% in S cream side and 93.1% in HC cream base side as shown on Table 2. The clinical improvement of both agents was shown in Fig. 4. No specific adverse events were recorded.

Discussion

The pathogenesis of AD results from the complex interaction between defects in skin barrier function, immune abnormalities, environmental and infectious agents. Skin barrier abnormalities appear to be associated with mutations within the filaggrin gene, which encodes a structural protein essential for skin barrier formation. These skin barrier abnormalities lead

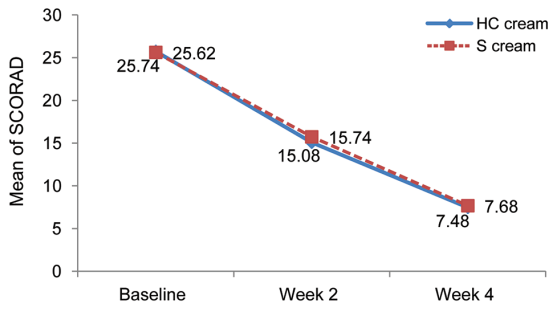

Fig. 1 The SCORAD score reduction of atopic dermatitis patients.

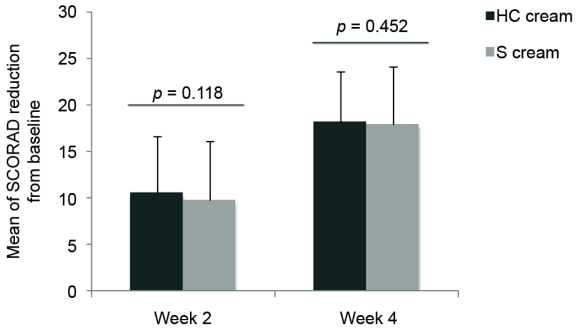

Fig. 2 Comparison of mean reduction from baseline between groups.

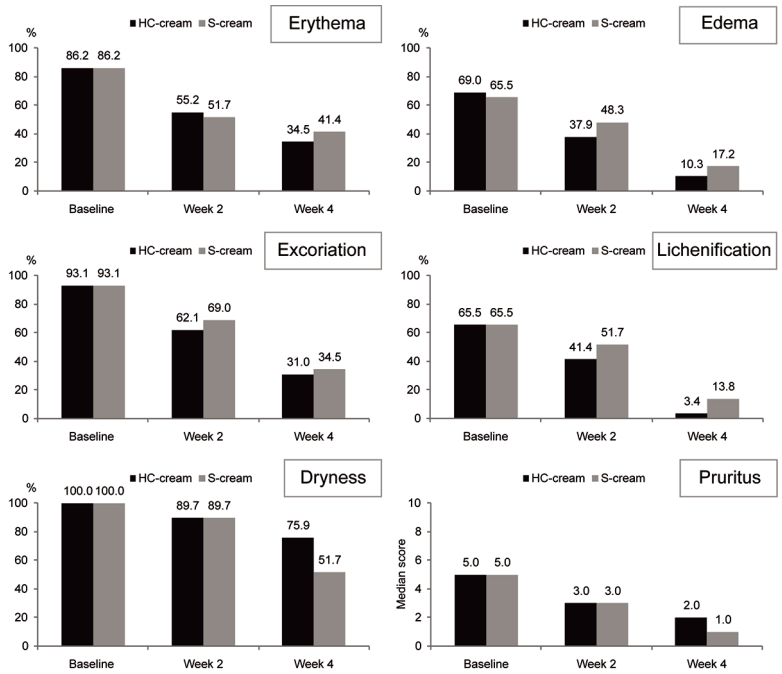

Fig. 3 The reduction in signs and symptoms present of atopic dermatitis patients.

to increase transepidermal water loss (TEWL) and heighten susceptibility to penetration of exogenous irritants, allergens, and microbes into the skin[12]. Additionally, it was discovered that the stratum corneum layer of AD patients experienced a decrease of intercellular lipid constituents (i.e., ceramide and linoleic acid), which this lipid decrease resulted in an increase of TEWL as well[13]. At the current time, based on information relating epidermal barrier dysfunction and AD, there were studies on the moisturizers' efficiency in treating AD. From those studies, it was discovered that moisturizers show clinical benefits in the treatments of both active and inactive AD[14-19]. Because of the limitations of topical steroid therapy, a nonsteroidal alternative moisturizer may play a major role for patients with mild to moderate AD[6].

