Pure Australian Tea Tree Oil

Personal Care Applications for Skin and Hair

In recent years, consumers have made a clear choice; personal care and cosmetic products with synthetic ingredients have declined in favour of products with naturally-based ingredients. However, formulators of these products often face significant challenges in incorporating naturally-derived ingredients into personal care formulations due to a lack of *in-vitro* research, let alone *in-vivo* clinical data validating the potential therapeutic properties of natural ingredients.

For one of the most popular natural ingredients in personal care, the essential oil of *Melaleuca alternifolia* (Tea Tree Oil), this is not the case. Indigenous to Australia, Pure Australian Tea Tree Oil is a prime example of an essential oil that has undergone extensive *in-vitro* and *in-vivo* clinical research over many years. Google Scholar lists a total of 5,610 articles, 787 of those articles since January 2014 (www.googlescholar.com; June 2015). Medical reference searches on PubMed for "Melaleuca" and "Tea Tree Oil" return 629 peer reviewed, published clinical studies evaluating the safety and efficacy of 100% Pure Australian Tea Tree Oil (www.pubmed.org; June 2015).

Pure Australian Tea Tree Oil offers proven properties as an effective antiseptic, antibacterial, antifungal, antiviral, and anti-inflammatory agent. These properties are highly valued in personal care formulations (Carson *et al.*, 2006). Tea Tree Oil is currently available worldwide as a "neat" oil and as an ingredient listing in a diverse range of products. The Personal Care Products Council has given Tea Tree Oil the INCI designation of *Melaleuca Alternifolia* (Tea Tree) Leaf Oil.

This White Paper is a summary of key scientific and clinical studies evaluating the efficacy and/or safety of Pure Australian Tea Tree Oil for topical personal care applications – Hair Care, Hand (and Body) Wash, and Acne. The intent of this white paper is to provide the reader with a basis of information necessary to consider the use of Tea Tree Oil in Personal Care product formulations.

Hair Care

Tea Tree Oil, a proven antifungal agent, is useful in the treatment of dandruff. Dandruff is generally considered to be caused by the yeast *Malassezia furfur.* The *M. furfur* yeast (previously known as *Pityosporum ovale*) is a lipophilic yeast which feeds on dermal lipids, releasing pro-inflammatory free fatty acids that cause both scalp dermal inflammation and tissue damage (Gemmer *et al*., 2002; Grimalt *et al*., 2007; Pooja *et al.,* 2013). An *in-vitro* study by Nenoff *et al.*, found that Tea Tree Oil had antifungal activity against the clinical fungal isolate *M. furfur* with the minimum inhibitory concentration between 556.2 and 4450.0 mg/ml, mean 1,261.5 (Nenoff *et al*., 1996). This was a landmark study of the efficacy of Tea Tree Oil for the treatment of dandruff. Tea Tree Oil was found to effectively inhibit growth of pathogenic fungi.

A prospective randomized, single-blinded parallel-group study by Satchell *et al*. (2004) found that a 5% Tea Tree Oil shampoo exhibited good overall effectiveness in inhibiting the growth of *M. furfur.* The study consisted of one hundred and twenty six male and female patients (n=126), aged 14 and older, randomized to receive either a 5% Tea Tree Oil shampoo or placebo, used daily for four weeks. It was found the 5% Tea Tree Oil shampoo group showed a 41% improvement compared with 11% in the placebo group, a statistically significant ($p<0.001$) improvement.

Hand Wash

Recent scientific studies, as well as mainstream media, suggest a move against the widespread use of antimicrobial agents in hand washes. Many such studies demonstrate a direct correlation between these agents and increased bacterial resistance, hormonal disturbances, and environmental disruption. There are even governments (such as Minnesota) which have banned their use entirely.

Regulatory health and environmental authorities, including the FDA and EPA, are working together to set restrictions on the use of common antimicrobial agents in soaps, hand washes, and similar personal care products (FDA Consumer Health Information, 2013), especially triclosan. Such agents generally offer a single mode of action. When these synthetic antimicrobial agents are used, surface residue is often left behind, imparting biological stress on exposed bacteria. As these stressors are one-dimensional, these bacteria can undergo non-lethal mutations, leading to resistance and reduced efficacy of these agents over time.

However as pure Tea Tree Oil is a combination of 113 compounds, the mode of antimicrobial activity is multi-dimensional, with bacterial resistance to pure Tea Tree Oil determined not to exist. Although one study (McMahon *et al*., 2007) in the literature proposed a possible link between sub-lethal concentrations of Tea Tree Oil and the development of antibiotic resistance in human pathogens, this hypothesis was thoroughly discredited by a prospective clinical trial published by Thomsen *et al*. (2013).

