

The therapeutic effect of topical *Hydnocarpus anthelminthicus* oil in combination with 0.1% triamcinolone acetonide in psoriasis; A Randomized Control Trial.

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ABSTRACT :

**SRISUWANWATTANA P, RAJATANAVIN N. THE THERAPEUTIC EFFECT OF TOPICAL
HYDNOCARPUS ANTHELMINTHICUS OIL IN COMBINATION WITH 0.1% TRIAMCINOLONE
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Background: *Hydnocarpus anthelminthicus*, krabao in Thai, a herbal medicine, has been used mainly for the treatment of leprosy. Oil extracted from its seeds “chaulmoogra oil ” administered orally shown an anti-inflammatory and anti-nociceptive activities in animal model. Psoriasis is a chronic inflammatory disease which involves multiple immune mechanisms which cause abnormal keratinocytes proliferation and differentiation. Chaulmoogra oil has been used in Thai herbal remedies for psoriasis but its efficacy has never been elucidated.

Objectives: to determine whether topical chaulmoogra oil can enhance the efficacy of topical steroid in the treatment of psoriasis.

Materials and methods: Randomized double-blinded intra-individual control trial was conducted in 27 patients with symmetrical stable chronic plaque type psoriasis. Half-body lesions were randomized to treat with topical 0.1 percent o/w triamcinolone acetonide in chaulmoogra oil or 0.1 percent o/w triamcinolone acetonide in mineral oil, which served as control, twice daily for 4 weeks. Local psoriasis severity index and physician’s global assessment were evaluated at baseline, and at the second and fourth week by investigators and photographs. Patient satisfaction was evaluated at the last visit.

Results: 24 patients completed the study. Both 0.1 percent o/w triamcinolone acetonide in chaulmoogra oil and control regimen significantly reduced erythema, thickness and scales of index lesions (p -value < 0.0011, p -value= 0.0038 and p -value= 0.0038, respectively). In contrast, the mean difference in areas of index lesion after treatment was significantly increased in the chaulmoogra oil treated side. However, after combining all parameters, the PASI score reduced significantly from the baseline on both side (p -value =0.0001). There were significant improvements of physician’s global assessment and visual analogue scale of itchiness and irritation in both sides. Overall satisfaction scores of the treated group and the controlled group were not significant difference, 6.87(±2.10) and 7.30(±1.93), respectively (p -value = 0.12).

Conclusion: 0.1 percent o/w triamcinolone acetonide in chaulmoogra oil or in mineral oil demonstrated similar efficacy in term of erythema, thickness scales and reduction of psoriatic index lesions. The effect of triamcinolone acetonide in chaulmoogra oil preparation was not superior to the standard preparation of 0.1% triamcinolone acetonide cream.

Keyword: psoriasis, chaulmoogra oil, krabao, *Hydnocarpus anthelminthicus* oil

บทคัดย่อ :

พลอยชมพู ศรีสุวรรณวัฒนา ภัฏฐา รัชตะนาวิณ การศึกษาแบบมีกลุ่มเปรียบเทียบ เพื่อประเมินประสิทธิภาพของน้ำมันสกัดจากเมล็ดกระเบาในการเสริมฤทธิ์การรักษาโรคสะเก็ดเงินร่วมกับ 0.1% ไตรแอมซิโนโลน วารสารโรคผิวหนัง 2559; 32: 116-129.

หน่วยโรคผิวหนัง ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล

ผื่นสะเก็ดเงินเกิดจากเซลล์เคอราติโนไซต์ (keratinocyte) แบ่งตัวมากผิดปกติเป็นผลจากความผิดปกติทางพันธุกรรมร่วมกับสิ่งกระตุ้นต่อทีเซลล์ (T cell) ทำให้เกิดการอักเสบเรื้อรัง น้ำมันสกัดจากเมล็ดกระเบามีฤทธิ์ลดการอักเสบ จึงถูกนำมาใช้รักษาโรคติดเชื้อหลายชนิด เช่น โรคเรื้อน ซิฟิลิส หรือใช้เป็นยาสมานแผล และโรคสะเก็ดเงินแต่ไม่เคยมีการศึกษาประสิทธิภาพของน้ำมันสกัดเมล็ดกระเบาในการรักษาโรคสะเก็ดเงินมาก่อน

วัตถุประสงค์ : เพื่อประเมินประสิทธิภาพของน้ำมันสกัดจากเมล็ดกระเบาในการรักษาโรคสะเก็ดเงินร่วมกับ 0.1 เปอร์เซ็นต์ ไตรแอมซิโนโลนอะเซโตนไนด์