In the present study, it was demonstrated that treatment with the S cream could equally decrease SCORAD score in mild-to-moderate AD comparing with the HC cream. At all post-baseline visits (week 2 and week 4), all investigation parameters (erythema, edema, excoriation, lichenification, dryness, and pruritus) were improved with statistically significant difference in both the S cream and the HC cream groups. Comparing the mentioned parameters between the two sides, it was found that the decreases of values between both sides were not different with statistical significance, except for the skin dryness value in week 4. Here, it was discovered that the S cream side had a lower dryness value than that of the HC cream side with statistical significance. This was owing to an effect of saccharide isomerate in the S cream, which acted as a humectant to keep the skin moist.

The results gained from the present studies displayed the anti-inflammatory effects the S cream in treating mild-to-moderate atopic dermatitis. Many research works have displayed that linoleic acid, which is the main component in the S cream, has anti-inflammatory effects[20]. There were some clinical studies demonstrated the effect of linoleic acids in the treatment of AD. It was discovered that the patients who received treatment with evening primrose oil, which were rich in linoleic acids both orally or topically had beneficial effects of treatment[21-23]. In addition, linoleic acid was a lipid that helped to repair skin barrier functions[9].

Studies of recurring rashes discovered that in patients who were remitted in four weeks, none of the patients suffered from recurring rashes for both the HC cream side and the S cream side treatments during the next four weeks. Up to present, no study about the efficacy of the S cream has been conducted. From the present study, it was recommended that the duration

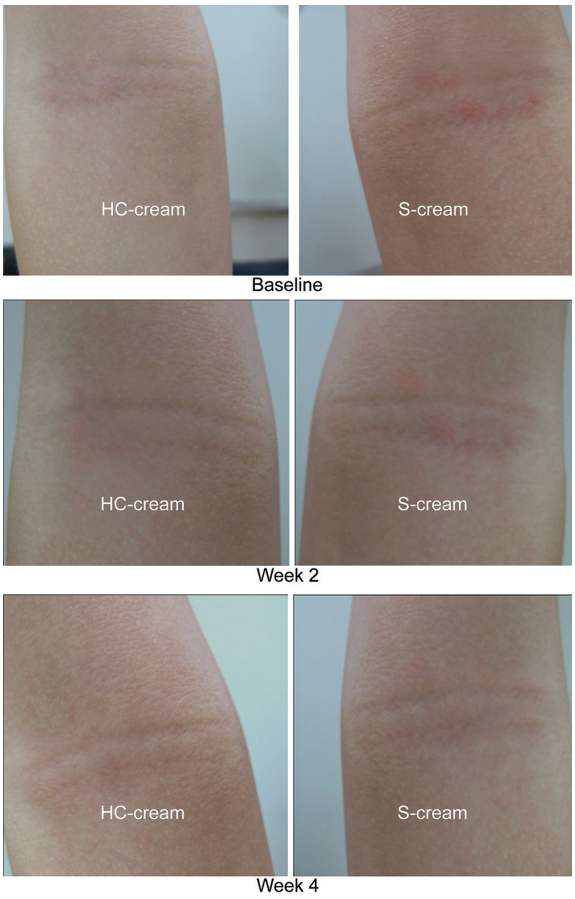

Fig. 4 The clinical response of atopic dermatitis patient at week 2 and 4.

of maintenance period trial should be longer for observing recurrence of the disease in order to obtain more accurate results. There was no adverse event observed from both agents.

The limitations of the present research was that the objective evaluations such as TEWL and erythema index should be measured. Additionally, the length of the observation period for recurrences should be increased for results that are more precise.

In conclusion, it was suggested that the S cream could be used as an alternative treatment for both acute and maintenance phases in children with mild-to-moderate AD.

What is already known on this topic?

AD is a chronically relapsing inflammatory skin disease. Topical steroid has been used as standard therapy. However, long-term treatment with topical steroid limits its use. The use of moisturizers is considered standard therapy for the treatment of AD by improving dry skin and preventing recurrence of inflammation, and reducing the amount of topical steroid usage. Previous researches[14-19] discovered that moisturizer containing non-steroidal anti-inflammatory agents such as licochacone A, dexpanthenol were able to improve mild-to-moderate severity of which might be used as an alternative treatment instead of topical steroid like hydrocortisone.

What this study adds?

This study showed that the S cream composed of linoleic acids, which had anti-inflammatory action, clinically improved the mild to moderate AD. Therefore, this agent may be used as alternative treatment for mild to moderate AD, in order to reduce adverse effects from the long-term use of topical steroids.

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Potential conflicts of interest

None.

