The Comparative Study of Topical Therapy on Striae Alba between a Herbal Extract Cream and 0.1% Tretinoin Cream in Adolescence

Prapote Asawaworarit MD*, Suwadee Chuanchaiyakul PhD**,
Nanticha Kamanamool MD*, Tanaporn Piyavechvirat MD*, Montree Udompataikul MD*

** Skin Center, Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand*
*** Department of Anatomy, Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand*

Background: *Striae are commonly developed in adolescence as a result of active growth spurt. Although they create little physical health issue, they are cosmetic concerns to the patients. Effective striae treatment can help improve their mental health and personality.*

Objective: *To compare the effects of a herbal extract cream and 0.1% tretinoin cream in the treatment of striae alba.*

Material and Method: *Forty eight participants aged between 10 - 19 years old, with striae alba at their thighs were randomized into two groups. Each group was separately treated with 0.1% tretinoin and herbal extract for 16 weeks. The width, length and surface roughness of the lesions were assessed including histological evaluation and participants' satisfaction.*

Results: *Thirty nine participants completed the study after 16 weeks. Compared to initial lesions, the striae width was reduced by 9.01% ($p = 0.002$) in tretinoin group and 13.09% ($p<0.001$) in herbal extract group. The length was reduced by 9.54% in tretinoin group ($p<0.001$) and 8.73% in herbal extract group ($p<0.001$). The surface roughness assessed by Visioscan VC98 was reduced by 13.70% in tretinoin group ($p = 0.036$) and 17.24% in herbal extract group ($p<0.001$). From H&E staining, the mean difference of epidermal thickness was 4.79±7.15 microns in tretinoin group and 14.22±16.98 microns in herbal extract group.*

The mean difference of collagen amount was 13.75±6.02 units in tretinoin group and 6.60±4.92 units in herbal extract group. From Masson trichrome staining, the mean difference of collagen amount was 6.75±3.50 units in tretinoin group and 12.20±7.73 units in herbal extract group. From Verhoff van Gieson staining, the mean difference of elastin amount was 2.25±3.30 units in tretinoin group and 5.40±4.16 units in herbal extract group. There was no statistical significant difference between two groups in histological evaluation. The herbal extract caused irritant contact dermatitis only 4.55% in contrast to 72.73% from the tretinoin group. Most participants from both groups had moderate to high satisfaction according to the efficacy of their treatments.

Conclusion: *The herbal extract cream is as effective as 0.1% tretinoin cream in the treatment of striae alba. As tretinoin can cause skin irritation, the herbal extract can be a better alternative treatment.*

Keywords: *Striae alba, Stretch marks, Centellaasiatica, Aloe vera, Tretinoin*

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Striae alba is a common skin condition that usually begins to develop in adolescence from an active growth spurt or in pregnancy. The abrupt stretching of the skin can cause this condition[1,2]. Striae are classified into two stages: striae rubra and striae alba. Early lesions (striae rubra) are red or purple elevated lines and can be pruritic. Overtime, they become atrophic with a fine wrinkled appearance and the color is gradually faded as they become striae alba, which are usually permanent[3]. Striae alba are presented as linear depression of the skin caused by changes to the reticular collagen[4]. Histopathology of striae rubra begins with dermal edema and perivascular lymphocytic infiltration[5]. In straie alba, epidermal atrophy and loss of rete ridges

Correspondence to:
Udompataikul M, Skin Center, Faculty of Medicine, Srinakharinwirot University, Bangkok 10110, Thailand.
Phone: +66-2-2594260
E-mail: umontree@gmail.com

can be observed[6]. Although striae cause little physical health issues, they are mainly a cosmetic concern for patients. Striae rubra usually last for a few weeks and then become striae alba which are more common and more difficult to treat. The treatments of striae include topical and laser therapy. Regarding laser treatments, 1540-nm non-ablative fractional laser[7], pulse dye laser, intense pulsed light[8] and 308-nm excimer laser have been tried. All of these therapies demonstrated variable effectiveness. Moreover, they are associated with side effects such as skin burn, postinflammatory hyperpigmentation and postinflammatory hypopigmentation[9]. Concerning the topical treatments, 0.1% tretinoin[10], glycolic acid and ascorbic acid[11] were used. There were some studies demonstrating that topical 0.1% tretinoin were effective, however, skin irritation caused by this drug limited its use particularly in the case of striae rubra[10-13]. Therefore, a novel of herbal extract has been developed for an alternative treatment.