วิธีการศึกษา : ผู้ป่วยสะเก็ดเงินชนิดปื้นหนาเรื้อรัง (plaque) ที่ผื่นกระจายเท่ากันทั้งสองข้างจำนวน 27 คน ฝั่งด้านหนึ่งรักษาด้วยยาทาไตรแอมซิโนโลนอะเซโตนไนด์ 0.1 เปอร์เซ็นต์ (0.1% Triamcinolone acetonide cream) ผสมน้ำมันสกัดจากเมล็ดกระเบา อีกด้านเป็นกลุ่มควบคุมรักษาด้วยยาทาไตรแอมซิโนโลนอะเซโตนไนด์ 0.1 เปอร์เซ็นต์ผสมน้ำมันมินเอร์รัล (mineral oil) ทาวันละ 2 ครั้ง เป็นเวลา 4 สัปดาห์ ประเมินผลหลังรักษา 2 และ 4 สัปดาห์ โดยประเมินคะแนนรวมของความแดง ความหนา และขุย วัดพื้นที่รอยโรคด้วยโปรแกรมโฟโต้ช็อป (photoshop) และ ประเมินอาการโดยแพทย์ (Physician's Global Assessment) ร่วมกับการประเมินผลการรักษาโดยผู้ป่วย

ผลการศึกษา : ผู้ป่วยสะเก็ดเงิน จำนวน 24 คน ได้รับการรักษาครบ 4 สัปดาห์ ผลการรักษาของยาทาไตรแอมซิโนโลนอะเซโตนไนด์ 0.1 เปอร์เซ็นต์ ผสมน้ำมันสกัดจากเมล็ดกระเบาและยาทาไตรแอมซิโนโลนอะเซโตนไนด์ 0.1 เปอร์เซ็นต์ ผสมน้ำมันมินเอร์รัลมีประสิทธิภาพในการลดความแดง ความหนาและขุย ได้อย่างมีนัยสำคัญทางสถิติหลังการรักษา 4 สัปดาห์ ($p\text{-value} < 0.0001$, $p\text{-value} = 0.0038$ and $p\text{-value} = 0.0038$ ตามลำดับ). แต่ไม่มีการเปลี่ยนแปลงของพื้นที่รอยโรค ทั้ง 2 ด้าน ประเมินอาการหลังการรักษาโดยแพทย์ (Physician's Global Assessment) ด้านที่ให้การรักษาและด้านควบคุมอาการดีขึ้นอย่างมีนัยสำคัญทางสถิติ ($p\text{-value} < 0.0001$ และ $p\text{-value} < 0.0001$) ตามลำดับ แต่ไม่มีความแตกต่างระหว่างสองด้าน หลังการรักษา 4 สัปดาห์ ระดับความคันระคายเคืองของรอยโรคลดลงอย่างมีนัยสำคัญทางสถิติทั้งด้านที่ให้การรักษาและด้านควบคุม ($p\text{-value} = 0.0270$ และ $p\text{-value} = 0.0434$) ซึ่งทั้งสองด้านไม่มีความแตกต่างกัน คะแนนความพึงพอใจในการรักษาที่ทาน้ำมันสกัดจากเมล็ดกระเบาและด้านควบคุมมีค่าเฉลี่ย 6.897 (ส่วนเบี่ยงเบนมาตรฐาน 2.10) และ 7.30 (ส่วนเบี่ยงเบนมาตรฐาน 1.93) ตามลำดับ ไม่พบผลข้างเคียงรุนแรงจากการรักษา ($p\text{-value} = 0.12$).

สรุปผล: ยาทาไตรแอมซิโนโลนอะเซโตไนด์ 0.1 เปอร์เซ็นต์ผสมน้ำมันสกัดจากเมล็ดกระเบามีประสิทธิภาพไม่แตกต่างจากยาทาไตรแอมซิโนโลนอะเซโตไนด์ 0.1 เปอร์เซ็นต์ผสมน้ำมันมินอ์รรัลในการลดความแดง ความหนา และพุพองรอยโรคได้อย่างมีนัยสำคัญทางสถิติหลังการรักษา 4 สัปดาห์

คำสำคัญ: กระเบา, โรคสะเก็ดเงิน, น้ำมันสกัดจากเมล็ดกระเบา, ไตรแอมซิโนโลนอะเซโตไนด์