References

1. Kay J, Gawkrodger DJ, Mortimer MJ, Jaron AG. The prevalence of childhood atopic eczema in a general population. J Am Acad Dermatol 1994; 30: 35-9.
2. Langeveld-Wildschut EG, Bruijnzeel PL, Mudde GC, Versluis C, Van Ieperen-Van Dijk AG, Bihari IC, et al. Clinical and immunologic variables in skin of patients with atopic eczema and either positive or negative atopy patch test reactions. J Allergy Clin Immunol 2000; 105: 1008-16.
3. Eichenfield LF, Hanifin JM, Luger TA, Stevens SR, Pride HB. Consensus conference on pediatric atopic dermatitis. J Am Acad Dermatol 2003; 49: 1088-95.
4. Van Bever HP, Llanora G. Features of childhood atopic dermatitis. Asian Pac J Allergy Immunol 2011; 29: 15-24.
5. Johnson AW. Cosmeceuticals: function and skin barrier. In: Draelos ZD, editor. Cosmeceuticals. Philadelphia: Elsevier Saunders; 2005: 11-7.

6. Valencia IC, Kerdel FA. Topical glucocorticoids. In: Freedberg IM, Aisen AZ, Wolff K, Austen DF, Goldsmith LA, Katz SI, editors. Dermatology in general medicine. 6th ed. New York: McGraw-Hill; 2003: 2324-7.
7. Williams HC. Clinical practice. Atopic dermatitis. N Engl J Med 2005; 352: 2314-24.
8. Calder PC. Polyunsaturated fatty acids and inflammation. Biochem Soc Trans 2005; 33: 423-7.
9. Elias PM, Brown BE, Ziboh VA. The permeability barrier in essential fatty acid deficiency: evidence for a direct role for linoleic acid in barrier function. J Invest Dermatol 1980; 74: 230-3.
10. Akihisa T, Kojima N, Kikuchi T, Yasukawa K, Tokuda H, Masters T, et al. Anti-inflammatory and chemopreventive effects of triterpene cinnamates and acetates from shea fat. J Oleo Sci 2010; 59: 273-80.
11. Simpson EL, Hanifin JM. Atopic dermatitis. Med Clin North Am 2006; 90: 149-67.
12. Watson W, Kapur S. Atopic dermatitis. Allergy Asthma Clin Immunol 2011; 7 (Suppl 1): S4.
13. Coderch L, López O, de la Maza A, Parra JL. Ceramides and skin function. Am J Clin Dermatol 2003; 4: 107-29.
14. Udompataikul M, Limpa-o-vart D. Comparative trial of 5% dexpanthenol in water-in-oil formulation with 1% hydrocortisone ointment in the treatment of childhood atopic dermatitis: a pilot study. J Drugs Dermatol 2012; 11: 366-74.
15. Eberlein B, Eicke C, Reinhardt HW, Ring J. Adjuvant treatment of atopic eczema: assessment of an emollient containing N-palmitoylethanolamine (ATOPA study). J Eur Acad Dermatol Venereol 2008; 22: 73-82.
16. Chamlin SL, Kao J, Frieden IJ, Sheu MY, Fowler AJ, Fluhr JW, et al. Ceramide-dominant barrier repair lipids alleviate childhood atopic dermatitis: changes in barrier function provide a sensitive indicator of disease activity. J Am Acad Dermatol 2002; 47: 198-208.
17. Boguniewicz M, Zeichner JA, Eichenfield LF, Hebert AA, Jarratt M, Lucky AW, et al. MAS063DP is effective monotherapy for mild to moderate atopic dermatitis in infants and children: a multicenter, randomized, vehicle-controlled study. J Pediatr 2008; 152: 854-9.
18. Udompataikul M, Srisatwaja W. Comparative trial of moisturizer containing licochalcone A vs. hydrocortisone lotion in the treatment of childhood atopic dermatitis: a pilot study. J Eur Acad Dermatol Venereol 2011; 25: 660-5.
19. Wananukul S, Chatproedprai S, Chunharas A, Limpongsanuruk W, Singalavanija S, Nitiyarom R, et al. Randomized, double-blind, split-side, comparison study of moisturizer containing licochalcone A and 1% hydrocortisone in the treatment of childhood atopic dermatitis. J Med Assoc Thai 2013; 96: 1135-42.
20. Horrobin DF. Essential fatty acid metabolism and its modification in atopic eczema. Am J Clin Nutr 2000; 71 (1 Suppl): 367S-72S.
21. Guenther L, Wexler D. Efamol in the treatment of atopic dermatitis. J Am Acad Dermatol 1987; 17: 860.
22. Senapati S, Banerjee S, Gangopadhyay DN. Evening primrose oil is effective in atopic dermatitis: a randomized placebo-controlled trial. Indian J Dermatol Venereol Leprol 2008; 74: 447-52.
23. Anstey A, Quigley M, Wilkinson JD. Topical evening primrose oil as treatment for atopic eczema. J Dermatol Treat 1990; 1: 199-201.