The results of the Thomsen study, specifically designed to test for changes in antibiotic resistance following a sub lethal Tea Tree Oil formulation challenge, firmly rebutted the bacterial resistance to Tea Tree Oil theory by McMahon. The authors concluded that they could not identify any change in genetic mutation nor any causal link between sub-lethal concentrations of Tea Tree Oil and habitual antibiotic resistant human pathogens.

Additionally, the data from an *in-vitro* study by Hammer *et al*. (2008) suggested that Gram-positive organisms such as *Staphylococcus* and *Enterococcus spp*. have very low frequencies of resistance to pure Australian Tea Tree Oil. This study was conducted to determine the frequencies at which single-step mutants resistant to Tea Tree Oil and rifampicin occurred amongst the Gram-positive organisms *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Enterococcus faecalis*. For Tea Tree Oil, resistance frequencies were very low at <10−9. Single-step mutants resistant to Tea Tree Oil were undetectable at two times MIC for *S. aureus* RN4220 and derivative mutator strains, or at 3× MIC for the remaining *S. aureus* strains, including a clinical *methicillin-resistant S. aureus* (MRSA) isolate. Similarly, no mutants were recovered at 2× MIC for *S. epidermidis* or at 1× MIC for *E. faecalis.* Resistance frequencies determined *in vitro* for rifampicin (8× MIC) ranged from 10−7 to 10−8 for all isolates, with the exception of the *S.aureus* mutator strains, which had slightly higher frequencies. These data suggest that Gram-positive organisms such as *Staphylococcus* and *Enterococcus spp.* have very low frequencies of resistance to pure Australian Tea Tree Oil.

Hammer *et al*. (2011) conducted a study which examined the effect of sub inhibitory *Melaleuca alternifolia* (Tea Tree) essential oil on the development of *Staphyloccus aureus* and *Escherichia coli*. This study found that neither pure Australian Tea Tree Oil nor its major component, terpinene-4-ol, have any perceptible impact on the development of antimicrobial resistance and susceptibility.

Tea Tree Oil has a considerable history of being used as an effective antimicrobial agent in hand wash formulations. Like other antimicrobial active agents, this effect is achieved when in formulations at bactericidal concentrations. (Bassolé & Juliani, 2012).

Transient Microorganisms	Range (%)	MIC_{90} (%)
Acinetobacter baumannii	0.06 – 1	1
Escherichia coli	0.12 – 0.25	0.25
Klebsiella pneumoniae	0.12 – 0.5	0.25
Pseudomonas aeruginosa	2 – 5	3
Serratia marcescens	0.25 – 0.5	0.25
Staphylococcus aureus	0.12 – 0.5	0.5
Methicillin-Resistant *Staphylococcus aureus* (MRSA)	0.25	0.25

Furthermore, Tea Tree Oil has been found to not disrupt commensal bacterial populations, improving the natural symbiotic skin flora activity. More information can be found in Hammer, *et al.*, "Susceptibility of transient and commensal skin flora to the essential oil of *Melaleuca alternifolia* (tea tree oil)," American Journal of Infection Control, 1996.