Introduction

Oil extracted from seeds of *Hydnocarpus anthelminthicus*, chaulmoogra oil, Krabao name in Thai, is extensively used in Thai herbal remedies for several years. It had been used in various skin and infectious diseases¹⁻², and was well documented in leprosy³⁻⁴. Its active ingredients are chaulmoogric acid, hydnocarpic acid and gorlic acid. Oral administration of chaulmoogra oil showed an anti-inflammatory and peripheral antinociceptive in animal model⁵. Cottle W. reported the use of chaulmoogra oil in the treatment of leprosy, eczema, rheumatism, gout and psoriasis. In case of psoriasis, chaulmoogra ointment treatment yielded a good outcome.²

Psoriasis is a chronic inflammatory disease which choice of treatment ranges from topical or systemic medication, phototherapy and biologic agents. None of the treatment can cure the disease. Topical steroids are the mainstay in management of psoriasis. However, long-term used may cause local cutaneous side effects, such as, atrophy, striae, telangiectasia and skin hypopigmentation. Rarely, systemic absorption could occurred.

Plant derived compounds that already established in psoriasis treatment are dithranol (anthralin) from

araroba tree bark (*Andira araroba*), salicylic acid derived from white willow bark (*Salix alba*) and 8-methoxy psoralen a furocoumarin from *Ammi majus*⁶. Recently, a randomized double-blind, placebo-controlled study of a topical 10% Oregon grape root (*Mahonia aquifolia*) cream in 200 psoriasis patients confirmed the efficacy and safety⁷.

Chaulmoogra oil is one of the Thai herbal medicine that has been used as home remedies for several skin infection and inflammation including psoriasis. Our purpose was to determine therapeutic effects of topical chaulmoogra oil in combination with topical steroid in the treatment of psoriasis. The randomized controlled trial to demonstrate the therapeutic effects of chaulmoogra oil in psoriasis has never been conducted before.

Materials and methods

Study design

The study was a randomized, double-blind intra-individual control study and was carried out between July 2011 and March 2012.

Study population

Patients with stable chronic plaque type psoriasis were recruited from the Dermatology out patient clinic, Ramathibodi hospital, Faculty of Medicine, Mahidol

University. The inclusion criterias were i) chronic stable plaque type psoriasis with lesion distributed symmetrically ii) less than 10 percent of body surface area involvement iii) systemic medication or phototherapy was discontinued for at least 1 month iv) age at least 18 year-old. Patients were excluded if they had at least one of the following criterias i) pregnancy or lactation ii) previous allergic to topical steroids or

chaulmoogra oil iii) concurrent immunosuppressive or immunomodulatory drugs therapy iv) HIV infection v) other underlying inflammatory or infectious skin diseases. All patients had a 2-week washout of any topical treatment for psoriasis prior to receiving the study drugs. During wash out period patients were allowed to apply cream base twice daily. (figure 1)

