World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:10, No:12, 2016

An Open-Label Pilot Study of Efficacy and Safety of 2% *Curcuma aeruginosa* Roxb. Extract Cream in the Treatment of Mild to Moderate Facial Seborrheic Dermatitis

Kulaya Wimolwat, Panlop Chakravitthamrong, Neti Waranuch

International Science Index, Pharmacological and Pharmaceutical Sciences Vol:10, No:12, 2016 waset.org/Publication/10005869

***Abstract*—**Background: Seborrheic dermatitis is a common chronic skin condition affecting the face, scalp, chest, and trunk. The cause of seborrheic dermatitis is still unknown. Sebum production, lipid composition, hormone levels, and *Malassezia* species have been suggested as important factors in the development of seborrheic dermatitis. *Curcuma aeruginosa* Roxb. extract-containing cream with anti-inflammatory and anti-androgenic properties may be beneficial for treating mild to moderate facial seborrheic dermatitis. Objectives: We evaluated the efficacy and safety of 2% *C. aeruginosa* Roxb. extract-containing cream in the treatment of mild to moderate seborrheic dermatitis. Methods: This was a prospective, open-label, and non-comparative study. Ten adult patients clinically diagnosed with mild to moderate seborrheic dermatitis were enrolled in a four-week study. The 2% *C. aeruginosa* Roxb. cream was applied twice daily to a lesional area on the face for four weeks. The Scoring Index (SI) ranking system on days 14 and 28 was compared with that at baseline to determine the efficacy of treatment. The adverse events (burning sensation and erythema) were evaluated on days 14 and 28 to determine the safety of the treatment. Results: Significant improvement was observed in the reduction of the mean SI at day 14 (2.9) and 28 (1.4) compared to that at baseline (4.9). An adverse reaction was observed on day 14 (mild erythema 20% and mild burning sensation 10%) and was resolved by the end of the study. Conclusion: This open-label pilot study has shown that there was a significant improvement in the severity in these seborrheic patients and most reported they were satisfied with it. Reported adverse events were all mild.

***Keywords*—**Anti-androgenic, antifungals, anti-inflammatory, *Curcuma aeruginosa*, seborrheic dermatitis, efficacy, safety.

I. Introduction

SEBORRHEIC dermatitis is a common chronic inflammatory dermatologic condition. The characteristic symptoms are erythema, scaling, and pruritus. The condition usually appears on areas of the body with a large density of sebaceous glands, such as the face, scalp, chest, back, axilla, and groin [1]. Its prevalence is 1–3% in the general population and 34–83% in immunocompromised individuals [2].

K. W. is with the Chulabhorn International College of Medicine, Thammasat University, Pathum thani, Thailand (phone: +66(0)25644440; fax: +66(0)29869213; e-mail: kulayawimolwat@ hotmail.com).

P. C. was with Chulabhorn International College of Medicine, Thammasat University, Pathum thani, Thailand (phone: +66(0)25644440; fax: +66(0)29869213; e-mail: panlop078@ yahoo.com).

N. W. is with the Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok, Thailand (e-mail: netiw@nu.ac.th).

The cause of seborrheic dermatitis remains unknown. Hormone levels, sebum production, lipid composition on the skin surface, *Malassezia* species, and patient predisposition to immune or inflammatory reactions have been suggested as important factors in the development of seborrheic dermatitis [3]-[5].

Effective therapies for seborrheic dermatitis include corticosteroids (1% hydrocortisone) [6], [7], antifungals (2% ketoconazole cream, 1% cyclopiroxolamine cream, 1% terbinafine cream) [6], [8], [9], and keratolytic agents (selenium sulfide, tar shampoo) [10].

Curcuma aeruginosa Roxb. (Zingiberaceae) is a native tropical plant of the Southeast Asia, including Myanmar, Cambodia, Vietnam, Malaysia, Indonesia and Thailand. This plant is commonly known as Waan-Ma-Haa-Mek (Thai), Mahamek (Hindi), and "pink and blue ginger" (English). In the present study, the anti-inflammatory actions of this plant were investigated in experimental animals. Germacrone, the most active component, showed possible anti-inflammatory activity [11] and anti-androgenic activity [12], [13].