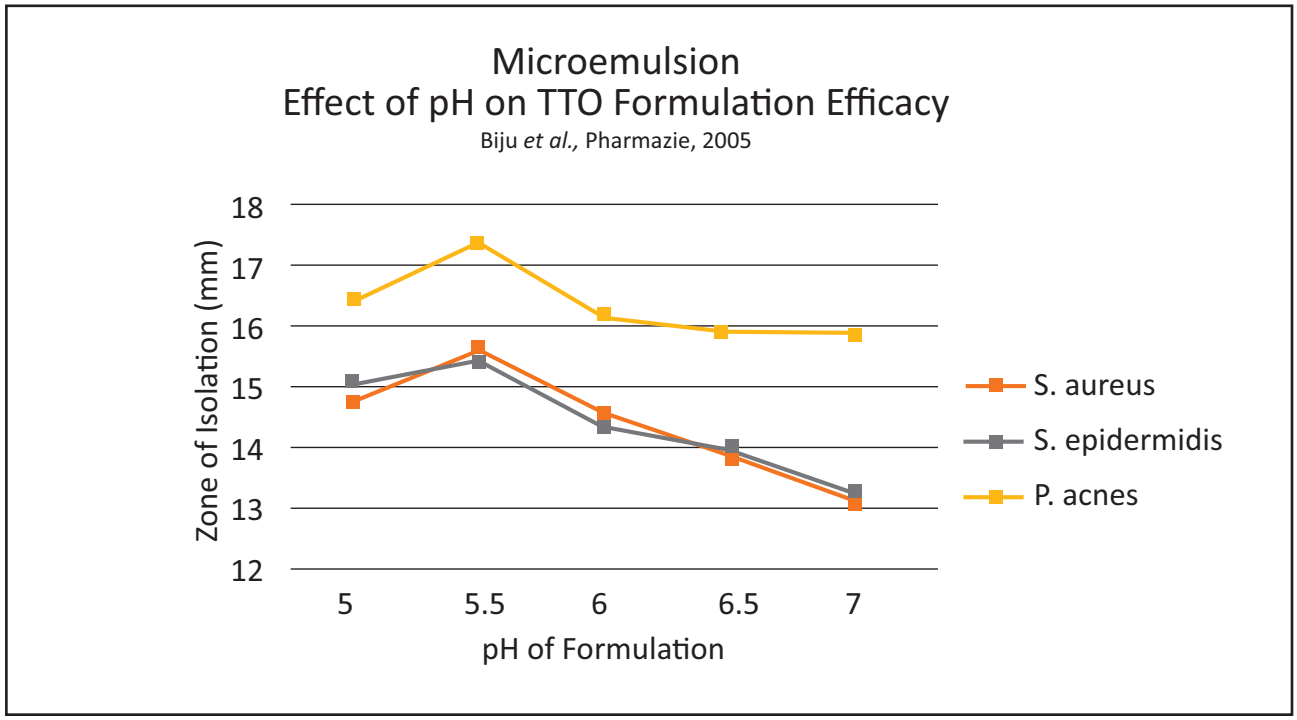
Acne

Acne is a skin affliction common to most adolescents and many adults. It is caused by a mix of clinical conditions affecting the pilosebaceous unit, comprised of the hair shaft, follicle, and associated sebaceous gland and erector pili muscle. These clinical conditions include: hyperkeratinization (excess keratin cells overlaying the follicle/gland), excess sebum production, presence and proliferation of *Propionibacterium acnes,* and inflammation. Pure Australian Tea Tree Oil provides a natural alternative for the treatment of these conditions due to its antimicrobial and anti-inflammatory properties.

One clinical study to assess the efficacy of Tea Tree Oil in the treatment of acne was conducted by Basset *et al.* (1990). The study performed a blinded, randomized clinical trial on 124 patients to evaluate the efficacy and skin tolerance of a 5% Tea Tree Oil gel against a 5% benzoyl peroxide lotion. Basset *et al.* concluded that both treatments had a positive effect in reducing the number of inflamed and non-inflamed lesions, yet the 'onset of action' for the tea tree oil took longer to come into effect.

A randomized clinical study by Enshaieh *et al.* (2007) concluded that topical 5% Tea Tree Oil is an effective treatment for mild to moderate acne vulgaris. A total of 60 patients with mild to moderate acne vulgaris were divided into two groups and treated with Tea Tree Oil gel (n=30) or placebo (n=30). The study was evaluated by the total acne lesions counting (TLC) and acne severity index (ASI). Tea Tree Oil gel was found to be more effective than the placebo – 3.55 times in terms of TLC and 5.75 in terms of ASI. The authors concluded that a topical 5% Tea Tree Oil is an effective treatment for mild to moderate acne vulgaris.

In the Journal of Dermatology, Kwon *et al.* (2014) reported on the comparative results of Tea Tree Oil against a new trial compound from the native Korean plant *Chamaecyparis obtusa*. The authors constructed an eight week, double-blind controlled trial of 34 participants with existing chronic acne (revised Leeds acne score 4.0±1.2; inflammatory lesions, 30.6±10.6). Results of the study confirmed Tea Tree Oil's performance as an effective natural acne treatment, with Leeds acne and inflammation scores achieving statistically significantly reductions at a 4-week trial time period, with further improvements observed between 4



and 8 weeks of treatment. Unfortunately the authors did not detail the composition of the Tea Tree product used, nor did they include a placebo arm to the trial, so it is difficult to deduce the beneficial effect of the Tea Tree Oil product over no treatment.

A study by Malhi *et al*. (2016), published in the Australian Journal of Dermatology also confirmed the use of Australian Tea Tree Oil products to significantly improve mild to moderate acne. In an open-label uncontrolled phase II pilot study, 18 participants were divided into two study arms applying Tea Tree Oil gel (200mg/g) and face wash (7mg/g) to their face daily. They were assessed after a 4, 8 and 12 week period. The mean total lesion counts were 23.7 at baseline, 17.2 at 4, 15.1 at 8 and 10.7 at 12 weeks. The authors concluded that the use of Tea Tree Oil products significantly improved mild to moderate acne and that the products were well tolerated.