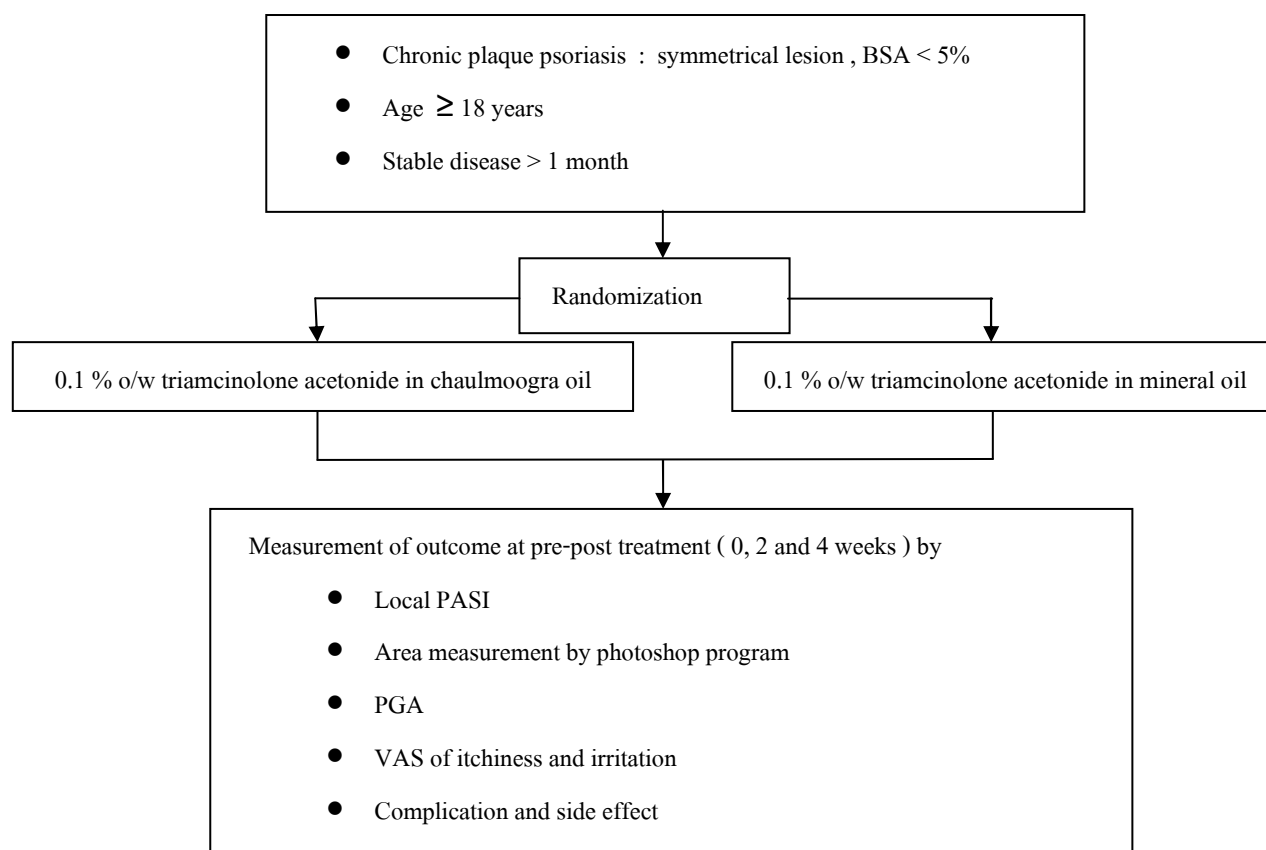


Figure 1 Flow chart of the study protocol

Table1 Demographics data

Mean age (years), SD	50.71, 13.06
Male:Female (number of patients)	12:12
Mean duration of disease (years), min,max	11.94; 1.5,39
Previous treatment(percent)	
Topical treatment	100
Traditional systemic therapy	29.17
Phototherapy	29.17

Table 2 Baseline characteristic of target lesions

	chaulmoogra oil side mean;SD	mineral oil side mean;SD	p-value
Local PASI* (0-12)	5.58;1.21	5.58;1.21	1.0000
Erythema (0-4)	2.04;0.62	2.08;0.65	0.5748
Thickness (0-4)	1.92;0.58	1.92;0.58	1.0000
Scale (0-4)	1.63;0.71	1.58;0.72	0.5748
Area,cm ² ,mean;range	7;0.35,25.20	6.54; 0.29, 25.96	0.5841
PGA [§]	3.75;1.19	3.75;1.22	1.0000

Local PASI* is a sum of erythema (score 0-4), thickness (score 0-4) and scale (score 0-4) of index lesion.

Physician global assessment (PGA)[§] ; 0 to 6 (0: clear, 1: almost clear, 2: mild disease, 3: mild to moderate disease, 4: moderate disease, 5: moderate to severe disease, 6: severe disease)

Assessments

We examined and took photographs of patients at baseline (2 weeks after wash out) and after 2 and 4 weeks of therapy.

Primary outcome of this study were local psoriasis severity index (local PASI), areas of index lesion, physician's global assessment (PGA) and visual analogue scale (VAS) of itchiness and irritation, all outcomes were measured at baseline, weeks 2 and 4.

Local PASI is a sum of erythema (score 0-4), thickness (score 0-4) and scale (score 0-4) of index lesion.

Area of index lesions were measured by adobe photoshop CS3 10 extended version. Each index lesion was measured twice to minimize measurement error.

PGA score ranged from 0 to 6 (0: clear, 1: almost clear, 2: mild disease, 3: mild to moderate disease, 4:

moderate disease, 5: moderate to severe disease, 6: severe disease)

VAS of itchiness and irritation ranged from 0 (minimum) to 10 (maximum).

The study was approved by the ethics committee of Faculty of Medicine Ramathibodi Hospital, Mahidol University (protocol number ID 09-54-27) and all patients gave written informed consent. The study was conducted in accordance with the ICH Guideline for

Good Clinical Practice for the clinical testing of drugs and the Declaration of Helsinki.

Statistical analysis

We used descriptive analysis for qualitative data. Comparison between groups was done by paired *t*-tests for variables with normal distribution and Wilcoxon signed-rank test for variables that did not present a normal distribution. For all tests, statistical significance was established at $p < 0.05$.