There are many reports about various biological activities of *Curcuma aeruginosa* such as anti-microbial activities [14], [15], anti HIV [16], anti-oxidation activity [17], platelet activating factor inhibition [18], inhibition of nitric oxide production [19], anti-inflammatory [20], [21], anti-androgen [12], [13], uterine relaxation [22], and hair growth promoter [13].

Regarding the causes of seborrheic dermatitis, particularly inflammation and androgenic levels, the pharmacological effect of *C. aeruginosa* Roxb. extract may improve clinical outcomes in seborrheic dermatitis patients and prevent complications related to the long-term use of steroids. Therefore, more novel selective anti-androgenic compounds are needed, and natural products may fulfill this requirement. In this open-pilot study, the efficacy and safety of 2% Curcuma aeruginasa Roxb. cream was investigated in the treatment of seborrheic dermatitis.

II. Methods

A. Study Protocol

This was a prospective, open-label, non-comparative study. This study was approved by the ethics committee of the Thammasat University. All candidates were supplied with

International Science Index, Pharmacological and Pharmaceutical Sciences Vol:10, No:12, 2016 waset.org/Publication/10005869

detailed information regarding the aims of the study and informed consent was provided by each patient. A pilot study was conducted involving 10 subjects diagnosed with mild to moderate seborrheic dermatitis. Each patient received 2% *C. aeruginosa* Roxb. extract-containing cream applied on lesional areas of the face twice daily. Adverse reactions such as burning, irritation, and erythema were assessed on days 14 and 28.

B. Patient Selection

Inclusion criteria included that patients be aged ≥18 years with a 14-day washout period of topical or systemic medications and clinically diagnosed with mild (Scoring Index, SI 0–4) or moderate (SI 5–8) seborrheic dermatitis on the face.

Exclusion criteria included any concomitant dermatitis (acne, rosacea, contact dermatitis) on the face, suspected hypersensitivity to any constituent of study medication, and any woman who was pregnant, breast-feeding, or planning on becoming pregnant during the study period.

C. Assessments

To determine the severity of seborrheic dermatitis, the SI ranking system was used as described by Koca et al. [8]. According to this system, erythema, scaling, pruritus, and irritation of each area was ranked from 0–3: none = 0, mild = 1, moderate = 2, severe = 3. The sum of these values was regarded as an SD rank based on three ranges: 0–4 (mild), 5–8 (moderate), and 9–12 (severe). SI was assessed by dermatologist at baseline and on days 14 and 28. Compliance was monitored by recording the frequency of application of study medication and the amount of medication used.

Adverse reactions, such as erythema and burning sensation (grading none, mild, moderate, and severe), were evaluated on days 14 and 28 to determine safety.

Patient satisfaction with the cream was also evaluated at the end of the treatment and was categorized as no-change, mild, moderate, and good.

D. Safety and Tolerability

All adverse events (erythema, burning, irritation) reported by patients or observed by investigators were recorded.

E. Statistical Methods

Statistical analysis was performed using STATA version 14 (StataCorp, College Station, TX, USA). Descriptive statistical analysis was used to evaluate safety and patient satisfaction. Categorical data were reported as percentages. Continuous data were reported as the mean and SD. Kruskal-Wallis and multi-level regression analysis were used to compare scores on days 0, 14, and 28 of follow-up. A P-value of < 0.05 was considered significant.

III. Results

A. Patient Population

A total of 10 patients with mild to moderate seborrheic dermatitis were enrolled in this study. The mean age of subjects was 44.8 ± 14.5 years. Most common age group is between 30 years to 49 years. Sixty percent of all subjects were men. Baseline demographics showing underlying diseases (30% hypertension, 20% diabetes, and 10% dyslipidemia), current medication (30% antihypertensives, 20% antidiabetics, and 10% anticholesterolemics), lesional area of the disease (10% hairlines, 10% glabella, 70% nasolabial folds, and 10% mixed areas) and mean SI was 4.9.