When formulating with Tea Tree Oil for effective acne treatments, not only the concentration but the pH and product format should be considered. Biju *et al*. (2004) conducted an *ex-vivo* dermal study to understand the adsorption rate of Tea Tree Oil components. They used multiple methods to quantify the differential concentration of Tea Tree Oil via different forms of delivery – colloidal bed, microemulsion, multiple emulsion, and liposomal dispersion. The colloidal bed format showed the best follicular adsorption score at 0.43±0.01mg TTO/g sebum plug, followed closely by the microemulsion method (0.41±0.009). The other two formats showed significantly lower concentrations (0.21 and 0.16, respectively). This study demonstrates the need to consider the delivery format, optimal pH, as well as ingredient concentration in developing effective formulations.

Overall, Tea Tree Oil offers effective and demonstrated relief from the symptoms leading to acne. It is mild on the skin and presents little to no irritancy nor skin sensitization at effective concentrations under 10% (Grieg *et al*., 1999).

A Note about Pure Australian Tea Tree Oil

All references in this paper have used 100% Pure Australian Tea Tree Oil.

Tea Tree Oil is a natural compound known as an essential oil, which is steam distilled from the leaves of the *Melaleuca alternifolia* tree. The properties of Tea Tree Oil are documented in the standard ISO4730. This standard details the acceptable percent range of the 15 most common components as well as physical parameters including optical rotation and specific gravity. Research into this native Australian essential oil has determined a combination of 113 different compounds, which contribute to the many ways in which Tea Tree Oil yields its antimicrobial efficacy. In effect, bacteria are unable to adapt given Tea Tree Oil's many different mechanisms of activity.

As Tea Tree Oil has become more popular, adulterated versions of this oil have appeared on the market. These versions are often comprised of compounds from other industrial, sometimes waste, processes. There are documented safety issues, including burns and allergic reactions, with adulterated Tea Tree Oil which do not occur with Pure Australian Tea Tree Oil. **To combat this, an updated ISO standard will be released in 2016, tightening the acceptable component ranges and incorporating a simple and inexpensive method to identify adulteration, called Chiral Testing. Contact Down Under Enterprises to obtain a White Paper on the new ISO Standard and Chiral Testing.**

The Australian Tea Tree Industry Association (www.ATTIA.org) offers a wealth of information on the beneficial use of Pure Australian Tea Tree Oil. Their Code of Practice (COP) is a documented quality system which covers the entire production, processing, and packaging of Tea Tree Oil. COP-certified producers and distributors undergo annual audits. Approved organizations, including Down Under Enterprises, may display the ATTIA COP logo.

References:

Bassett IB, Pannowitz DL, Barnetson RS, 1990, A comparative study of tea-tree oil versus benzoyl peroxide in the treatment of acne. *Medical Journal Australia,* 153(8)455-8.

Bassolé IHN, Juliani HR, 2012, Essential Oils in Combination and Their Antimicrobial Properties. *Molecules*, 17(12)3989–4006.

Biju SS, Ahuja A, Khar RK, 2005, Tea tree oil concentration in follicular casts after topical delivery: determination by high-performance thin layer chromatography using a perfused bovine udder model. *J Pharm Sci*, 94(2)240-5.

Biju SS, Ahuja A, Khar RK, 2005, Formulation and evaluation of an effective pH balanced topical antimicrobial product containing tea tree oil. *Pharmazie*, 60(1)208-11.

Carson CF, Hammer KA, Riley TV, 2006, *Melaleuca alternifolia* (Tea Tree) Oil: a Review of Antimicrobial and Other Medicinal Properties. *Clinical Microbiology Reviews*, 19(1)50-62.

Enshaieh S, Jooya A, Siadat AH, Iraji F, 2006, The efficacy of 5% topical tea tree gel in mild to moderate acne vulgaris: A randomized, double-blind placebo-controlled study. *Indian J Dermatol*, 73(1)22-25.

FDA Consumer Health Information, 2013, FDA Taking a Closer Look at 'Antibacterial' Soap, US Food and Drug Administration.

Gemmer CM, DeAngelis YM, Theelen B, Boekhout T, Dawson, Jr. TL, 2002, Fast, Noninvasive Method for Molecular Detection and Differentiation of *Malassezia* Yeast Species on Human Skin and Application of the Method to Dandruff Microbiology. *J Clin Microbiol*, 40(9)3350–3357.

Greig JE, Carson CF, Stuckey MS, Riley TJ, 1999, Skin sensitivity testing for tea tree oil, Australian Government RIRDC Publication No 99/076.

