Efficacy of *Melaleuca alternifolia* Essential Oil in the Treatment of Facial Seborrheic Dermatitis: A Double-blind, Randomized, Placebo-Controlled Clinical Trial

Beheshti Roy A (Dermatologist.)[1], Tavakoli-far B (Ph.D.)[2]*, Fallah Huseini H (Ph.D.)[3], Tousi P (M.D.)[1], Shafigh N (M.D.)[1], Rahimzadeh M (Ph.D.)[4]

1- Dermatology Department, Boali Hospital, Qazvin University of Medical Science, Qazvin, Iran
2- Physiology and Pharmacology Department, Alborz University of Medical Science, Karaj, Iran
3- Pharmacology & Applied Medicine Department of Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran
4- Department of Social Determination of Health Research Center, Alborz University of Medical Science, Karaj, Iran
* Corresponding author: Physiology & Pharmacology Department, Alborz University of Medical Science, Karaj, Iran
Tel: +98-26-34336007
E mail: tavakkolifarb@yahoo.com

Received: 19 Aug. 2013 **Accepted:** 19 Aug. 2014

Abstract

Background: ***Melaleuca alternifolia*** **(tea tree) essential oil has been traditionally used in the ayurvedic system of medicine for healing burns, infections and seborrheic dermatitis. But yet, no controlled human study has determined its efficacy.**

Objective: The goal of the current study was to compare the efficacy of 5% tea tree essential oil (TTO) gel with placebo in the treatment of mild to moderate facial seborrheic dermatitis.

Methods: Fifty four patients with mild to moderate facial seborrheic dermatitis reffered to Skin Diseases Research Center, in the Qazvin city, Iran, were randomly divided into two groups and treated with either 5% TTO gel or placebo three times daily for 4 weeks. The patients follow-ups were conducted in both groups after 2 and 4 weeks with evaluating of erythema, scaling, itching and greasy crusts.

Results: Forty two patients completed the treatment course. There were significant differences between the TTO and placebo groups in the improvement of erythema, scaling, itching and greasy crusts ($p < 0.05$). Allergic side - effects were seen in neither group.

Conclusions: 5% TTO gel is effective in the treatment of mild to moderate facial seborrheic dermatitis.

Keywords: ***Melaleuca alternifolia*****, Facial seborrheic dermatitis, Tea tree oil gel, Topical treatment**

Introduction

Seborrheic dermatitis is a chronic, relapsing, inflammatory skin disorder. The prevalence of adult seborrheic dermatitis is estimated to be between %2 and 5% [1]. The symptoms of the disease include scaling, erythema, itching and greasy crusts. Although the exact cause of seborrheic dermatitis is yet to be understood, *Malassezia* yeasts, hormones (androgens), sebum levels and immune response are known to play important roles in its development. Additional factors, including drugs, winter temperatures and stress may exacerbate the disease [2].

An association is believed to exist between *malassezia* yeasts and seborrheic dermatitis, which may, in part be due to abnormal or inflammatory immune response against these yeasts [3].

Although topical antifungal agents such as ketoconazole are used for treatment of seborrehic dermatitis, but other treatment modalities including low-potency topical steroids and calcineurin inhibitors (immunomodulators) are also used [4].

Tea tree oil (TTO) is essential oil from the *Melaleuca alternifolia* tree, which is native to Australia [5–7]. This oil has been traditionally used for treatment of burns, infections and seborrheic dermatitis [8,9]. However the antibacterial, antifungal and anti-inflammatory activities of TTO have been reported in several experimental studies [10-13]. Recent studies have revealed that TTO has antifungal activity against *Malassezia* yeasts; it may thus be beneficial in the treatment of seborrheic dermatitis [3]. The goal of the present study is to investigate the efficacy and tolerability of 5 % TTO gel in patients with mild to moderate facial seborrheic dermatitis.

Materials and Methods

Drugs: TTO 5% and placebo gels (vehicle hydroxypropyl cellulose) were provided by Dr. Jahangir's Company, Parmoon (Tehran, Iran). The TTO and placebo gels were prepared with same colour, texture and packing shape but different labels. The composition of *M. alternifolia* oil used in TTO gel is given by Company is presented in table 1.