TABLE I
BASELINE DEMOGRAPHICS OF SEBORRHEIC DERMATITIS PATIENTS

Characteristic	10 seborrheic dermatitis patients, n (%)
Gender	
Male	4 (40.0)
Female	6 (60.0)
Age in years, mean(SD)	44.8 (14.5)
Age group, year	
18-29	1(10.0)
30-49	6(60.0)
50-64	1(10.0)
More than 65	2(20.0)
Underlying disease	
Hypertension	3 (30.0)
Diabetes mellitus	2 (20.0)
Allergy	0 (0)
Dyslipidemia	1 (10.0)
Current medication	
Antihypertensives	3 (30.0)
Antidiabetics	2 (20.0)
Anticholesterolemics	1 (10.0)
Area of lesion	
Hair line	1(10.0)
Glabella	1(10.0)
Nasolabial	7(70.0)
Nasolabial and glabella	1(10.0)
Scoring index, mean(SD)	4.9 (1.1)
Severity	
Mild	2 (20.0)
Moderate	8 (80.0)

SD = standard deviation

B. Treatment Efficacy

A statistically significance with p value of 0.007 was observed in the mean SI between baseline and days 14 and 28 after treatment. The mean SI values were 4.9, 2.9, and 1.4 on days 0, 14, and 28 after treatment, respectively, (Table II and Fig. 1). This result was the same as that of the multi-level regression analysis of mean SI on days 14 and 28 after treatment and was significantly reduced compared to day 0 ($p = 0.0004$) with values of 2.2 and 3.1, respectively.

The clinical appearances of the patients with seborrheic dermatitis at baseline, days 14, and 28 after treatment with 2% *C. aeruginosa* Roxb. extract-containing cream were demonstrated in Figs. 2-5.

TABLE II
SI BEFORE AND AFTER TREATMENT

Day	Scoring index	p-value
Beginning day, mean(SD)	4.9(1.1)	
14th day, median(IQR)	2.9(2-5)	0.0007
28th day, median(IQR)	1.4(0-2)	

IQR=interquartile range

International Science Index, Pharmacological and Pharmaceutical Sciences Vol:10, No:12, 2016 waset.org/Publication/10005869

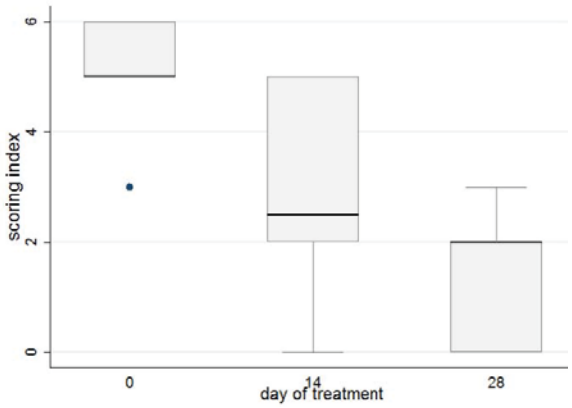


Fig. 1 Changes of scoring index from baseline to days 14 and 28

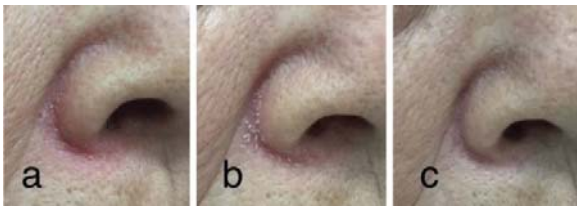


Fig. 2 Clinical appearance of the patient with seborrheic dermatitis at base line (a), days 14 (b), and 28 (c) after treatment with 2% *C. aeruginosa* Roxb. extract-containing cream

