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Effect of *Citrullus lanatus* seed oil on xerosis in leprosy patients

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ABSTRACT

Xerosis in leprosy patients may result from defects in sweat gland function. Red watermelon (*Citrullus lanatus*) seed oil a lot of contains linoleic acid, which can hydrate the skin and reduce trans-epidermal water loss (TEWL). This study aimed to evaluate the effect of *C. lanatus* seed oil administration in leprosy patients with xerosis. It was a clinical study with one group pretest posttest control group design involving 30 leprosy patients with xerosis at the Department of Dermatology and Venereology, Dr. Pirngadi Medan Hospital, the Polyclinic of Dermatology and Venerology, Universitas Sumatera Utara Hospital and the Department of Dermatology and Venerology, H. Adam Malik General Hospital, Medan, Indonesia. Patients were asked to topically administration of 2 mL *C. lanatus* seed oil to the right and left legs for two times daily for 4 weeks. Specified symptom sum score (SRRC) and skin capacitance (SCap) were then measured before the intervention at the first visit (week 0), week 2, and week 4. A significantly different on SRRC and SCap of the leprosy patients was observed on the 2nd and 4th week after *C. lanatus* oil administration compared to week 0 ($p<0.001$). No side effects of erythema, blistering, and burning were observed. However, a mild degree itching was observed in 2 (6.7%) patients. Majority of leprosy patients feel good satisfaction (83.4%), followed by a moderate (13.3%) and a low satisfaction (3.3%). In conclusion, topically administration of red watermelon (*C. lanatus*) seed oil can reduce the xerosis degree in leprosy patients as indicated by the decrease of SRRC and the increase of SCap. The seed oil is well tolerated and gives a good satisfaction on the patients.

ABSTRAK

Xerosis pada pasien kusta kemungkinan terjadi akibat gangguan fungsi kelenjar keringat. Minyak biji semangka merah (*C. lanatus*) mengandung banyk asam linoleat yang dapat mempertahan kulit lembap dan menurunkan kehilangan air trans epidermal. Penelitian ini bertujuan mengkaji pengaruh pemberian minyak biji semangka merah (*C. lanatus*) terhadap xerosis pada pasien kusta. Penelitian ini merupakan penelitian klinik menggunakan rancangan *one group pretest posttest control group* yang melibatkan 30 pasien kusta dengan xerosis dari Departemen Dermatologi dan Venereologi, Rumah Sakit Dr. Pirngadi Medan, Poliklinik Dermatologi dan Venerologi, Rumah Sakit Universitas Sumatera Utara dan Departemen Dermatologi dan Venerologi, Rumah Sakit Umum Pusat H. Adam Malik, Medan, Indonesia. Pasien diminta memberikan secara topikal 2 mL minyak biji semangka merah (*C. lanatus*) pada tungkai bawah kanan dan kiri sebanyak 2 kali sehari selama 4 minggu. *Specified symptom sum score* (SRRC) dan *skin capacitance* (SCap) kemudian diukur sebelum perlakuan pada kunjungan pertama (minggu 0), minggu ke 2 dan ke 4. Perbedaan nyata pada SRRC dan SCap pasien kusta teramati pada minggu ke 2 dan ke 4 setelah pemberian minyak biji semangka merah (*C. lanatus*) dibandingkan dengan minggu ke 0 ($p<0.001$). Tidak dijumpai efek samping berupa eritema, lepuh dan rasa terbakar. Namun demikian rasa gatal derajat sedang dijumpai pada 2 pasien. Sebagian besar pasien merasakan tingkat kepuasan yang baik (83,4%), diikuti sedang (13.3%), dan rendah (3,3%). Dapat disimpulkan, pemberian secara topikal minyak biji semangka merah (*C. lanatus*) dapat menurunkan derajat xerosis pasien kusta sebagaimana ditunjukkan dengan penurunan SRRC dan kenaikan SCap. Minyak biji ini ditoleris dengan baik dan memberikan kepuasan yang baik pada penderita.