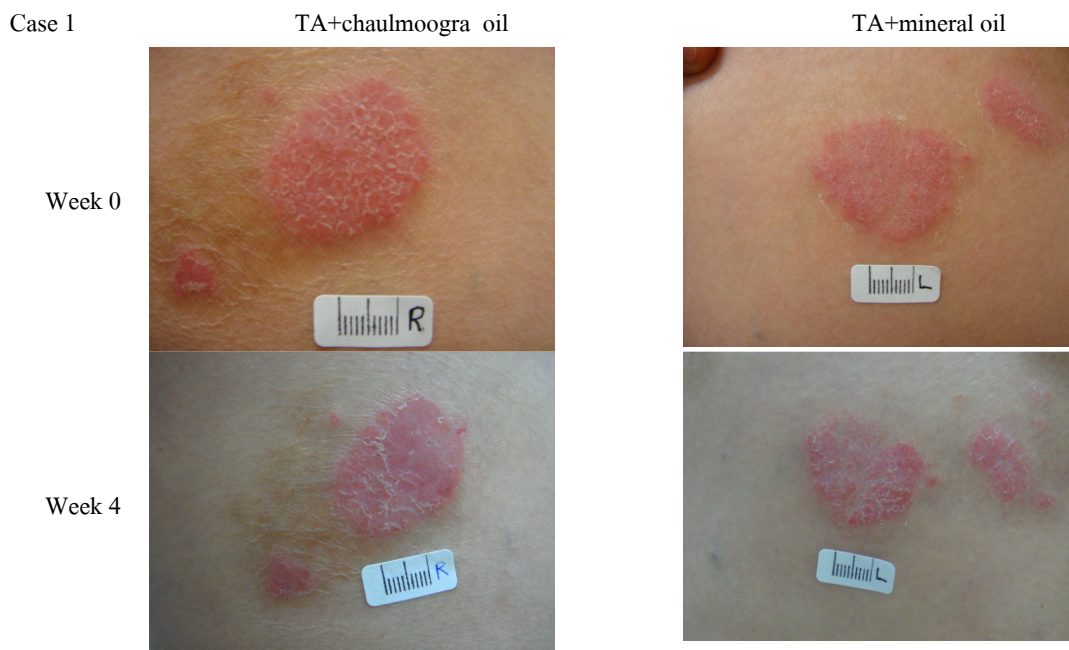


Figure 2 Pre and 4 weeks post treatment

Results

Twenty seven patients were enrolled. Three patients dropped out before completion of the study. Data from twenty four patients were analyzed. Demographics data were presented in table 1. The mean age of patients was 50.71 years (± 13.06). Twelve (fifty percent) were male.

The mean duration of disease was 11.94 years (range 2.5,39). All patients had received topical medications before the study, seven out of twenty-four (29.17 percent) had been treated with systemic medications (7 with methotrexate, 1 with acitretin, and 1 with hydroxylurea), seven patients were previously treated

with phototherapy. There were no significant differences between the treated and the controlled sides in term of local PASI, areas of index lesion, PGA, VAS

of itchiness and irritation at baseline. Baseline characteristic of patients were shown in table 2.

Primary outcome (figure2,3,4)