Centella asiatica, which is the main active ingredient of the trial herbal extract cream, contains asiaticoside which stimulates collagen type I production enhancing scar maturation and wound healing[14]. Madecassosidein *Centella asiatica* stimulates both collagen type I and type III synthesis[15,16]. It improves the tensile strength of newly formed skin and also inhibits inflammation[17]. *Aloe vera*, another active ingredient, has been reported to increase re-epithelialization, provide anti-inflamatory effects and improve dermal perfusion in tissue repair process. It also stimulates fibroblast activity and collagen synthesis[18-20]. Palmitoyl tripeptides are in small peptide molecules and have lipophilic properties which accelerate delivery across the skin. The peptides stimulate transforming growth factor-beta that enhance collagen and elastin production[21]. Hydroxyprolisilane has been reported to help the wound healing process and prevent hypertrophic scarring from the polarization of silicone[22,23]. Panthenol has been used topically to improve hydration and reduce inflammation[24]. Both *Centella asiatica* and *Aloe vera,* the main active ingredients used in the present study, are grown in Thailand and would be great advantage for further plant industrial investment in Thailand.

The aim of the present study is to compare the effectiveness of the herbal extract cream and 0.1% tretinoin cream in the treatment of striae alba.

Material and Method

This was a randomized double-blind study. The sample size was calculated from the following research article. The data obtained from Kang et al. study[10], the mean difference of the lesions' length reduction between 0.1% tretinoin cream group and the control group was 14% (8 millimeters) with the standard deviation of difference in the response of 3. The sample size of 40 subjects was required with 95% confidence and 80% power. Sample size was calculated using PS (Power and Sample Size Calculations) program version 3.0.43. With a dropout rate of 20%, samples of 48 patients had to be recruited, 24 in each group. The present study was approved by the Srinakharinwirot University Ethical Committee. Each subject was counseled about the study and informed consent from the guardians was obtained. Participants aged 10-19 years old (average 18 years) who had been medically identified with striae alba on upper thighs were recruited into the study. Exclusion criteria were history of collagen or elastin disorders, or usage of any stretch mark treatments in the past six months. No other treatment of stretch mark or any other topical products was allowed during the study. Pregnant and breast-feeding women were also excluded.

The participants were randomized into two groups. All participants were assigned by a third person using computerized block randomization method and the encoding was disclosed when the study ended. One group received 0.1% tretinoin cream and the other received the herbal extract cream for 16 weeks. The herbal extract cream contains *Centella asiatica*, *Aloe vera*, paper mulberry, palmitoyl tripeptide, hydroxyprolisilane, squalene oil, and panthenol (Centria, Bangkok Botanica LTD, Thailand). The clinical evaluation photography; striae width and length; and surface roughness were obtained at baseline and every 4 weeks until 16 weeks. The width and length were measured by a digital vernier caliper. The roughness was assessed by a UVA-light video camera (Visioscan VC98; Courage-Khazaka, Koln, Germany).When the study ended, participants' satisfaction was graded in the treatment effectiveness and adverse effects. Histological processing and evaluation with H&E staining was done from 5 of each group at baseline and 16 weeks to compare the epidermal thickness and the subjective amount of collagen and elastin. The differential

determination of collagen and elastin were confirmed by staining with Masson Trichrome and Verheoff van Gieson staining respectively.

The epidermal thickness was measured from five areas with 50 microns apart using Olympus BX50 microscope. The microscopic image files were accessed with Adobe Photoshop CS6 program and each image was designed to have 70 square grids with seven rows and ten columns. Collagen and elastin were randomly counted from 35 out of 70 grids. The subjective amounts of collagen and elastin bundles were predicted as units instead of bundles. A unit was defined as the full bundle presented in a grid or when more than half of the visible bundle appeared in a grid, or a bundle passed at least two sides of a square grid.