Keywords:
C. lanatus;
leprosy;
watermelon seed oil;
xerosis;
side effects

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INTRODUCTION

Leprosy, caused by *Mycobacterium leprae*, has been known for a long time, even years before Christ. Indonesia is the third in the world after India and Brazil regarding leprosy patients. The prevalence rate of leprosy in Indonesia in 2017 was 0.70 cases/10,000 population with a new case finding rate of 6.08 cases per 100,000 population.[1]

Xerosis is a common skin disorder in the general population. This condition has clinical characteristics of rough skin, scaly, and sometimes itchy. In leprosy lesions, there is a decrease in epidermal proliferative activity, and a reduction of sphingolipids in stratum corneum (SC), which can further change epidermal function.[2] The mechanism contributing to decreased SC hydration is defect in sweat gland function and decrease active osmotic components that contribute to the development of xerosis. The sphingolipid content in leprosy patients with and without lesions is lower than that in normal people. Lipid changes in SC, especially sphingolipids, are caused by cornification and loss of sweat gland function due to nerve damage in leprosy.[3] Studies found that patients with xerosis cutis showed higher psychosocial burden than participants without xerosis cutis which could lead to reduced quality of life of the patients.[4]

Red watermelon (*C. lanatus*) seed oil has been used to treat skin disease since ancient Egyptian times. Komane *et al*.[5] reported that *C. lanatus* seed oil contains linoleic acid as the primary fatty acid that can hydrate and soften the skin and reduce transepidermal water loss (TEWL). Visual moisture efficacy examination showed that *C. lanatus* seed oil increased the skin's water content, thereby improving skin barrier function. This oil can also increase the natural moisturizing factor because it has a low viscosity and low molecular weight to retain moisture in the skin.[5] This study aimed to investigate the effect of red watermelon (*C. lanatus*) seed oil on skin capacitance in leprosy patients with xerosis.

MATERIALS AND METHODS

Study design

It was a clinical study with pre experimental design using one group pretest and posttest design. The pre-test was conducted before applying the red watermelon (*C. lanatus*) seed oil and the post-test was performed after administration of the red watermelon (*C. lanatus*) seed oil for 2 and 4 wk.

Extraction preparation

The extract of the red watermelon seed oil was produced by the Association of Indonesian Traditional Herb Medicine (ASPETRI/*Asosiasi Pengobat Tradisonal Ramuan Indonesia*).

Subjects

Leprosy patients with xerosis from the Department of Dermatology and Venereology, Dr. Pirngadi Medan Hospital, the Polyclinic of Dermatology and Venerology, Universitas Sumatera Utara Hospital and the Department of Dermatology and Venerology, H. Adam Malik General Hospital, Medan, Indonesia were involved in this study. The diagnosis of leprosy was performed by a dermatologist based on anamnesis, physical and microscopic examinations. Patients who were hypersensitive to *C. lanatus* seed oil, who had previously other skin conditions (such as psoriasis, ichthyosis, or atopic dermatitis), who had comorbidities (such as chronic kidney disease, diabetes, chronic liver disease, hypothyroid, malignancy, AIDS/HIV), who had already used other topical preparation on the skin two weeks before, and who had to consume hormonal

therapy, retinoid, antihistamine, antidiuretic, and antihypertension treatment for the last one month were all excluded from the study.

The application of watermelon seed oil (*C. lanatus*)

Red watermelon (*C. lanatus*) seed oil at dose of approximately 0.1 mL was administered to cover an area of 5.7 cm x 3.7 cm of the right and left legs. The seed oil applied topically by using fingers on the xerotic area, twice daily immediately after the morning bath (08.00 AM) and in the afternoon (04.00 PM). The subjects were asked to apply the seed oil for four wk. The evaluation of specified symptom sum score (SRRC) and skin capacitance (SCap) was conducted at the first visit (week 0), week-2, and week-4.

The subjective examination of xerosis using SRRC

Xerosis is a dry skin condition of the patient that consists of dull, rough, fissured, and scaly skin appearance. Clinical evaluation of xerosis on both lower limbs of the patients was performed visually and tactilely to calculate SRRC. The score ranges from 0 to 16.

The objective examination of xerosis using corneometer

SCap is the ability of the stratum corneum to bind water, and its value describes the water content in the stratum corneum. The CM825 corneometer (C&K, Courage-Khazaka, Köln, J Germany) was used to measure skin capacity. The measurements were conducted three times on mid-point of both lower limbs, and then the mean value was taken. The average result of three measurements was expressed in arbitrary units (AU) which was divided into three degrees of dryness i.e. <30AU (very dry), 30-45AU (dry), >45AU (normal).