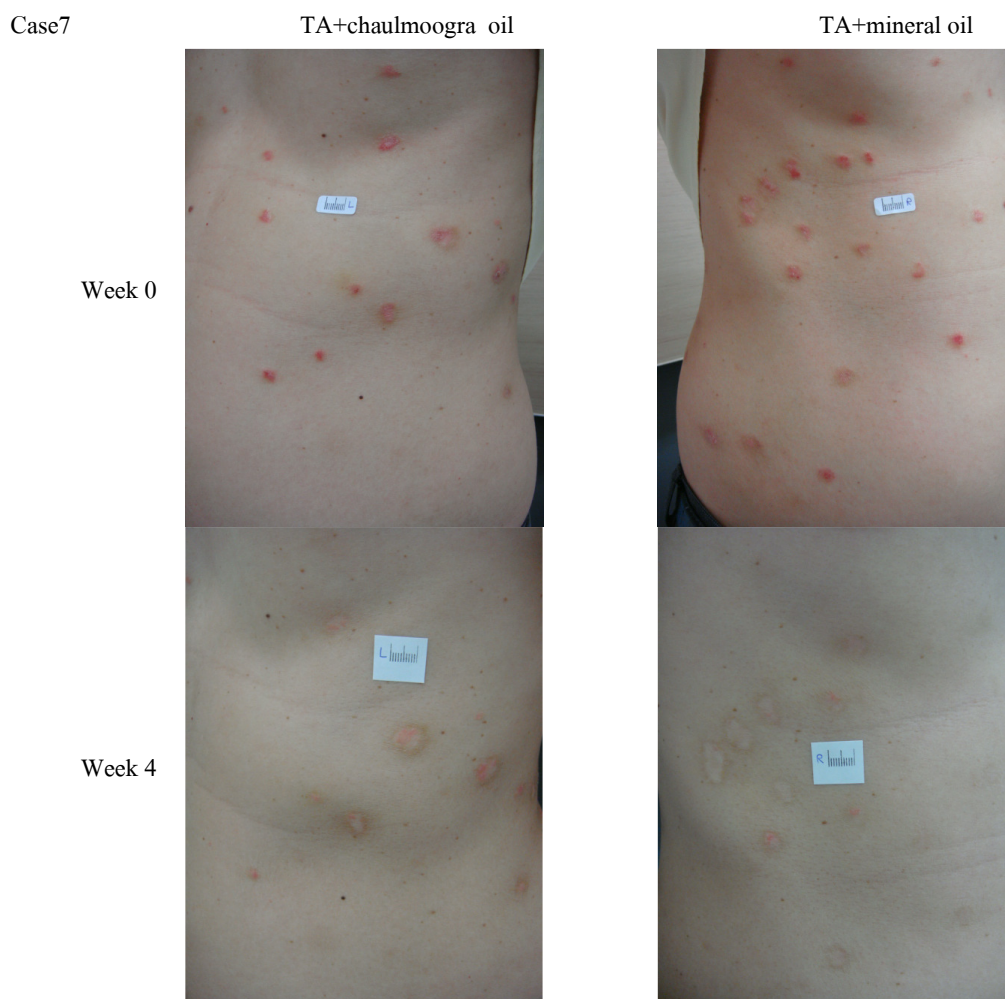


Figure 3 Pre and 4 weeks post treatment

Local PASI

Baseline local PASI in the treated and the controlled sides were equal to 5.58 (± 1.21). At the end of the study local PASI in both sides reduced significantly from baseline to 3.87 ± 1.63 , $p < 0.0001$ and 3.87

± 1.58 , $p = 0.001$, respectively (table 3). However, no significant difference between active and control side ($p = 0.1$, table 4)

Area of index lesions

Area of index lesion in the treated and the controlled sides at baseline were comparable, 7 cm² and 6.54 cm², respectively ($p = 0.5841$, table 4). At the end of the study mean area of index lesion in the treated and the controlled sides were significant difference (figure 5),

8.81 cm² (range 0, 42.89) and 6.20 cm² (range 0, 24.16), respectively ($p = 0.02$, table 4). On the contrary, there was no significant difference of the area from the baseline on both side, $p = 0.18$ and $p = 0.66$, table 3.

Case 14

TA+chaulmoogra oil

TA+mineral oil

Week 0



Week 4



Figure 4 Pre and 4 weeks post treatment

Comparison of the mean difference in area of index lesion at baseline and week 4

$$\frac{= (A_4 - A_0)_1 + (A_4 - A_0)_2 + (A_4 - A_0)_3 + \dots + (A_4 - A_0)_N}{N}$$

A_0 : area of index lesion at baseline

A_4 : area of index lesion at week 4

N : number of patient

If difference in area of index lesion was +: area of index lesion was increased. If difference in area of index lesion was -: area of index lesion was reduced.

The mean difference in area of index lesion in the treated side was 1.98 cm^2 , indicating an increase contradict to the controlled side which the mean different in area of index lesion was -0.24 cm^2 . Compared between both sides the mean difference of area of index lesion in the treated side significantly increased. ($p = 0.0161$, table 4, figure 5)

PGA

Case 10

TA+chaulmoogra oil

TA+mineral oil

Week 0



Week 4



Figure 5 Pre and 4 weeks post treatment

Table 3 Pre and post treatment comparison; local PASI, erythema, thickness, scale, area and physician global assessment (PGA)