Statistical Analysis

The demographic data was reported in proportion and percentage. One-way repeated measured ANOVA was used to compare the mean changes of the lesions' width, length and surface roughness within the treatment groups and Two-way repeated measured ANOVA was used to compare between two groups. Regarding histological evaluation, Independent t-test or Wilcoxon rank-sum test was used to compare the mean difference or the median difference at week 16 from baseline between two groups. Chi-square test was used to compare satisfaction and side effects between the two treatments. Statistical significant would be reported if *p*-valve was of less than 0.05. SPSS program version 19.0 was used for data analysis.

Results

Forty six females and two males were included in the present study. The demographic data of the two groups did not differ in age, sex, skin type, previous treatment and striae age as shown in Table 1. At the end of the study, nine participants were withdrawn from analysis because they did not attend schedule visits. There were 19 from the tretinoin group and 20 from the herbal extract group completed the study.

The mean width of the lesions was decreased each visit in tretinoin group ($p = 0.002$) and in the herbal extract group ($p<0.001$) which were statistically significant different from baseline. There was no statistically significant difference between two groups ($p = 0.783$) (Fig. 1). The mean length of the lesions was reduced each visit in tretinoin group ($p<0.001$) and in the herbal extract group ($p<0.001$) which were statistically significant different from baseline. There was no statistically significant difference between the two groups ($p = 0.651$) (Fig. 2). The surface roughness was decreased each visit from baseline in tretinoin group ($p = 0.036$), and the herbal extract group ($p<0.001$) as well. There was no statistically significant difference between two groups ($p = 0.892$) (Fig. 3). The pictures of the striae roughness captured by Visioscan VC98 were illustrated in Fig. 4. Regarding the histological change from H&E staining, the median difference of epidermal thickness after 16 weeks was-7.74 (-9.34 to -0.25) micronsin tretinoin group and -13.18 (-37.16 to -0.94) microns in herbal extract group.The mean difference of collagen amount was -13.75±6.02 units in tretinoin group and -6.60±4.92 units in herbal extract group.

From Masson trichrome staining, the mean difference of collagen amount was -6.75±3.50 units in tretinoin groupand -12.20±7.73 units in herbal extract group.

From Verhoff van Gieson staining, the mean difference of elastin amount was -2.25±3.30 units in tretinoin group and -5.40±4.16 units in herbal extract group. Comparing all the histologic changed variables, there was no significant difference between both groups (Table 2).

From the post-treatment survey, 72.73% of the tretinoin group and 81.82% of the herbal extract group had moderate to very high level of satisfaction in the treatment efficacy. There was no statistically significant difference between the two groups ($p = 0.35$).

There were 72.73% of the subjects in the tretinoin group who experienced skin irritation, redness or scaling. In contrary, 4.55% of subjects in the herbal extract group had mild skin irritation from the treatment with statistically significant difference between both groups ($p<0.001$).

Discussion

Regarding topical striae treatments, there were several previous studies reported with variable results. Ash et al. conducted a 12-week clinical study of ten participants with striae alba using 20% glycolic acid/0.05% tretnoin compared with 20% glycolic acid/10% L-ascorbic acid. The results from both groups

showed that the lesions were significantly improved by visual grading but there was no significant difference between both groups[11]. In contrast to the study of Pribanich et al., tretinoin cream was used for seven months in a double-blind, placebo-controlled study in 11 women who had abdominal striae alba but there was no difference or improvement in the treated group compared with controlled group[25]. The study of Rangel et al was done in 26 one-week-post-partum women with abdominal striae alba. Tretinoin cream was used for 12 weeks and the targeted lesion decreased in length by 20% with statistically significant difference[13]. Kang et al did a study using tretinoin on 26 subjects with striae rubra. It was demonstrated that the width and the length were reduced by 8% and 14% respectively after 24 weeks with statistical significant[10].