The measurement technique of corneometer

The capacitance of a dielectric medium, in this case, the stratum corneum, the top layer of the skin, was used to make the measurement. As hydration increases, its dielectric properties change. The dielectric constant of water is higher than that of most other substances (mostly 7). An electric field with the alternating attraction between the tracks created by gold tracks on top of the probe head, separated from the skin by a glass lamina. One track accumulates electrons in excess (minus charge), whereas the other accumulates electrons in deficit (plus charge). When applied to the skin, the scattered field penetrates the very first layer. The Corneometer® CM825 detects the change in dielectric constant caused by the capacitance of a precision capacitor changing owing to skin surface moisture. The device can detect even the tiniest variations in hydration levels.[6]

The evaluation of side effect

Side effects are unwanted events during the use of the substance being tested in the experimental study. They were assessed and documented based on anamnesis and dermatological examination to seek any erythema, blisters, burning, and itching sensation during the study period. The side effects that appeared were classified into 0 (none), 1 (mild), 2 (moderate), and 3 (severe). The evaluation of side effects was conducted after the 2nd and 4th weeks of use.

The evaluation of patient satisfactory

Patient satisfaction regarding their xerotic skin changes after using the red watermelon seed oil was asked after the end of the study. Patients were asked to classify their level of satisfaction on

a scale of 0 (dissatisfied), 1 (slightly), 2 (moderate), 3 (good), 4 (very satisfied).

Ethic committee

This clinical trial did not conflict with any human values and the research code of ethics. This study has been approved by the Research Ethics Committee, Universitas Sumatra Utara, Medan (reff. number 323/KEP/USU/2021 dated 23 April 2021).

Statistical analysis

Shapiro Wilk test was performed to evaluate the normality of the data. The data was normally distributed if $p > 0.05$. Repeated analysis of variance or the Friedman alternative test was applied to evaluate the effect of red watermelon (*C. lanatus*) seed oil on the degree of xerosis based on SRRC or on SCap in leprosy patients at the first visit (week 0), week 2, and week 4. Wilcoxon post hoc test was applied to evaluate the effect of red watermelon (*C. lanatus*) seed oil on the degree of xerosis based on SRRC or on SCap in leprosy patients at each measurement time.

RESULTS

This study involved 30 leprosy patients with xerosis with mean age of 36 yo and males majority (70%). All patients underwent anamnesis and physical examination to establish the diagnosis of leprosy with xerosis. All patients could finish their involvement in this study without drop out.

Effect of red watermelon (*C. lanatus*) seed oil on SRRC

The effect of red watermelon (*C. lanatus*) seed oil topically administration to the skin of the right and left legs on the degree of xerosis based on SRRC was observed in three different measurement times (TABLE 1). On the week 0, the median degree of xerosis was 10.75 (min-max: 4.00-16.00). After two weeks of administration, there was a decrease in the degree of xerosis to 8.5 (4.00-16.00). On the week 4, the median degree of xerosis decreased to 6.75 (2.00-15.00). A significantly decrease on SRRC of xerosis in leprosy patients after watermelon (*C. lanatus*) seed oil topically administration was observed ($p<0.001$).

TABLE 1. Effect of red watermelon (*C. lanatus*) seed oil administration on SRRC in leprosy patients

Time of assessment	n	Median	Min-Max	p[a]
Week-0	30	10.75	4.00-16.00	
Week-2	30	8.50[b,c]	4.00-16.00	<0.001
Week-4	30	6.75[d]	2.00-15.00	

[a]Friedman test was applied

The statistical analysis of SRRC was continued by using the post-hoc Wilcoxon test, a significantly different of SRRC in leprosy patients between week 0 and week 2, week 0 and week 4 as well as week 2 and week 4 were observed ($p<0.001$).

Effect of red watermelon (*C. lanatus*) seed oil on SCap in leprosy patients

The effect of red watermelon (*C. lanatus*) seed oil topically administration on SCap of the right and left legs based was observed in three different

measurement times (TABLE 2). On the week 0, the median SCap was 36.25AU (19.00-42.250AU). After two weeks of red watermelon (*C. lanatus*) seed oil topically administration, an increase in SCap to 40.67AU (22.50 – 44.85 AU) was observed. On week 4, the median SCap increased to 43.83AU (26.65-50.15AU). A significantly increase on SCap of xerosis in leprosy patients after watermelon (*C. lanatus*) seed oil topically administration was observed ($p<0.001$). The hydration status of the right lower leg of the leprosy patients was still classified as dry (30-45 AU).