		Pre treatment	4 wks post treatment	p- value
Local PASI (0-12)	chaulmoogra oil side mean;SD	5.58;1.21	3.87;1.63	<0.0001
	mineral oil side mean;SD	5.58;1.21	3.87;1.58	0.0001
Erythema (0-4)	chaulmoogra oil side mean;SD	2.04;0.62	1.39;0.78	0.0011
	mineral oil side mean;SD	2.08;0.65	1.43;0.73	0.0019
Thickness (0-4)	chaulmoogra oil side mean;SD	1.92;0.58	1.48;0.59	0.0254
	mineral oil side mean;SD	1.92;0.58	1.48;0.67	0.0254
Scale (0-4)	chaulmoogra oil side mean;SD	1.63;0.71	1.00;0.67	0.0038
	mineral oil side mean;SD	1.58;0.72	0.96;0.64	0.0038
Area (cm ²)	chaulmoogra oil side mean;SD	7;0.35,25.20	8.81; 0, 42.89	0.1831
	mineral oil side mean;SD	6.54; 0.29, 25.96	6.20;0, 24.16	0.6612
PGA (0-6)	chaulmoogra oil side mean;SD	3.75;1.19	3.17;1.34	0.0149
	mineral oil side mean;SD	3.75;1.22	3,1.41	0.0122
VAS of itch/irritation (0-10)	chaulmoogra oil side mean;SD	5.04;0,10	3.30;0,9	0.0326
	mineral oil side mean;SD	5.02;0,10	3.13;0,9	0.0122

Table 4 Active and control side comparison; local PASI, erythema, thickness, scale, area and physician global assessment (PGA)

Physician assessments		chaulmoogra oil side mean;SD	mineral oil side mean;SD	p-value
Local PASI (0-12)	Pre treatment	5.58;1.21	5.58;1.21	1.0000
	2 weeks post Rx	5;1.54	4.68;1.62	0.0312
	4 weeks post Rx	3.87;1.63	3.87;1.58	1.0000
Erythema (0-4)	Pre treatment	2.04;0.62	2.08;0.65	0.5748
	2 weeks post Rx	1.82;0.69	1.77;0.69	0.3287
	4 weeks post Rx	1.39;0.78	1.43;0.73	0.5753
Thickness (0-4)	Pre treatment	1.92;0.58	1.92;0.58	1.0000
	2 weeks post Rx	1.86; 0.35	1.64;0.49	0.0215
	4 weeks post Rx	1.48;0.59	1.48;0.67	1.0000

Physician assessments		chaulmoogra oil side mean;SD	mineral oil side mean;SD	p-value
Scale (0-4)	Pre treatment	1.63;0.71	1.58;0.72	0.5748
	2 weeks post Rx	1.32;0.78	1.27;0.77	0.5758
	4 weeks post Rx	1.00;0.67	0.96;0.64	0.5637
Area (cm ²)	Pre treatment	7;0.35,25.20	6.54; 0.29, 25.96	0.5841
	2 weeks post Rx	9.73; 0.42,37.14	8.49; 0.17, 24.73	0.4342
	4 weeks post Rx	8.81; 0, 42.89	6.20;0, 24.16	0.0211
	Change of area after treatment,cm ²	1.98	-0.24	0.0161
PGA pre treatment		3.75;1.19	3.75;1.22	1.0000
PGA 4 weeks post treatment		3.17;1.34	3,1.41	0.1035

Baseline PGA of the treated and the controlled were 3.75±1.19 and 3.75±1.22, respectively. At week 4, PGA score of treated and control sides were significantly decreased to 3.17±1.34 and 3.0±1.41, respectively. (p= 0.01,table3) There was no significant difference of PGA score of index lesion compared between the treated and the controlled side at week 4. (p= 0.1035, table4)

Patient self-assessment

VAS of itchiness and irritation

VAS of itchiness and irritation in the treated side was significantly reduced from 5.04 (range 0.10) to 3.30 (range 0,9), p=0.0326 and 5.25 (range 0,10) to 3.13 (range 0,9) in the controlled side, p=0.0122. There was no significant difference in the VAS between both sides at week 4.

Patient satisfactory score

Patient satisfactory score were in a good range in both sides; 6.87(±2.1) and 7.30(±1.93). There was no significant difference in the score between both sides at week 4 (p =0.12).

Mild side effects were reported from 4 patients. One patient reported itchiness on both side and another one only on the chaulmoogra side. Three patients experienced mild redness, one on both side another two on active treatment side. All these side effects resolved spontaneously.

Discussion

Herbal remedies gain popularity in both cosmetic and dermatology diseases. Plant derived compounds which have proven efficacy in psoriasis treatment are dithranol (anthralin) from araroba tree bark (Andira araroba), salicylic acid derived from white willow bark (Salix alba) and 8-methoxy psoralen a furocoumarin

from *Ammi majus*⁶. Although, various new herbal medicines have been used for psoriasis very limited numbers were through roughly evaluated by a RCT method⁶⁻⁷. In addition, majority of botanical medication studies were done in a small group of patients without control.

