

A Double-Blind Randomized Controlled Trial of the Efficacy of 5% Tea Tree Oil Cleanser versus Mild Cleanser in the Treatment of Mild-Moderate Facial Seborrheic Dermatitis

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ABSTRACT

Background: Seborrheic dermatitis is a chronic, relapsing, inflammatory disease characterized by erythema, scaling, pruritus over the areas of the scalp, face, ears, sternum and upper back. Tea tree oil is rich in terpene alcohols such as terpinen-4-ol which is thought to be the active germicidal component.

Objective: To determine the efficacy of 5% tea tree oil cleanser in the treatment of mild-moderate facial seborrheic dermatitis and to determine the adverse side effects.

Methods: Forty-five patients with clinical signs of seborrheic dermatitis were randomly assigned to one of the two treatment groups: mild cleanser and the 5% tea tree oil group. This study was done as a double-blind randomized controlled trial for 4 weeks. The parameters – area involved, erythema, scaling, and Seborrhea Area and Severity Index were taken at baseline and weekly for 4 weeks. At the end of 4 weeks, the difference of the two groups were compared using paired t-test.

Results: After 4 weeks, significant clinical improvement of the area involved, erythema, and scaling and the reduction of Seborrhea Area and Severity

Conclusion: The use of 5% tea tree oil cleanser provides significant improvement in the treatment of mild-moderate facial seborrheic dermatitis with no adverse side effects.

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Clinical Question

Is 5% tea tree oil cleanser effective in the treatment of mild-moderate facial seborrheic dermatitis?

Tea tree oil, an essential oil, which is clear to pale yellow in color, is distilled from the leaves and terminal branches of *Malaleuca alternifolia*, an Australian tree. Traditionally, it has a wide range of topical applications and is commonly used to treat skin and respiratory infections.

Among the 100 components of tea tree oil, *terpinen-4-ol*, α -pinene and β -pinene, and *1,8-cineol* showed the most activity, with minimum inhibitory concentrations and minimum fungicidal concentrations. An in vitro antifungal activity of tea tree oil against 26 strains of dermatophyte species, 54 yeasts, and 22 different *Malassezia furfur* strains, showed that the lipophilic yeast, *M. Furfur* seemed to be most susceptible to tea tree oil. MIC values between 556.2 and 4,450.0 $\mu\text{g/ml}$ (geometric mean 1,261.5 $\mu\text{g/ml}$) were found against the tested *M. furfur* strains, corresponding to 0.5-0.44% tea tree oil content. These values are far below the usual relatively high therapeutic concentrations of the agent; approximately 5-10% solution or even the concentrated essential oil are used for external treatment.

Seborrheic dermatitis is a chronic, relapsing inflammation of sebum-rich areas of the scalp, face, and trunk. It is commonly aggravated by changes in humidity, changes in seasons, trauma, or emotional stress. The severity varies from mild dandruff to exfoliative erythroderma.

This condition is associated with normal levels of *Malassezia* but an abnormal immune response. Helper T cells, phytohemagglutinin and concanavalin stimulation, and antibody titers are depressed compared with those of control subjects. There is increased sebum production, which may come from its lipase activity—releasing inflammatory free fatty acids—and from its ability to activate the alternative complement pathway. Persons prone to this dermatitis also may have a skin-barrier dysfunction. Various medications may flare or induce seborrheic dermatitis.

The prevalence rate of seborrheic dermatitis is 3-5%, with a worldwide distribution. Dandruff, the mildest form of this dermatitis, is probably far more common and is present in an estimated 15-20% of

the population. It occurs in persons of all races and affects more males than females. It has two peak periods – infancy and adulthood. The adult type is chronic and peaks during the fourth to sixth decade of life.

Clinically, facial seborrheic dermatitis manifests as erythematous, inflamed skin topped with branny or greasy scales. There is accompanying pruritus of variable degree. Distribution follows the oily and hair-bearing areas of the face, such as the forehead, the eyebrows, the lash line, the nasolabial folds, the beard, and the postauricular skin. An extension to submental skin can occur.