In the present study, 0.1% tretinoin cream and a cream containing *Centella asiatica*, *Aloe vera*, paper mulberry, palmitoyl tripeptide, hydroxyprolisilane, squalene oil, and panthenol were compared. There were statistically improvements of the lesional width, length, surface roughness, and histological changes in both groups. The key ingredients of the herbal extract to improve striae alba are *Centella asiatica* which promotes collagen synthesis, improves tensile strength of the newly formed skin and also *Aloe vera* which has a wound healing promotion and stimulates the fibroblast and collagen production.

Though tretinoin cream has been used for the treatment, its side effects limited the use. In contrast, the herbal extract used in the present study showed minimal side effects. Hence the use of the herbal extract cream results in better participants' compliance.

It was also demonstrated that there was no significant difference in the efficacy of the herbal extract cream compared to the tretinoin cream in the present study. The histological changes in this study were not significantly different from baseline except for the amount of collagen bundles. This might be due to the small sample size for skin biopsy. Increasing sample size may clearly identify the remarkable changes. Hence, further studies with longer period of follow-up and increased histological sample sizes should be conducted. Moreover, studies designed to use the herbal extract cream in conjunction with other treatments such as light and laser therapies should also be investigated.

Conclusion

The herbal extract cream containing of *Centella asiatica* and *Aloe vera* as active ingredients can reduce the width, the length and surface roughness of striae alba as effective as 0.1% tretinoin. As tretinoin can cause skin irritation, the herbal extract can be a better alternative topical treatment for striae alba.

What is already known on this topic?

Striae alba is a common skin condition. Laser treatments have demonstrated some improvements but they are associated with postinflammatory hyperpigmentation and skin burn. Topical products such as tretinoin can be used to improve the lesion but can produce irritant contact dermatitis.

Table 1. Baseline characteristicsof the participants

	0.1% Tretinoin	Herbal extract	*p* -value
	n = 19	n = 20	
Age, year, mean (SD)	18.86 (0.37)	18.82 (0.40)	0.741
Sex			1.000
Male, n (%)	1 (5.26)	1 (5.00)	
Female, n (%)	18 (94.74)	19 (95.00)	
Duration of lesion, year, mean (SD)	4.18 (2.04)	5.04 (2.03)	0.181
Skin type			0.429
Type III, n (%)	6 (31.58)	9 (45.00)	
Type IV, n (%)	13 (68.42)	11 (55.00)	

Table 2. Comparison of histological changes at 16 weeks from baseline

Histological evaluation	0.1% Tretinoin (n = 4)	Herbal extract (n = 5)	Mean difference between groups (95%CI)	*p*-value
Epidermal thickness, micron, median (IQR)	-7.74 (-9.34 to -0.25)	-13.18 (-37.16 to -0.94)	-9.42 (-31.09 to 12.25)	0.327
Collagen (H&E), unit, mean (SD)	-13.75 (6.02)	-6.60 (4.92)	7.15 (-1.45 to 15.75)	0.090
Collagen (Masson trichrome), unit, mean (SD)	-6.75 (3.50)	-12.20 (7.73)	-5.45 (-15.40 to 4.50)	0.236
Elastin, unit, mean (SD)	-2.25 (3.30)	-5.40 (4.16)	-3.15 (-9.20 to 2.90)	0.258

data was presented as mean difference (SD) or median (Interquartile ranges)

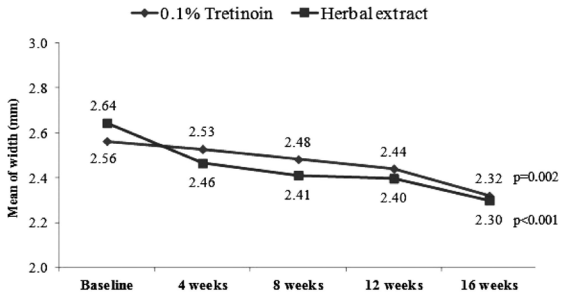

Fig. 1 Mean width of the lesions at baseline, 4 weeks, 8 weeks, 12 weeks and 16 weeks after treatment between 0.1% tretinoin and herbal extract.