Inclusion criteria: Patients aged 18-45 years with mild-to-moderate facial seborrheic dermatitis and no localized or systemic infections.

Exclusion criteria: Compromised immune system; definitive cutaneous findings such as erythroderma, acne, psoriasis and known allergy to lotions or moisturizers; pregnancy or breastfeeding; use of products for seborrheic dermatitis within the past 2 weeks or treatment with systemic steroids and current treatment with a medication that causes flushing.

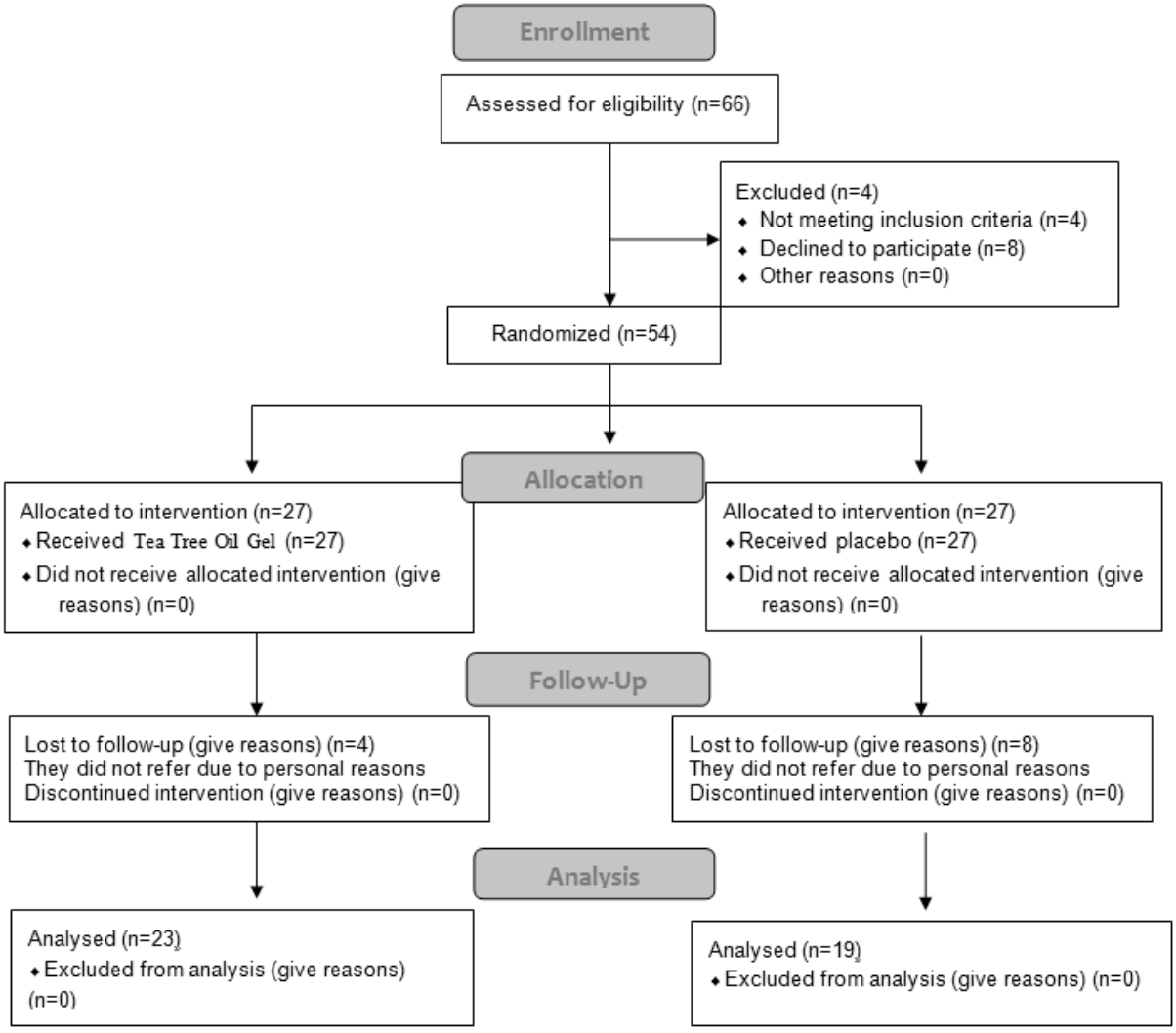
Protocol: Fifty four patients meeting the inclusion criteria who were referred to the Skin Diseases Research Center of the university-affiliated hospital in the Qazvin city, Iran, from September 2013 to December 2013 were selected. The medical ethics committee of the Skin Diseases Research Center affiliated with Qazvin university approved the protocol. Written informed consent was obtained from all patients prior to the study.