The use of mild topical corticosteroids +/- antifungal is still the gold standard. Mild cleanser, an adjuvant to the treatment regimen helps decrease inflammation and helps veer away from the vicious cycle of seborrhoea elicited by the use of harsh soaps commonly used by patients with seborrheic dermatitis. The objective of this study was to determine the efficacy and safety of 5% tea tree oil cleanser in the treatment of mild-moderate facial seborrheic dermatitis compared with mild cleanser as to improvement of area involved, erythema, and scaling and the reduction of the seborrhea area and severity index.

METHODOLOGY

The ethics committee approved the study. Patients were diagnosed clinically based on the location of the lesions, the erythema, scaling, and pruritus. All patients, male and female, twelve years and older, who were systematically well, with no known allergies to tea tree oil and were not taking arsenic, gold, methyldopa, cimetidine, and neuroleptics were invited to enter the study and informed consent was obtained. (*Appendix A*)

Randomization was made through the Research Randomizer. The total number of subjects intended for the study was entered and was divided into 2. Subject was asked to pick a number from 1-140 and was assigned to the set where his/her preferred number fell. The subjects were randomly assigned to receive either 5% tea tree oil cleanser or the vehicle mild cleanser. Subjects were then given their treatment sample by the secondary investigator.

Patients were instructed to wash their face twice a day for 3 minutes before rinsing off with tap water. Male subjects were free to shave but were prohibited

the use of shaving cream, after-shave lotion, toner, or astringents. Female subjects were free to use face powder but were likewise prohibited the use of toner or astringents. The primary investigator and an assistant (blinded) assessed the patients (blinded) at baseline and weekly for 4 weeks based on the Seborrhea Area and Severity Index. (Appendix B). Photographic documentations on selected patients were done baseline, and weekly until week 4. (Appendix D)

It was determined that a sample size of 45 patients per treatment group would be required to detect a difference of 30% in the proportion of clearance of symptoms and 80% clearance in the 5% Tea Tree Oil Cleanser and 50% clearance in cleanser alone. (Using a power of 80% and $\alpha = 0.05$)

Paired T-test was used to determine the difference between baseline and week 4 of the areas involved, erythema, scaling, and SASI for the 5% tea tree oil and mild cleanser.

Independent T-test was used to determine mean difference in area involved, erythema, scaling and SASI scores between the 5% tea tree oil cleanser and mild cleanser

RESULTS

A total of ninety-five subjects were enrolled in the study, ninety of which finished the four-week period. Sixty-three males and twenty-seven females ranging from 18 to 68 years entered the study. Forty-eight subjects were randomly assigned to the mild cleanser group (A) while forty-seven were randomly assigned to the 5% tea tree oil (B). The mild cleanser group had thirty-five males and ten females. While, the 5% tea tree oil cleanser had twenty-eight males and seventeen females. There were three drop-outs for the mild cleanser group and two for the 5% tea tree oil group. The drop-outs were lost to follow-up. Demographic data are shown in Table I.

Statistically significant improvements were observed in the area involved, erythema and scaling and Seborrhoea Area and Severity Index for both groups.

For the 45 patients using the mild cleanser, the area involved was 3.2 at baseline, and 2.24 after 4 weeks, a 30% reduction. In the 45 patients using the 5% tea tree oil cleanser, the score for the area involved fell from an average of 3.36 at baseline to

1.62 after 4 weeks, a 52% drop in the mean score. (Graph A)

The score for the erythema for the mild cleanser group fell from 3.04 at baseline to 1.96 at week 4. A 36% drop in the mean score The score for the erythema for the patients using the 5% tea tree oil fell from an average of 3.13 at baseline to 1.02 after 4 weeks. A 67% improvement in the mean score. (Graph B)

In the mild cleanser group, the score was 2.955 at baseline and 1.84 at week 4, while in the 5% tea tree oil, the score for the scaling at baseline was 3.07 and 0.73 at the end of 4-weeks, 38% and 76% drop in the mean score respectively. (Graph C)

The primary objective efficacy variable was the improvement in Seborrhea Area and Severity Index (SASI), the SASI rates both the degree of involvement and severity.

The scores for the Seborrhea Area and the Severity Index were significantly improved in both the mild cleanser and the tea tree oil groups. The score for the mild cleanser at baseline was 10.13 and at week 4 – 4.93, a 51% improvement. The tea tree oil score fell from an average of 10.8 baseline to 1.61 at week 4, an improvement of 85% in the Seborrhea Area and Severity Index. (Graph D)

The difference were likewise calculated to show the mean percentage improvement from the baseline to week 4 for the mild cleanser group and the 5% tea tree oil cleanser group.