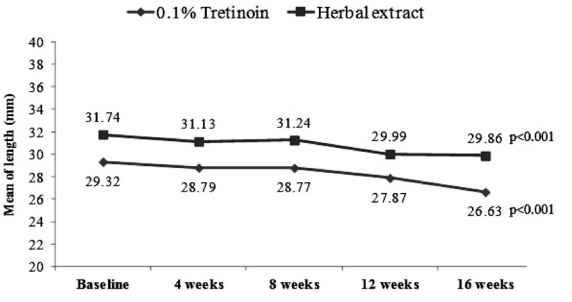

Fig. 2 Mean length of the lesions at baseline, 4 weeks, 8 weeks, 12 weeks and 16 weeks after treatment between 0.1% tretinoin and herbal extract.

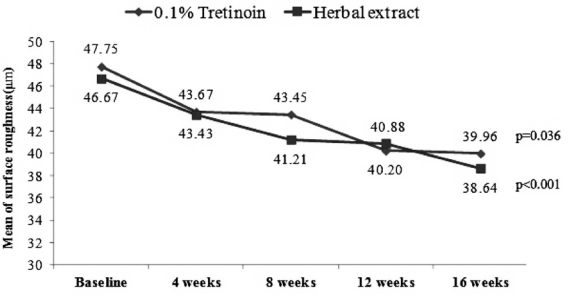

Fig. 3 Mean surface roughness at baseline, 4 weeks, 8 weeks, 12 weeks and 16 weeks after treatment between 0.1% tretinoin and herbal extract.

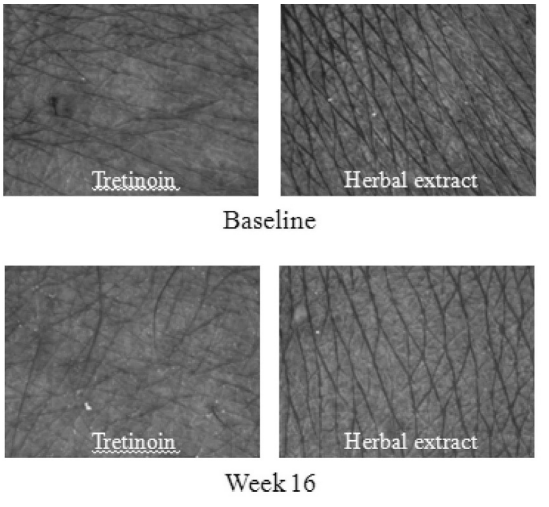

Fig. 4 The changes in surface roughness between baseline and week 16. The striae have fewer wrinkles after 16 weeks of treatment in two groups.

What is this study adds?

The cream containing*Centella asiatica* and *Aloe vera* can improve striaealba effectively. It can be used as an alternative treatment.

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Potential conflicts of interest

None.

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การศึกษาเปรียบเทียบประสิทธิภาพของครีมสมุนไพร และเทรทิโนอินครีม 0.1% ในการรักษารอยแตกลายในวัยรุ่น

ประโพธ อัศวรฤทธิ์, สุวดี ชวนไชยะกูล, นันทิชา คมนามูล, ธนาพร ปิยะเวชวิรัตน์, มนตรี อุดมเพทายกุล

ภูมิหลัง: *รอยแตกลายเป็นภาวะที่เกิดจากการยืดตัวของผิวหนังมากกว่าปกติสามารถพบได้ตั้งแต่ช่วงวัยรุ่น แม้จะไม่มีผลทางด้านสุขภาพกายแต่มีผลต่อสุขภาพทางจิตใจ การรักษาภาวะรอยแตกลายที่มีประสิทธิภาพจะสามารถลดความกังวลและมีส่วนช่วยในการพัฒนาบุคลิกภาพของกลุ่มคนดังกล่าวได้*

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพการรักษารอยแตกลาย โดยการใช้ครีมสมุนไพร เทียบกับเทรทิโนอินครีม 0.1%*