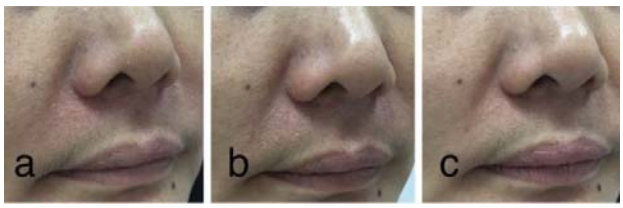


Fig. 3 Clinical appearance of the patient with seborrheic dermatitis at base line (a), days 14 (b), and 28 (c) after treatment with 2% *C. aeruginosa* Roxb. extract-containing cream



Fig. 4 Clinical appearance of the patient with seborrheic dermatitis at base line (a), days 14 (b), and 28 (c) after treatment with 2% *C. aeruginosa* Roxb. extract-containing cream

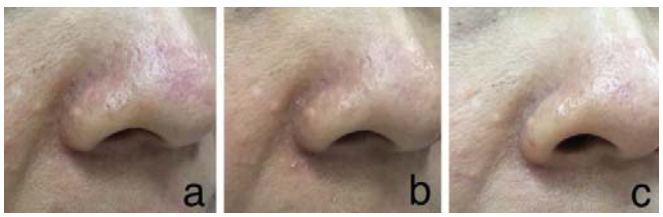


Fig. 5 Clinical appearance of the patient with seborrheic dermatitis at base line (a), days 14 (b), and 28 (c) after treatment with 2% *C. aeruginosa* Roxb. extract-containing cream

C. Safety and Patient Satisfaction

In this pilot study, some subjects experienced adverse reactions, such as mild erythema in 20% and mild burning sensation in 10% of subjects. All adverse reactions resolved spontaneously by day 28. Nine subjects continued the cream until the end of the study. One patient discontinued the study because of other medical conditions.

Most patients were satisfied with the treatment. The frequency distribution of patient satisfaction after using the 2% *C. aeruginosa* Roxb. extract-containing cream after 28 days of treatment is shown in Table IV.

TABLE III
PATIENTS FREQUENCY DISTRIBUTION ADVERSE REACTION AFTER TREATMENT ON 14TH AND 28TH DAYS OF TREATMENT

Adverse reaction	Seborrheic dermatitis patients n(%)	
	14th day N=10	28th day N=9
Erythema		
None	8(80.0)	9(100)
Mild	2(20.0)	0
Moderate	0	0
Severe	0	0
Burning sensation		
None	9(90.0)	9(100)
Mild	1(10.0)	0
Moderate	0	0
Severe	0	0

TABLE IV
PATIENTS FREQUENCY DISTRIBUTION CONSIDERING SATISFACTION AFTER TREATMENT ON 28TH DAYS OF TREATMENT

Satisfaction	9 seborrheic dermatitis patients n(%)
No change	0
Mild	1 (10.0)
Moderate	1 (10.0)
Good	7(70.0)

IV. DISCUSSION

This open-label pilot study showed statistically significant improvement in the reduction of the mean SI on day 28 of treatment. Thus, 2% *C. aeruginosa* Roxb. extract-containing cream is an effective topical agent for treating mild to moderate facial seborrheic dermatitis.

It is difficult to determine which compound in the extract was responsible for the improvement in seborrheic dermatitis in this study. The compound may have anti-inflammatory and anti-androgenic effects.

Although there is no clear correlation between sebum levels and seborrheic dermatitis development, the distribution of lesions on sites rich in sebaceous glands supports the idea that seborrhea is a probable predisposing factor. Suppression of sebum production by anti-andrgenic activity may in turn lead to an inhibition in the growth of the lipophilic organism *Malassezia*, which plays an important role in the pathogenesis of seborrheic dermatitis. In addition, this anti-inflammatory property may be a contributing factor to its efficacy in seborrheic dermatitis. This new natural product can be beneficial to patients, because it does not pose the same long-term risks associated with corticosteroid use.