The *independent group T-Test for means* was used to test the means of the two independent groups – the mild cleanser and the 5% tea tree oil cleanser, to determine if they are significantly different from one another.

The differences between the mean percentage change, 22.0 for the area involved, 31.0 for the erythema, 38.0 for the scaling and 34.0 for the seborrhoea area and severity index, were statistically significant with 95% confidence level and a P value of less than 0.05. (Table 2)

Tolerance of the 5% tea tree oil was excellent, no adverse reactions were reported by the subjects during the treatment period. No cutaneous adverse reactions were observed during the subsequent follow-ups after the study period.

DISCUSSION

Tea Tree Oil is a distillate, colorless to pale yellow in color with a characteristic strong fragrance attributed to *1,8-cineol* (eucalyptol). It is a complex mixture of over 100 different components, most of which being monoterpenes and sesquiterpene hydrocarbons and their alcohols. *Terpinen-4-ol* is thought to be the active germicidal component. Traditionally, the Bundjalung Aborigines of northern New South Wales were the first to use the leaves of this tree. Tea Tree Oil was named by Captain James Cook when he first visited Australia in the 18th century. In 1923, Dr. Penfold proved that tea tree oil was 13 times stronger than the antiseptic of that time carbolic acid and that it did not burn the skin. And during WW II, tea tree oil was issued to Australian soldiers for use as antiseptics.

Tea tree oil is active against all three categories of infectious organisms: bacteria, viruses and fungi.

A study by KA Hammer et al, published in 2003 investigated the *in vitro* antifungal activity of tea tree oil. It was shown that among the 100 components of tea tree oil, *terpinen-4-ol*, α -*terpineol*, *linalool*, α -*pinene* and β -*pinene*, and *1,8-cineole* showed the most activity, with minimum inhibitory concentrations and minimum fungicidal concentrations. It was concluded that all tea tree oil components, except β -*myrcene*, had antifungal activity.

Another paper by the same authors showed that tea tree oil has both inhibitory and fungicidal properties. Tea tree oil MICs for all fungi ranged from 0.004% to 0.25% and minimum fungicidal concentrations (MFCs) ranged from <0.03% to 8.0%. Time-kill experiments with 1-4 x MFC demonstrated that 3 out of 4 test organisms were still detected 8 hrs post treatment, but not after 24 hours.

With the antifungal evidences of tea tree oil, a randomized, placebo-controlled, double-blinded study was done for the treatment of interdigital tinea pedis with 25% and 50% tea tree oil solution. One hundred fifty-eight patients with tinea pedis were randomized to received either the placebo, 25% or 50% tea tree oil solution. Patients were instructed to apply the solution twice a day for 4 weeks. A marked clinical response was seen in 68% of the 50% tea tree oil group, 72% of the 25% tea tree oil group, and 39% in the placebo group. Mycological cure rate was 64% in the 50% tea tree oil compared to 31% in

the placebo group. Four patients developed moderate-severe dermatitis that improved on stopping the study medication.

Locally, a randomized double blind clinical trial on the efficacy and safety of tea tree oil in the treatment of tinea corporis by Drs. P Nagbuya-Cebrian, E. Morales, J. Dizon showed that tea tree oil 2% cream is effective and safe for the treatment of tinea corporis. It has a comparable efficacy and safety with miconazole 2% cream.

In the study by Satchell AC et al, one hundred twenty-six subjects with mild to moderate dandruff were randomly distributed to receive either the placebo or the 5% tea tree oil shampoo. They were assessed after a four-week period. Those using the 5% tea tree oil shampoo significantly improved. 5% tea tree oil: baseline score 91.0; down to 53.0 after 4 weeks versus placebo: baseline score of 99.7; down to 88.2 after 4 weeks; P < .001. Unfortunately, this study was not double-blind.