Grimalt R, 2007, A Practical Guide to Scalp Disorders. *J Invest Derm Symp Proc,* 12(2)10-14.

Hammer KA, Carson CF, Riley TV, 1996, Susceptibility of transient and commensal skin flora to the essential oil of *Melaleuca alternifolia* (tea tree oil). *American Journal of Infection Control*, 24(3)186-9.

Hammer KA, Carson CF, Riley TV, 2008, Frequencies of resistance to Melaleuca alternifolia (tea tree) oil and rifampicin in *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Enterococcus faecalis*. *Int J Antimicrob Agents,* 32(2)170-3.

Hammer KA, Carson CF, Riley TV, 2011, Effects of *Melaleuca alternifolia* (tea tree) essential oil and the major monoterpene component terpinene-4-ol on the development of the single-and multi-step antibiotic resistance and antimicrobial susceptibility. *Antimicrobial Agents and Chemotherapy*, 56(2)909-915.

Kwon HH, Yoon JY, Park SY, Min S, 2014, Comparison of Clinical and Histological Effects between *Lactobacillus*-Fermented *Chamaecyparis obtusa* and Tea Tree Oil for the Treatment of Acne: An-Eight Week Double-Blind Randomized Controlled Split-Face Study. *Journal of Dermatology,* 229(2)102-9.

Malhi, HK, Tu J, Riley T, Kumarasinghe SP, Hammar KA, 2016, Tea tree oil gel for mild to moderate acne; a 12 week uncontrolled, open-label phase II pilot study. *Australas J Dermatol,* 57(2).

McMahon MAS, Blair IS, McDowell DA, 2007, Habituation to sub-lethal concentrations of tea tree oil *(Melaleuca alternifolia)* is associated with reduced susceptibility to antibiotics in human pathogens. *Journal of Antimicrobial Chemotherapy.* 59(1)125-127.

Messager S, Hammer KA, Carson CF, Riley TV, 2004, Effectiveness of hand-cleansing formulations containing tea tree oil assessed ex vivo on human skin and in vivo with volunteers using European standard EN 1499. *J Hosp Infect,* 59(1)220-28.

Messager S, Hammer KA, Carson CF, Riley TV, 2005, Assessment of the antibacterial activity of tea tree oil using the European EN 1276 and EN 12054 standard suspension tests. *J Hosp Infect,* 59(1)113–25.

Nenoff P, Haustein UF, Brandt W, 1996, Antifungal activity of the essential oil of *Melaleuca alternifolia* (tea tree oil) against pathogenic fungi in vitro. *Skin Pharmacol,* 9(6)388-394.

Pooja A, Arun N, Maninder K, 2013, Screening of plant essential oils for antifungal activity against *Malassezia furfur*. *International Journal of Pharmacy and Pharmaceutical Science,* 5(2)70.

Ravichandran G, Bharadwaj VS, Kolhapure SA, 2004, Evaluation of the clinical efficacy and safety of "Anti-Dandruff Shampoo" in the treatment of dandruff, *The Antiseptic,* 201(1) 5-8.

Riley TV, 2003, Antimicrobial activity of tea tree oil against oral microorganisms, *RIRDC Report,* Publication number 03/019.

Santamaria Jr. M, Petermann KD, Vedoveloo SA, Degan V, Lucato A, Franzini CM, 2014, Antimicrobial effect of *Melaleuca alternifolia* dental gel in orthodontic patients. *Am J Orthod Dentofacial Orthop*, 145(1)198-202.

Satchell AC, Saurajen A, Bell C, Barnetson RS, 2002, Treatment of dandruff with 5% tea tree oil shampoo. *Journal of the American Academy of Dermatology,* 47(6)852-855.

Thomsen NA, Hammer KA, Riley TV, Carson CF, 2013, Effect of habituation of tea tree *(Melaleuca alternifolia)* oil on the subsequent susceptibility of *Staphylococcus spp*. to antimicrobials, tricolosan, tea tree oil, terpinene-4-ol

About Us

For over 15 years, Down Under Enterprises has focused on three key goals: provide the best quality essential oils and native Australian ingredients; provide these ingredients directly from the plantation (our family and friends); and, with an exceptional level of customer service. We must be doing something right because we have fantastic customers – true partners – whom we have been working with for years – and adding more every day. For us, it is much more than the sale, it is about taking a holistic approach to building and maintaining long term relationships.

We love what we do and love helping our customers achieve their goals. Down Under Enterprises is dedicated to delivering quality, native Australian ingredients to the world.

We offer Certificates of Analysis on every batch of product we sell, our systems enable full supply chain traceability, and we adamantly support efforts to stamp out adulteration.

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