The statistical analysis of SCap was continued by using the post-hoc Wilcoxon test, a significantly different of SCap in leprosy patients between week 0 and week 2, week 0 and week 4 as well as week 2 and week 4 were observed ($p<0.001$).

Side effects of red watermelon (*C. lanatus*) seed oil after topically administration

No side effect related to erythema, blistering, and burning was observed after red watermelon (*C. lanatus*) seed oil topically administration. Meanwhile, the incidence of itchy were found in 2 patients (6.7%) as shown in TABLE 3.

TABLE 2. The effect of red watermelon seed oil (*C. lanatus*) administration on SCap) in leprosy patients

Time of assessment	n	Median	Min-Max	p[a]
Week-0	30	36.25	19.00-42.50	
Week-2	30	40.67[b,c]	22.50-44.85	<0.001
Week-4	30	43.83[d]	22.65-50.15	

[a]Friedman test was applied

TABLE 3. Side effects of red watermelon (*C. lanatus*) seed oil after topically administration in leprosy patients

Side effects	None n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
Erythema	30 (100)	0 (0)	0 (0)	0 (0)
Blister	30 (100)	0 (0)	0 (0)	0 (0)
Burning	30 (100)	0 (0)	0 (0)	0 (0)
Itching	28 (93.3)	2 (6.7)	0 (0)	0 (0)

Patient's satisfaction after red watermelon (*C. lanatus*) seed oil topically administration

All subjects were asked to give their opinion regarding their satisfaction related to changes on their skin. The majority of patients (25 or 83.4%) stated that they had a good level of satisfaction, followed by a moderate level of satisfaction in 4 (13.3%) and low level of satisfaction in 1 (3.3%) (FIGURE 1).

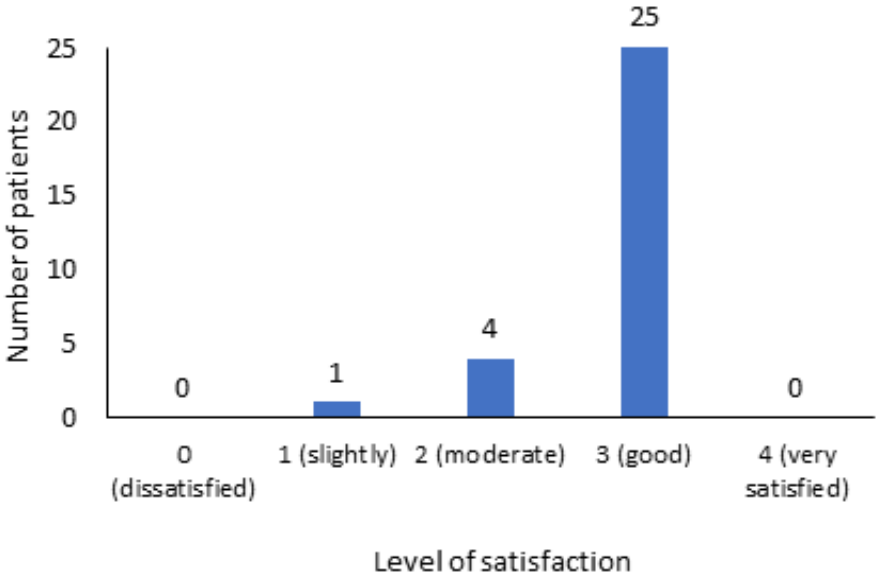

FIGURE 1. The level of leprosy patients' satisfaction after red watermelon (*C. lanatus*) seed oil topically administration

DISCUSSION

This study was dominated by male leprosy patients (70%). Oliveira and Romanelli reported that the incidence of leprosy is higher in men than women in Brazil.[7] In most Asian countries, leprosy is more common in men than women, while in Africa, the number of women affected by leprosy is more than men. However, men are diagnosed with multibacillary (MB) more often than women.[8] This condition could be affected by social, cultural, and educational factors. In certain cultures, women's access to health services is minimal. The higher incidence of leprosy in men could also be associated with the fact that man had greater mobility and chance of contact with leprosy patients. In addition, men are also more active in seeking treatment and get diagnosed.[9]

Dry skin, or xerosis, has the potential to become a more severe condition due to its tendency to break and the possibility of inflammation.[10] In leprosy, chronic fissures in dry skin could be a significant problem. This study showed that red watermelon (*C. lanatus*) seed oil is effective in treating xerosis in leprosy proved by improvement in xerosis level measured by SRRC method and corneometer. It is in line with study conducted by Ekayanti *et al.*[11] who found that moisturizing cream preparation containing watermelon (*C. lanatus*) water extract can maintain skin hydration as assessed using AUC value. Increasing the concentration of the extract in the preparation decreases the total AUC value.[11]