The antifungal activity of tea tree oil against yeasts (*Candida spp.*) and dermatophytes (*Microsporum spp.* And *Trichophyton spp.*) is reported in the study of KA Hammer et al.. This study documented the ability of tea tree oil to inhibit *Candida albicans* conversion from yeast form to the pathogenic mycelial form. These results, along with the lipophilic nature of the tea tree oil, which enables it to penetrate the skin, makes it suitable for topical use for the treatment of fungal mucocutaneous infections.

The adverse side effects of the use of tea tree oil were mostly of the allergic contact dermatitis. This reaction is a well-documented phenomenon and has been described in several reports since the early 1990's. In a paper published by The University of Western Australia Tea Tree Oil Research Group, they found that "*1,8-cineol* (eucalyptol) which gives eucalypts their characteristic strong fragrance and medicinal properties, was the allergen.". "*Aromadendrene*, α -*terpinene*, *d-limonene*, and *eucalyptol* have been all suggested as primary sensitizers" in a case presented by YM Monthrope and JC Shaw in 2004. In the study done by Cebrian et al, they note "worsening of erythema and pruritus and hyperpigmentation" which "upon discontinuation of the given medicines, reactions spontaneously resolved".

CONCLUSION

This study has shown that 5% tea tree oil cleanser is an effective and safe treatment for mild-moderate facial seborrheic dermatitis.

It is recommended that for the succeeding study, a larger sample population and longer follow-up period for at least 12 months to determine the incidence of recurrence and to determine the mean period of remission.

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TABLES AND GRAPH

Table 1. Demographic Data of the 5% Tea Tree Oil and Mild Cleanser Groups

	MILD CLEANSER	5% TEA TREE OIL CLEANSER
Gender		
Male	35	28
Female	10	17
Age	39.31±9.73	41.02±13.40

Graph A. Change in Area Involved

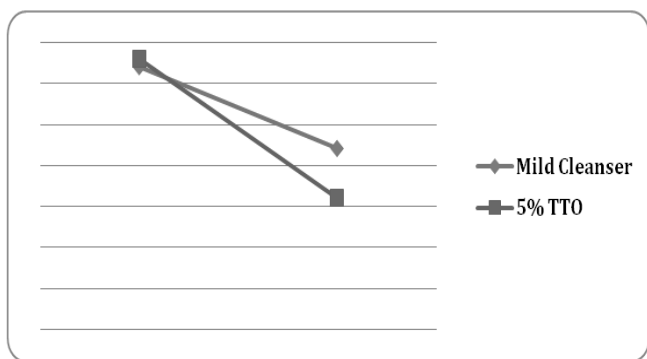


Table A

	MILD CLEANSER	5% TEA TREE OIL CLEANSER
Baseline	3.2±1.32	3.35±1.13
Week 4	2.24±1.22	1.62±0.88
Percentage Mean Score	30%	52%

Graph B. Change in Erythema

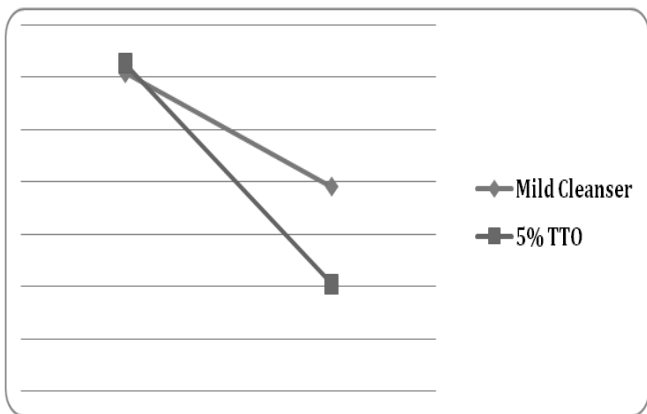


Table B

	MILD CLEANSER	5% TEA TREE OIL CLEANSER
Baseline	3.04±0.63	3.13±0.63
Week 4	1.95±0.74	1.02±0.45
Percentage Mean Score	36%	67%