International Science Index, Pharmacological and Pharmaceutical Sciences Vol:10, No:12, 2016 waset.org/Publication/10005869

Further studies are necessary to evaluate the efficacy of *C. aeruginosa* Roxb. extract-containing cream in comparison with standard treatments, corticosteroids, and antifungals.

V. Conclusion

The results of this pilot study support the efficacy and safety of 2% *C. aeruginosa Roxb*. cream in the treatment of mild to moderate facial seborrheic dermatitis.

Reported adverse events at day 14 after treatment were mild erythema and mild burning sensation. These results suggest that the *C. aeruginosa* Roxb. extract-containing cream is a promising new nonsteroidal therapy for patients with seborrheic dermatitis, and further investigation into its efficacy and safety, as monotherapy or in combination with other therapies for patients with seborrheic dermatitis, is warranted.

Acknowledgment

The study was supported by the faculty of pharmaceutical sciences, Naresuan University who provided the hydrophilic base of 2% *Curcuma Aeruginosa* Roxb. extract-containing cream, respectively.

The authors would like thank the patients for agreeing to take part in this study. The authors are grateful to Dr. Bob Taylor, and Dr. Jitlada Meephansan, for reviewing the manuscript.

The authors acknowledge the contribution of Asst. Prof. Kumpol Amnuaypattanapon who provided support for statistical analysis.

References

[1] G. W. Clark, S. M. Pope, and K. A. Jaboori, "Diagnosis and treatment of seborrheic dermatitis," Am. Fam. Physician. vol. 91(3), pp. 85–190, 2015

[2] A. K. Gupta, R. Bluhm, J. O. Barlow, A. B. Fleischer, Jr., and S. R. Feldman, "Prescribing practices for seborrheic dermatitis vary with the physician's specialty: implications for clinical practice," J. Dermatol. Treat. vol. 15(4), pp. 208–213, 2004.

[3] A. K. Gupta, M. Richardson, and M. Paquet, "Systematic review of oral treatments for seborrheic dermatitis," J. Eur. Acad. Dermatol. Venereol. vol. 28(1), pp. 16–26, 2014.

[4] G. K. Kim, "Seborrheic dermatitis and Malassezia species: how are they related?" J. Clin. Aesthet. Dermatol. 2009; 2(11):14-17.

[5] A. K. Gupta, S. E. Madzia, and R. Batra, "Etiology and management of Seborrheic dermatitis," Dermatology. vol. 208(2), pp. 89–93, 2004.

[6] J. D. Stratigos, C. Antoniou, A. Katsambas, K. Bohler, P. Fritsch, A. Schmolz, et al., "Ketoconazole 2% cream versus hydrocortisone 1% cream in the treatment of seborrheic dermatitis. A double-blind comparative study," J. Am. Acad. Dermatol. vol. 19 (5 Pt 1), pp. 850–853, 1988.

[7] A. Firooz, A. Solhpour, F. Gorouhi, M. Daneshpazhooh, K. Balighi, K. Farsinejad, et al., "Pimecrolimus cream, 1%, vs hydrocortisone acetate cream, 1%, in the treatment of facial seborrheic dermatitis: a randomized, investigator-blind, clinical trial," Arch. Derm. vol. 142(8), pp. 1066–1067, 2006.

[8] M. Goldust, E. Rezaee, S. Masoudnia, and R. Raghifar, "Clinical study of sertaconazole 2% cream vs. hydrocortisone 1% cream in the treatment of seborrheic dermatitis," Ann. Parasitol. vol. 59(3), pp. 119–123, 2013.

[9] L. Naldi, "Seborrhoeic dermatitis," BMJ Clin. Evid. vol. 2010, 2010.

[10] A. K. Gupta and R. Bluhm, "Seborrheic dermatitis," J. Eur. Acad. Dermatol. Venereol. vol. 18(1), pp. 13–26; quiz 19–20, 2004.