Komane *et al.*[5] also investigated the efficacy and safety of *C. lanatus* seed extract on the skin. The participants were asked to wash the calf area 2-4 times a day using a soap bar and apply moisturizer of 0.1 mL twice daily at five random locations tested (with an area of 5.7 cm x 3.7 cm) in a circular motion for seven days straight. Skin examinations were conducted on day 1, 2, 3, 4, 5, 8, 10, and 12. It was found that all products caused a significant decline in dryness from day one compared to day 12 (mean value of 2.4 vs 1.6, respectively).[5] These findings confirm the ability of *C. lanatus* seed extract oil to enrich the water content in the skin, which allows for an increase in

the skin barrier function by increasing the natural moisture factor due to its low viscosity and low molecular weight.[12,13]

Yusuf *et al.*,[14] also assessed the efficacy of oil extracts as a therapy for dryness in leprosy patients using virgin coconut oil. This study found a significant effect of virgin coconut oil on the skin of leprosy patients based on the overall dry skin score (ODS). This moisturizing effect of coconut oil was obtained from the high content of lauric acid. Komane *et al.*[5] reported that red watermelon seed extract oil also contains many acids that help increase skin moisture and prevent TEWL. One of the highest is the linoleic acid content of 41.5%.

In cosmetics and dermatology, skin moisture is an essential parameter. It has led to the development of tools for measuring skin moisture. Corneometer is one of the most commonly used tools to measure skin moisture. This technique determines the skin capacitance due to its behavior as a dielectric medium which can detect water content as deep as 10–20 μm in the stratum corneum layer. Although this tool assesses the skin's water content, it can also indirectly evaluate the skin's barrier function. Higher values indicate higher moisture and better skin barrier function.[15]

A statistically significant difference effect of red watermelon (*C. lanatus*) seed oil on SCap based on the corneometer in leprosy patients during eight weeks administration. This result is supported by Komane *et al.*,[5] who reported that red watermelon (*C. lanatus*) seed oil extract reduced skin dryness significantly between the first and the 12th day (16.44 vs 18.74, respectively). The effect of increasing the moisture content is due to the presence of stearic acid (6.3%), which can prevent TEWL.[5]

No side effects related to erythema, blistering, and burning were observed among 30 leprosy patients in this study. However, 2 patients had experienced a mild degree of itching. Loden *et al.*[16] reported that a common side effect of using moisturizers is a subjective sensation of burning. Humectants such as lactic acid and urea could also cause a burning sensation. Piraccini *et al.*[17] reported that the allergic contact dermatitis, burning sensation, and itching could emerge from using urea. Purnamawati *et al.*,[18] also reported that petrolatum causes folliculitis. This study showed that red watermelon (*C. lanatus*) seed oil is considered safe and only caused a few side effects.

The itching side effect can be attributed to the high linoleic acid content in red watermelon (*C. lanatus*) seed oil. Rahman *et al.*[19] reported that linoleic acid has the potential to scavenge free radicals that can trigger an anti-inflammatory effect on the skin and reduce irritation.[19] Zielińska *et al.*[20] found that oils with a high linoleic acid content are considered excellent skin treatments. In addition, Lima *et al.*[12] also reported that linoleic acid has properties that can trigger emollient substances.

All subjects were asked to provide their opinion on satisfaction related to their skin changes. The majority of patients (83.4%) stated that they had a good level of satisfaction, followed by a moderate level of satisfaction of 13.3% and a low level of satisfaction of 3.3%. This result is in line with conducted by Dewi *et al.*[21] concerning the effect of pumpkin (*Cucurbita moschata*) seed extract on xerosis in geriatrics. It was reported that participants claimed to be satisfied with a good satisfaction level of 85.7%; a moderate level of 11.4% and a mildt level of 2.8%. This showed that the use of plant seed extract oil generally has a good satisfaction level.

CONCLUSION

Red watermelon (*C. lanatus*) seed oil can improve xerosis degree in leprosy patients as indicated by the decrease in the degree of xerosis measured

subjectively by SRRC and objectively by the SCap. The topically administration of red watermelon (*C. lanatus*) seed may cause mild temporary itching. However, majority of leprosy patients feel good satisfaction.

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