Recently, a randomized double-blind, placebo-controlled study of a topical 10% Oregon grape root (*Mahonia aquifolia*) cream in 200 psoriasis patients confirmed its efficacy and safety⁷. However, RCT studies of some botanical products have demonstrated conflicting results. For example, Aloe vera was one of the botanical agents that conflicting result from 2 RCT studies were observed⁸⁻⁹.

In this study, twenty four psoriasis patients showed improvement of erythema, thickness and scaling of psoriasis lesions on both sides. In contrast, the mean difference of index lesion's areas in the active cream treated side significantly increased compared with the controlled side. This finding was also observed in the first few weeks of treatment with topical calcipotriol or systemic acitretin which are standard treatment of psoriasis worldwide. However, even though mean difference in area of index lesions in the treated side increased but erythema, thickness and scale score were reduced. After combining all parameters, the local PASI score was reduced and the lesions subsided.

We concluded that topical 0.1 percent o/w triamcinolone acetonide in chaulmoogra oil was not superior than 0.1 percent triamcinolone acetonide in

mineral oil after 4 weeks of treatment. However, longer treatment duration such as 8-12 weeks, the lesions may be cleared and the difference of our active cream may be observed. One confounding factor is narrow numerical assessment score which range from 0-4. Almost all targeted lesions if not cleared would range from 1-3, therefore it's unlikely to obtain statistically significant outcome. Another limitation was short period of study and using combination treatment with triamcinolone which is an active drug in psoriasis treatment.

The three main mechanisms of herbal remedies are anti-inflammation, antimicrobial and antioxidant. The mechanism of action of chaulmoogra oil in leprosy was from Hydnocarpic acid, a principle constituent, blocking the coenzymatic activity of biotin or inhibits microbial biotin synthesis³. *Hydnocarpus wightiana* is a tree in the same family which shows high antioxidant activity¹⁰. All these properties rarely come from a single active ingredient but from mixture of several ingredients in that plant. Preparation of herbal remedies by extracting only major active ingredient may, therefore, alter its efficacy. In addition, seasonal change may contribute to variation in efficacy of herbal preparation. At present, we need a scientific experiment that can explain the mechanism of action of chaulmoogra oil in psoriasis.

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References

1. Cottle W. Chaulmoogra Oil in Leprosy. Br Med J. 1879;1(965):968-9.
2. Cottle W. Chaulmoogra-Oil and Gynocardic Acid in the Treatment of Skin-Diseases. Br Med J. 1881;1(1069):999.
3. Jacobsen PL, Levy L. Mechanism by which hydnocarpic acid inhibits mycobacterial multiplication. Antimicrob Agents Chemother. 1973;3:373-9.
4. dos Santos FS, de Souza LP, Siani AC. [Chaulmoogra oil as scientific knowledge: the construction of a treatment for leprosy]. Hist Cienc Saude Manguinhos. 2008;15:29-47.
5. Lima JA, Oliveira AS, de Miranda AL, Rezende CM, Pinto AC. Anti-inflammatory and antinociceptive activities of an acid fraction of the seeds of *Carpotroche brasiliensis* (Raddi) (Flacourtiaceae). Braz J Med Biol Res. 2005;38:1095-103.
6. Reuter J, Merfort I, Schempp CM. Botanicals in dermatology: an evidence-based review. Am J Clin Dermatol. 2010;11:247-67.
7. Bernstein S, Donsky H, Gulliver W, et al. Treatment of mild to moderate psoriasis with Relieva, a *Mahonia aquifolium* extract: a double-blind, placebo-controlled study. Am J Ther 2006; 13 : 121-6
8. Syed TA, Ahmad SA, Holt AH, Ahmad SA, Ahmad SH, Afzal M. Management of psoriasis with Aloe vera extract in a hydrophilic cream: a placebo-controlled, double-blind study. Trop Med Int Health. 1996;1:505-9
9. Paulsen E, Korsholm L, Brandrup F. A double-blind, placebo-controlled study of a commercial Aloe vera gel in the treatment of slight to moderate psoriasis vulgaris. J Eur Acad Dermatol Venereol 2005; 19: 326-31.
10. Reddy SV, Tiwari AK, Kumar US, Rao RJ, Rao JM. Free radical scavenging, enzyme inhibitory constituents from antidiabetic Ayurvedic medicinal plant *Hydnocarpus wightiana* Blume. Phytother Res. 2005 ;19:277-81.