[11] C. F. Hossain, M. Al-Amin, A. S. Sayem, I. H. Siragee, A. M. Tunan, F. Hassan, et al., "Antinociceptive principle from Curcuma aeruginosa," BMC Complement. Altern. Med. vol. 15, pp. 191, 2015.

[12] N. Suphrom, G. Pumthong, N. Khorana, N. Waranuch, N. Limpeanchob, and K. Ingkaninan, "Anti-androgenic effect of sesquiterpenes isolated from the rhizomes of Curcuma aeruginosa Roxb.," Fitoterapia. vol. 83(5), pp. 864–871, 2012.

[13] G. Pumthong, P. Asawanonda, S. Varothai, V. Jariyasethavong, D. Triwongwaranat, P. Suthipinittharm, et al., "Curcuma aeruginosa, a novel botanically derived 5alpha-reductase inhibitor in the treatment of male-pattern baldness: a multicenter, randomized, double-blind, placebo-controlled study," J. Dermatol. Treat. vol. 23(5), pp. 385–392, 2012.

[14] Kamazeri TS, Samah OA, Taher M, Susanti D, Qaralleh H., "Antimicrobial activity and essential oils of Curcuma aeruginosa, Curcuma mangga, and Zingiber cassumunar from Malaysia," Asian Pacific journal of tropical medicine. vol. 5(3), pp. 202-209, 2012.

[15] Aspollah M, Suhaila, S., Nordin, S., Rahmani, L. M., Muse, R., Yusuf, U. K., Riyanto, S., "Chemical constituents and bioactivity of Curcuma aeruginosa Roxb.," Natural Product Sciences. vol. 3(13), pp. 175-179, 2007.

[16] Kitamura C, Nagoe T, Prana MS, Agusta A, Ohashi K, Shibuya H., "Comparison of Curcuma sp. in Yakushima with C. aeruginosa and C. zedoaria in Java by trnK gene sequence, RAPD pattern and essential oil component," Journal of Natural Medicines. vol. 61(3), pp. 239-243, 2007.

[17] Angel GR, Vimala, B., Nambisan, B., "Phenolic content and antioxidant activity in five underutilized starchy Curcuma species," International Journal of Pharmaceutical and Phytopharmacological Research. vol. 2(4), pp.69-73, 2012.

[18] Jantan I, Rafi IA, Jalil J., "Platelet-activating factor (PAF) receptor-binding antagonist activity of Malaysian medicinal plants," Phytomedicine. vol. 12(1-2), pp. 88-92, 2005.

[19] Moon-ai W, Niyomploy P, Boonsombat R, Sangvanich P, Karnchanatat A., "A superoxide dismutase purified from the rhizome of Curcuma aeruginosa Roxb. as inhibitor of nitric oxide production in the macrophage-like RAW 264.7 cell line," Applied biochemistry and biotechnology. vol 166(8), pp. 2138-2155, 2012.

[20] Reanmongkol W, Subhadhirasakul, S., Khaisombat, N., Fuengnawakit, P., Jantasila, S. and Khamjun, A., "Investigation the antinociceptive, antipyretic and anti-inflammatory activities of Curcuma aeruginosa Roxb. extracts in experimental animals," Songklanakarin J Sci Technol. vol. 5 (28), pp. 999-1008, 2006.

[21] Liu Y, Roy SS, Nebie RH, Zhang Y, Nair MG., "Functional food quality of Curcuma caesia, Curcuma zedoaria and Curcuma aeruginosa endemic to Northeastern Indi," Plant foods for human nutrition (Dordrecht, Netherlands). vol. 68(1), pp. 72-77,2013.

[22] Matangkasombut OP, Suckvanichsilp, N., Somanapan, A., "Postcoital contraceptive effect of Curcuma aeruginosa Roxb. in albino rat," Journal of the ASEAN Federation of Endocrine Societies. vol. (3), pp.117–118, 1983.