The study was double-blind and Block randomization was used for treatment allocation. Eighteen patients in each group was the sample size calculated to estimate 25% difference in total cure between the groups, considering type I error = 0.05 and 80% power. However 27 patients were selected in each group for any loss during the study. The CONSORT flowchart describing the progress

Table 1- Composition of *M. alternifolia* (tea tree oil)

Component	Composition (%)
	Typical composition
Terpinen-4-ol	41.1
γ-Terpinene	21.0
α-Terpinene	11.4
1,8-Cineole	4.7
Terpinolene	2.4
ρ-Cymene	2.6
α-Pinene	1.9
α-Terpineol	3.1
Aromadendrene	1.7
δ-Cadinene	1.0
Limonene	0.9

Figure 1: CONSORT flowchart diagram



of the participants through the trial is shown in Figure 1 . The patients and the investigators who carried out clinical assessments were unaware of treatment groups and type of medication. The patients were instructed to apply the TTO gel or placebo to the affected facial areas three times daily. The severity of seborrheic dermatitis was assessed in both groups by a dermatologist at 2 and 4 weeks following treatment initiation.

Skin involvement was assessed by a clinical score based on the extent of itching, erythema, scaling and greasy crusts as a primary outcome. During the initial evaluation, the area of involvement was measured using a scale of 1 to 5 representing ≤10%, 11% – 30%, 31% – 50%, 51% – 70% and >70% area involved, respectively [14]. At the 2 and 4 weeks following treatment initiation, assessment of patient satisfaction was conducted by the dermatologist as secondary outcome. A score of <25% was assigned to a rating of very bad, bad, no change or little improvement, 26% – 50% to mild improvement, 51% – 75% to good improvement, 76% – 99% to major improvement and 100% to total cure. The patients were also questioned about any side effects such as allergic irritation or inflammation on each visit as secondary outcome. For statistical analysis, t-test and paired t- test were employed using SPSS software. $p<0.05$ was considered as statistically significant.

Results

The demographic characteristics of the patients are shown in Table 2. Of the 54 patients enrolled in the study, 42 (77.7%) completed the treatment course. 4 patients from TTO and 8 from placebo groups failed to attend the follow-up visits.

The scores of itching, erythema, scaling, greasy crusts and scoring of patient satisfaction are shown in Table 3. Statistically significant decreases in the values of all parameters were observed after 2 weeks of treatment in the TTO group compared to the placebo group ($p< 0.05$). After 4 weeks of treatment, the values of all parameters in the TTO group decreased significantly ($p< 0.05$), compared with placebo group and compared with baseline values, but it was reverse in the placebo group after 2 or even 4 weeks of treatment ($p >0.05$). Scoring of patient satisfaction revealed total cure in 9 (39%) and 21 (91%) patients in the TTO group after 2 and 4 weeks of treatment, respectively. No allergic irritation or inflammation due to treatment was seen in both groups during the study.

