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File: ■ Tea Tree (*Melaleuca alternifolia*, Myrtaceae) ■ Acne

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RE: Tea Tree Oil Significantly Reduces Number of Acne Lesions

Malhi HK, Tu J, Riley TV, Kumarasinghe SP, Hammer KA. Tea tree oil gel for mild to moderate acne; a 12 week uncontrolled, open-label phase II pilot study. *Australas J Dermatol*. March 21, 2016; [epub ahead of print]. doi: 10.1111/ajd.12465.

Acne is a common skin condition caused by a combination of factors including excessive sebum production, an immunological response to the bacteria *Propionibacterium acnes*, inflammation, and abnormal desquamation of the follicular epithelium. Tea tree (*Melaleuca alternifolia*, Myrtaceae) leaf oil has demonstrated antimicrobial and anti-inflammatory activity. Clinical studies have evaluated the efficacy of tea tree oil in treating acne; however, they have investigated preparations that contain concentrations of tea tree essential oil (up to 5%) that are not available in commercial products. Hence, the purpose of this uncontrolled, phase II pilot study was to evaluate the efficacy and tolerability of a commercially available tea tree oil gel and facial wash for the treatment of mild to moderate acne.

Men and women (n = 18; 16-39 years old) with mild to moderate facial acne (defined as 10-100 facial lesions) were recruited from January to September 2014 via advertisements for this study conducted at 2 sites in Perth, Western Australia, Australia. Included subjects also had ≤ 2 nodules and an investigator global assessment (IGA) score of ≥ 2. Excluded subjects had a known allergy to tea tree oil, had another current skin disease, were currently using steroids or antibiotics, had severe underlying disease, were pregnant, were breastfeeding, or participated in another clinical trial within the previous 12 weeks.

The subjects received 200 mg/g Tea Tree Medicated Gel for Acne (Thursday Plantation; Integria Healthcare; Brisbane, Queensland, Australia) and 7 mg/g Tea Tree Face Wash for Acne (Thursday Plantation; Integria Healthcare). The products contained tea tree oil meeting the specifications of the *British Pharmacopoeia* monograph for tea tree oil, and both ISO 4730:2004 and Australian 2782-2009 standards for 'Oil of Melaleuca, terpinen-4-ol type' (tea tree oil). The other ingredients of the products were not reported. The subjects were instructed to use the products twice daily on their face by first washing their face with 1 pump of the face wash, patting it dry, and then applying a pea-sized amount of gel in a thin layer to acne-affected areas. They were instructed to leave the product on for at least 6 hours and wash it off only at the next application time.

The primary endpoints of total lesion count and IGA score were recorded at 0, 4, 8, and 12 weeks. The secondary endpoint of skin oiliness was recorded by the investigator at 0, 4, 8,

and 12 weeks. Study compliance was assessed via a daily diary and by the investigator weighing the remaining product at each visit. At the end of each week, subjects scored their acne on a 5-point scale ranging from worse to significantly better. Tolerability was assessed via adverse events and investigator score of erythema (redness), scaling, peeling, induration (hardness), and dryness on a 5-point scale.

The susceptibility of clinical isolates of *P. acnes* to non-formulated tea tree oil, the gel, and the face wash were assessed in triplicate using a standard broth microdilution method. The minimum inhibitory concentrations (MICs) of each product were determined visually after 48 h of anaerobic incubation.

The MIC of the unformulated oil (per volume) ranged from 0.25% to 1% (90% of the isolates inhibited by 1%). The MIC of the gel ranged from 0.062-0.5% (per volume) and the MIC of the face wash was < 0.25% (per volume).

Four subjects were discontinued from the study; 2 for protocol violations and 2 by request. Mean total lesion count significantly decreased at each visit compared with baseline; there was a 25% decrease at 4 weeks ($P < 0.05$), 37% decrease at 8 weeks ($P < 0.01$), and 54% decrease at 12 weeks ($P < 0.001$). IGA score was significantly better at weeks 8 and 12 ($P < 0.05$ for both) compared to baseline. Facial oiliness was significantly improved at week 12 ($P < 0.01$) compared to baseline. Clinical efficacy (defined as ≥ 40% decrease in lesion count at 12 weeks) was achieved for 79% (11/14) of subjects.

Based on diary data, 11 subjects (79%) were compliant for all 12 weeks; data for the remaining subjects were incomplete. The weekly opinion of the subjects most frequently recorded (46%) was that their acne was about the same or slightly improved (43%).

There were no serious adverse events. One subject reported minor itching within the first few days of applying the tea tree oil. At week 4, 1 subject experienced moderate scaling, 1 had moderate peeling, and 1 had moderate dryness. Mean tolerability scores for erythema ($P < 0.05$) and peeling ($P < 0.01$) were significantly decreased at week 12 compared to baseline. Product acceptability was assessed for the gel only; the lowest scores were for fragrance and ease of absorption and the highest scores were for texture, consistency, and ease of application.

The authors conclude that the use of a gel and face wash containing tea tree oil for 12 weeks significantly reduced the number of acne lesions and was well tolerated in subjects with mild to moderate acne. Both products showed significant antibacterial activity against *P. acnes* in vitro, suggesting that this may, in part, be the mechanism of action. An acknowledged limitation of the study was the lack of a control; "it remains possible that study factors such as the gel base product, or the regular, structured facial care routine contributed to the improvement in acne." The authors point out that a phase III, placebo-controlled, double-blind trial would be required to evaluate this possibility.

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—Heather S. Oliff, PhD

The American Botanical Council has chosen not to reprint the original article.