การศึกษาประสิทธิภาพของสารให้ความชุ่มชื้นที่มีส่วนประกอบของสเป็นเกรนแว็กซ์ เชียบัทเทอร์ และอาร์กาเนียสไปโนซ่า เคอร์เนวออย ในการรักษาโรคผื่นภูมิแพ้ผิวหนังในเด็กเทียบกับยาทา ไฮโดรคอร์ติโซน 1%

ปณยา จิรบันดาลสุข, สุวิราภร โอภาสวงศ์, มนตรี อุดมเพทายกุล

วัตถุประสงค์: *เพื่อศึกษาเปรียบเทียบประสิทธิภาพของสารให้ความชุ่มชื้นที่มีส่วนประกอบของสเป็นเกรนแว็กซ์ เชียบัทเทอร์ และอาร์กาเนียสไปโนซ่า เคอร์เนวออย กับ ไฮโดรคอร์ติโซน 1% ในการรักษาโรคผื่นภูมิแพ้ผิวหนังระดับความรุนแรงน้อยถึงปานกลาง*

วัสดุและวิธีการ: *ผู้ป่วยโรคผื่นภูมิแพ้ผิวหนัง (atopic dermatitis) ที่มีความรุนแรงเล็กน้อยถึงปานกลาง อายุตั้งแต่ 2 ปี ถึง 15 ปี จำนวน 29 ราย แบ่งบริเวณร่างกายเป็น 2 ข้าง และใช้การสุ่มโดยให้ข้างหนึ่งได้รับการรักษาด้วยสารให้ความชุ่มชื้นที่มีส่วนประกอบของสเป็นเกรนแว็กซ์ เชียบัทเทอร์ และอาร์กาเนียสไปโนซ่า เคอร์เนวออย และอีกข้างหนึ่งได้รับการรักษาด้วยไฮโดรคอร์ติโซน 1% วันละ 2 ครั้ง เป็นเวลา 4 สัปดาห์ เมื่อผื่นหายด้านที่ทาไฮโดรคอร์ติโซน 1% จะเปลี่ยนเป็นทาครีมเบสแทน ส่วนด้านที่ทาสารให้ความชุ่มชื้นที่มีส่วนประกอบของสเป็นเกรนแว็กซ์ เชียบัทเทอร์ และอาร์กาเนียสไปโนซ่าเคอร์เนวออย ให้ทายาเดิมต่อเป็นเวลา 4 สัปดาห์ เพื่อติดตามดูการกลับเป็นซ้ำ ประเมินผลโดยใช้คะแนน the scoring of atopic dermatitis (SCORAD) ประเมินผลทางสถิติโดยใช้สถิติเชิงพรรณนา paired student t-test, repeated analysis of varience (ANOVA) และ survival analysis โดยกำหนดระดับนัยสำคัญทางสถิติที่ $p<0.05$*

ผลการศึกษา: *สารให้ความชุ่มชื้นที่มีส่วนประกอบของสเป็นเกรนแว็กซ์ เชียบัทเทอร์ และอาร์กาเนียสไปโนซ่าเคอร์เนวออย และไฮโดรคอร์ติโซน 1% สามารถลดคะแนน SCORAD ลงได้อย่างต่อเนื่องทุก 2 สัปดาห์ และมีนัยสำคัญทางสถิติ ($p<0.001$) แต่อย่างไรก็ตามไม่พบความแตกต่างเมื่อเปรียบเทียบระหว่างสองกลุ่ม ($p>0.05$) เมื่อวิเคราะห์อัตราการหายของโรคพบว่าสารให้ความชุ่มชื้นที่มีส่วนประกอบของสเป็นเกรนแว็กซ์ เชียบัทเทอร์ และอาร์กาเนียสไปโนซ่าเคอร์เนวออย มีอัตราการหายมากกว่าไฮโดรคอร์ติโซน 1% แต่ไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p>0.05$)*

สรุป: *สารให้ความชุ่มชื้นที่มีส่วนประกอบของสเป็นเกรนแว็กซ์ เชียบัทเทอร์ และอาร์กาเนียสไปโนซ่า เคอร์เนวออยมีประสิทธิผลในการรักษาโรคผื่นภูมิแพ้ผิวหนังในเด็กที่มีความรุนแรงของโรคน้อยถึงปานกลางไม่แตกต่างจากไฮโดรคอร์ติโซน 1%*