Table 2- The demographic characteristics of the patients in the TTO and placebo groups

	Groups	
	TTO (N=23)	**Placebo (N=19)**
	Mean±SD	**Mean±SD**
Age **(year)**	31±10	28 ± 8
Disease duration **(years)**	3.0 ± 3.0	2.0 ± 2.2
Gender **(male/female)**	7 males, 16 females	6 males, 13 females

Table 3- The itching, erythema, scaling, greasy crusts and patient satisfaction scores in TTO and placebo groups in each visit

		Baseline	At 2 weeks	At 4 weeks
Itching (%)	TTO	1.52 ± 0.79	1.17 ± 0.71$^{\#}$	0.64 ± 0.34*$^{\#}$
	Placebo	1.7 ± 0.80	2.2 ± 1.2	2.2 ± 1.0
Erythema (%)	TTO	1.65 ± 0.77	1.47 ± 0.79$^{\#}$	0.69 ± 0.7*$^{\#}$
	Placebo	1.5 ± 0.62	2.4 ± 1.5*	2.2 ± 1.6*
Scaling (%)	TTO	1.02 ± 0.82	0.76 ± 0.31*$^{\#}$	0.55 ± 0.20*$^{\#}$
	Placebo	1.1 ± 0.91	1.8 ± 0.81*	1.9 ± 0.90*
Greasy crust (%)	TTO	0.84 ± 0.22	0.58 ± 0.39$^{\#}$	0.00 ± 0.00*$^{\#}$
	Placebo	0.7 ± 0.7	1.8 ± 0.5*	1.8 ± 0.3*
Scoring of patient satisfaction (%)	TTO	0.00 ± 0.00	39.3 ± 3.2*$^{\#}$	91.5 ± 4.1*$^{\#}$
	Placebo	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00

*= $p < 0.05$ (compared to baseline)
$^{\blacklozenge}$= $p < 0.05$ (compared to placebo at the same time)

Discussion

In the current 4 weeks intervention study the treatment of mild to moderate facial seborrheic dermatitis with topical 5% TTO gel reduced all the symptoms of facial seborrheic dermatitis without any allergic reaction. Although the numbers of patients in both groups were not in satisfaction range but all the patients in TTO group were satisfied of treatment. The present finding is supported by previous study which compared the effectiveness of a cream containing 5% TTO and 2 % butenafine hydrochloride in treatment of toenail fungal infection [15]. In another study, a cream containing 5% TTO was found to reduce the symptom of tinea pedis as effectively as 1% tolnaftate [16].

Although the exact mechanisms of TTO gel in treatment of seborrheic dermatitis is unknown, but several mechanisms may proposed.

Although the exact cause of seborrheic dermatitis has yet to be understood, *Malassezia* yeasts, hormones (androgens), sebum levels and immune response are known to play important roles in its development [3]. Previous study has shown that topical and systemic antifungal provide clinical benefit [4]. The antifungal effect of TTO has been reported in previous studies [15, 16]. The antifungal effect of many medicinal plants are attributed to their terpenoids content; however, terpenoids are major component in TTO (table 1) that, may support the efficacy of TTO in treatment seborrheic dermatitis [17,18]. Moreover seborrheic dermatitis is a chronic inflammatory disease and anti-inflammatory properties of TTO may be a factor in treatment of seborrheic dermatitis [13,19]. Of note our study had limitation such as small sample size, short duration and lack of additional group taking standard therapy. Considering the current study finding and previous data indicating TTO antifungal activity and its efficacy in treatment of other chronic skin disease such dandruff and acne [20, 21], TTO can be used as an alternative therapy for treatment seborrheic dermatitis if further large scale and long-term clinical study approved it.

Conclusion

In conclusion, the TTO gel appeared to be effective and well tolerated in the treatment of mild to moderate facial seborrheic dermatitis without any allergic reaction. Further large sample size and longer duration study on TTO gel comparing its efficacy to standard therapy is suggested.

References

1. Bikowski J. Facial seborrheic dermatitis: a report on current status and therapeutic horizons. *J. Drugs Dermatol*. 2008; 8: 125 - 33.

2. Del Rosso JQ. Adult seborrheic dermatitis. A status report on practical topical management. *J. Clin. Aesthet. Dermatol.* 2011; 4: 32-38.