วัสดุและวิธีการ: *มีการสุ่มเพื่อแบ่งอาสาสมัคร 48 รายออกเป็น 2 กลุ่ม กลุ่มที่หนึ่งได้รับเทรทิโนอินครีม 0.1% ส่วนกลุ่มที่สองได้รับครีมสมุนไพร กำหนดให้อาสาสมัครทาครีมที่ได้รับวันละหนึ่งครั้งเป็นระยะเวลา 16 สัปดาห์ โดยติดตามการรักษาทุก 4 สัปดาห์ ด้วยการวัดความกว้าง ความยาว และความหยาบของรอยแตกลาย และให้อาสาสมัครประเมินประสิทธิภาพของการรักษารวมถึงผลข้างเคียงในสัปดาห์ที่ 16 นอกจากนี้ยังได้มีการตัดชิ้นเนื้อจากอาสาสมัครกลุ่มละ 5 รายก่อนและหลังการศึกษาเพื่อประเมินลักษณะทางจุลพยาธิวิทยาของรอยแตกลาย*

ผลการศึกษา: *มีอาสาสมัครจำนวน 39 รายที่ได้มาติดตามการรักษาจนครบ 16 สัปดาห์ ความกว้างของรอยแตกลายลดลง 9.01% ($p = 0.002$) ในกลุ่มเทรทิโนอิน และลดลง 13.09% ($p<0.001$) ในกลุ่มครีมสมุนไพร ความยาวของรอยแตกลายลดลง 9.54% ($p<0.001$) ในกลุ่มเทรทิโนอิน และลดลง 8.73% ($p<0.001$) ในกลุ่มครีมสมุนไพร จากการวัดความหยาบของพื้นผิวรอยแตกลายด้วยเครื่องวิสิโอสแกนนั้น มีความหยาบที่ลดลง 13.70% ($p = 0.036$) ในกลุ่มเทรทิโนอิน และลดลง 17.24% ($p<0.001$) ในกลุ่มครีมสมุนไพร จากการศึกษาชิ้นเนื้อด้วยการย้อมเอช แอนด์ อี โดยการเทียบชิ้นเนื้อหลังการรักษา 16 สัปดาห์กับชิ้นเนื้อก่อนเริ่มการรักษา พบว่าความหนาของชั้นหนังกำพร้ามีค่า mean difference 4.79±7.15 ไมครอนในกลุ่มเทรทิโนอิน และ 14.22±16.98 ไมครอนในกลุ่มครีมสมุนไพร นอกจากนี้การเปลี่ยนแปลงของปริมาณคอลลาเจนนั้นมีค่า mean difference 13.75±6.02 หน่วยในกลุ่มเทรทิโนอิน และ 6.60±4.92 หน่วยในกลุ่มครีมสมุนไพร จากการย้อมชิ้นเนื้อด้วย Masson trichrome พบว่าปริมาณคอลลาเจนมีค่าเฉลี่ยของความแตกต่างระหว่างสองกลุ่ม(mean difference) 6.75±3.50 หน่วยในกลุ่มเทรทิโนอิน และ 12.20±7.73 หน่วยในกลุ่มครีมสมุนไพร สำหรับการย้อมชิ้นเนื้อด้วย Verhoff van Gieson ปริมาณอิลาสตินมีค่า mean difference 2.25±3.30 หน่วยในกลุ่มเทรทิโนอิน และ 5.40±4.16 หน่วยในกลุ่มครีมสมุนไพร จากการศึกษาชิ้นเนื้อที่กล่าวมาไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างสองกลุ่ม อาสาสมัครกลุ่มที่ใช้เทรทิโนอินมีผลข้างเคียง เช่น อาการคัน แสบ และผิวลอกเป็นขุย คิดเป็น 72.73% ในขณะที่อาสาสมัครกลุ่มที่ได้รับครีมสมุนไพรมีการระคายเคืองจากยาเพียง 4.55% อาสาสมัครในทั้งสองกลุ่มส่วนใหญ่มีความพึงพอใจต่อผลการรักษา*

สรุป: *ครีมสมุนไพรมีประสิทธิภาพในการรักษารอยแตกลายเทียบเท่ากับเทรทิโนอินแต่เนื่องจากเทรทิโนอินสามารถทำให้เกิดการระคายเคืองต่อผิวหนังมากกว่า ครีมสมุนไพรจึงเป็นทางเลือกที่ดีกว่า*