Graph C. Change in Scaling

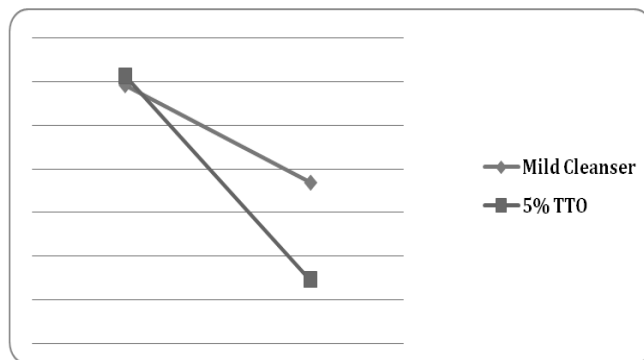


Table C

	MILD CLEANSER	5% TEA TREE OIL CLEANSER
Baseline	2.95±0.74	3.07±0.54
Week 4	1.84±0.90	0.73±0.45
Percentage Mean Score	38%	76%

Graph D. Change in SASI

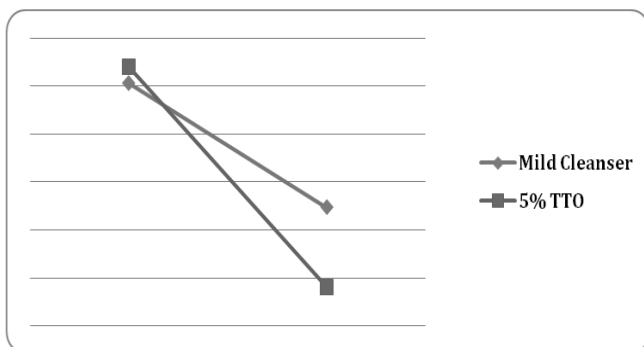


Table D

	MILD CLEANSER	5% TEA TREE OIL CLEANSER
Baseline	10.13±5.34	10.8±4.76
Week 4	4.93±3.40	1.61±1.07
Percentage Mean Score	51%	85%

Mean Difference**Table 2. Percent Improvement in Mean Difference in 5% Tea Tree Oil and Mild Cleanser**

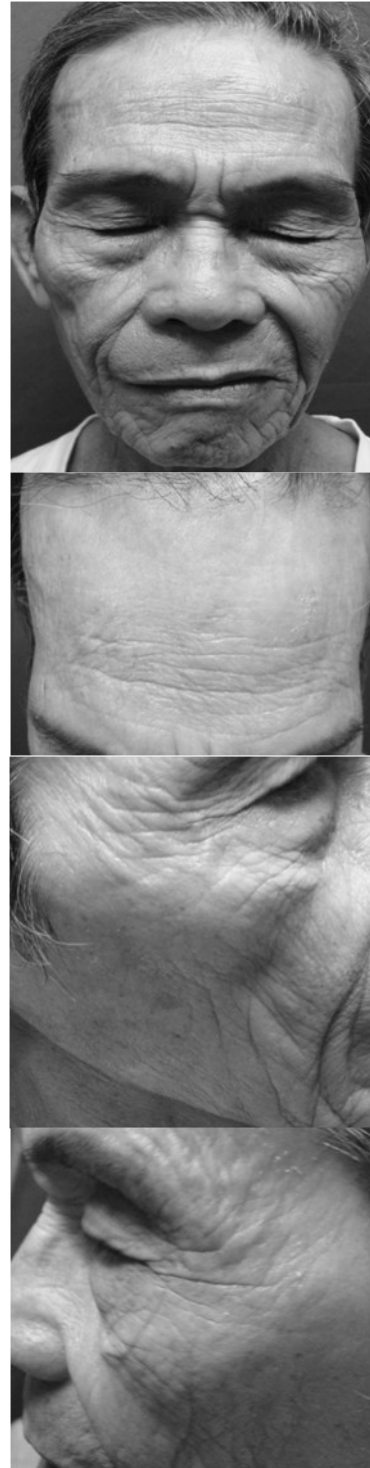
	MILD CLEANSER	5% TEA TREE OIL CLEANSER	DIFFERENCE BETWEEN MEAN PERCENTAGE CHANGE	P-VALUE
Parameters				
Area	30%	52%	22%	.000025
Erythema	36%	67%	31%	.000001
Scaling	38%	76%	38%	.000001
SASI	51%	85%	34%	.000003

Significant Difference p: < 0.05

APPENDIX A
MILD CLEANSER



BASELINE



WEEK 4

5% TEA TREE



BASELINE



WEEK 4