3. Gupta AK, Batra R and Bluhm R. Skin diseases associated with Malassezia species. *J. Am. Acad. Dermatol.* 2004; 51: 785 - 98.

4. Stefanaki I and Katsambasa A. Therapeutic update on seborrheic dermatitis. *Skin Therapy Lett.* 2010; 15: 1 - 4.

5. Saller R, Reichling J and Teebaum-Öl. Ein natürliches Universalheilmittel? *Deut. Apotheker Z.* 1995; 135: 40 - 8.

6. Galle-Hoffmann U, König WA and Ätherische Öle - Teebaumöl. *Deut. Apotheker Z.* 1999; 139: 64 - 72.

7. Jarmyn RJ. Vielseitig aber eigensinnig. Teebaumöl in Kosmetika und Körperpflegeprodukten. *Parfümerie und Kosmetik* 1998; 79: 22 - 6.

8. Osborne F and Chandler F. Australian tea tree oil. *Canadian Pharmaceut. J*. 1998; 131: 42 - 6.

9. Aburjai T and Natsheh FM. Plants used in cosmetics. *Phytotherapy Res*. 2003; 17: 987 - 1000.

10. Carson CF and Riley TV. The antimicrobial activity of the tea tree oil. *Med. J. Australia.* 1994; 160: 236 - 40.

11. Nenoff P, Haustein UF and Brandt W. Antifungal activity of the essential oil of *Melaleuca alternifolia* (tea tree oil) against pathogenic fungi in vitro. *Skin Pharmacol.* 1996; 9: 388 - 94.

12. Weseler A, Geiss HK, Saller R and Reichling J. Antifungal effect of Australian tea tree oil on malassezia pachydermatis isolated from canines suffering from cutaneous skin disease. *Schweiz Arch. Tierheilkd.* 2002; 144: 215 - 21.

13. Caldefie-Chézet F, Fusillier C, Jarde T, Laroye H, Damez M, Vasson MP and Guillot J. Potential anti-inflammatory effects of *Melaleuca alternifolia* essential oil on human peripheral blood leukocytes. *Phytother Res.* 2006; 20 (5): 364 - 70.

14. Khondker L, Choudhury AM, Wahab MA and Khan MSI. Efficacy of oral itraconazole in the treatment of seborrheic dermatitis. *J. Bangladesh College Physicians surgeons.* 2011; 29: 201 - 6.

15. Syed TA,Qureshi ZA, Ali SM, Ahmad S and Ahmad SA. Treatment of toenail onychomycosis with 2% butenafine and 5% *melaleuca alternifolia* (tea tree) oil in cream. Trop. *Med. Int. Health* 1999; 4: 284 - 7.

16. Tong, MM, Altman PM and Barnetson RS. Tea tree oil in the treatment of tinea pedis. *Aust. J. Dermatol*. 1992; 33: 145 – 9.

17. Brophy JJ, Davies NW, Southwell IA, Stiff IA and Williams LR. Gas chromatographic quality control for oil of melaleuca terpinen-4-ol type (Australian tea tree). *J. Agric. Food Chem*. 1989; 37: 1330 - 5.

18. Ishaq MS, Hussain MM, Afridi MS, Ali G, Khattak M, Ahmad S and Shakirullah. In vitro phytochemical, antibacterial, and antifungal activities of leaf, stem, and root extracts of *Adiantum capillus* veneris. *Scientific World J.* 2014; 28: 269 - 793.

19. Johnson BA and Nunley JR. Treatment of seborrheic dermatitis. *Am. Fam Physician* 2000; 61 (9): 2703 - 10.

20. Satchell AC, Saurajen A, Bell C and Barnetson RS. Treatment of dandruff with 5% tea tree oil shampoo. *J. Am. Acad. Dermatol*. 2002; 47: 852 - 5.

21. Bassett IB, Pannowitz DL and Barnetson RSTC. A comparitive study of tea-tree oil versus benzoylperoxide in the treatment of acne. *Med. J. Austral*. 1990; 153: 455 - 45.