



**Australian Government**  

---

**Rural Industries Research and  
Development Corporation**

Compilation and Review of  
**Published and Unpublished  
Tea Tree Oil Literature**

A report for the Rural Industries Research  
and Development Corporation

by CF Carson, KA Hammer, TV Riley

September 2005

RIRDC Publication No 05/151  
RIRDC Project No UWA-75A

© 2005 Rural Industries Research and Development Corporation.  
All rights reserved.

ISBN 1 74151 214 X  
ISSN 1440-6845

***Compilation and Review of Published and Unpublished Tea Tree Oil Literature***

*Publication No. 05/151*

*Project No. UWA-75A*

The views expressed and the conclusions reached in this publication are those of the author and not necessarily those of persons consulted. RIRDC shall not be responsible in any way whatsoever to any person who relies in whole or in part on the contents of this report.

This publication is copyright. However, RIRDC encourages wide dissemination of its research, providing the Corporation is clearly acknowledged. For any other enquiries concerning reproduction, contact the Publications Manager on phone 02 6272 3186.

**Researcher Contact Details**

TV Riley  
Microbiology (M502)  
School of Biomedical and Chemical Sciences  
The University of Western Australia  
35 Stirling Hwy  
Crawley WA 6009  
Australia

Phone: (08) 9346 3690

Fax: (08) 9346 2912

Email: [triley@cyllene.uwa.edu.au](mailto:triley@cyllene.uwa.edu.au)

In submitting this report, the researcher has agreed to RIRDC publishing this material in its edited form.

**RIRDC Contact Details**

Rural Industries Research and Development Corporation  
Level 1, AMA House  
42 Macquarie Street  
BARTON ACT 2600  
PO Box 4776  
KINGSTON ACT 2604

Phone: 02 6272 4539

Fax: 02 6272 5877

Email: [rirdc@rirdc.gov.au](mailto:rirdc@rirdc.gov.au)

Website: <http://www.rirdc.gov.au>

Published in September 2005  
Printed on environmentally friendly paper by Union Offset

# Foreword

The aim of this project was to assess, compile and review the available published and unpublished data on tea tree oil. This information is presented in the form of a Database of Tea Tree Oil Literature, a review of the literature for publication in a scientific journal and a Material Safety Data Sheet appropriate for use by all suppliers of tea tree oil.

There are now many scientific publications describing many aspects of tea tree oil, ranging from tree breeding, harvesting and oil distillation to its effectiveness in reducing inflammation, treating dandruff and cold sores. However, much of this scientific literature is not readily accessible for industry stakeholders. Similarly, no significant compilation and review of the data has occurred recently, meaning that areas of research that have been overlooked are not obvious. Finally, the compilation of available data into a standard tea tree oil Material Safety Data Sheet is useful to all industry stakeholders in the tea tree oil industry.

This report includes a review of the available tea tree oil literature (including eco-toxicity), a tea tree oil literature database, and a Material Safety Data Sheet created for tea tree oil.

This project was funded from industry revenue which is matched by funds provided by the Australian Government. This report, a new addition to RIRDC's diverse range of over 1500 research publications, forms part of our Tea tree oil R&D Program, which aims to support the continued development of a profitable tea tree oil industry.

Most of our publications are available for viewing, downloading or purchasing online through our website:

- downloads at [www.rirc.gov.au/reports/Index.htm](http://www.rirc.gov.au/reports/Index.htm)
- purchases at [www.rirc.gov.au/eshop](http://www.rirc.gov.au/eshop)

## **Peter O'Brien**

Managing Director  
Rural Industries Research and Development Corporation

# Acknowledgments

We would like to acknowledge the many publishers and authors who gave their permission to reproduce tea tree oil publications in the literature database. We are also grateful to The University of Western Australia and the Western Australian Centre for Pathology and Medical Research for institutional support.

## Abbreviations

---

|                   |  |
|-------------------|--|
| h                 | hour   |
| l                 | litre  |
| LC <sub>50</sub>  | Concentration per litre of aqueous solution lethal to 50% of test organisms  |
| LD <sub>50</sub>  | Dose per kilogram of body weight that is lethal to 50% of test organisms     |
| LC <sub>0</sub>   | Concentration per litre of aqueous solution lethal to 0% of test organisms   |
| LC <sub>100</sub> | Concentration per litre of aqueous solution lethal to 100% of test organisms |
| μ l               | microlitre   |
| min               | minute   |
| mg                | milligrams   |
| MSDS              | Material safety data sheet   |
| PDF               | portable document file   |
| ppm               | parts per million  |

---

# Contents

|  |     |
|--|-----|
| Foreword.....  | iii |
| Acknowledgments.....   | iv  |
| Abbreviations.....   | iv  |
| Executive Summary .....  | vii |
| Chapter 1. Introduction.....                                     | 1   |
| Chapter 2. Objectives.....                                       | 2   |
| Chapter 3. Review of literature.....                             | 3   |
| Chapter 4. Review of tea tree oil ecotoxicity data .....         | 20  |
| 4.1 Acute toxicity of tea tree oil to aquatic organisms .....    | 20  |
| 4.2 Acute toxicity of tea tree oil to terrestrial insects.....   | 23  |
| 4.3 Other acute toxicity data.....                               | 25  |
| 4.4 Conclusions .....  | 25  |
| Chapter 5. Literature Database .....                             | 26  |
| 5.1 Methods.....   | 26  |
| 5.2 Results .....  | 27  |
| Chapter 6. Material safety data sheet.....                       | 28  |
| Chapter 7. Recommendations for further studies .....             | 29  |
| References .....   | 30  |
| Appendix 1 – Literature database .....                           | 40  |
| Appendix 2 – Responses of publishers to permission requests..... | 66  |
| Appendix 3 – Material Safety Data Sheet .....                    | 72  |



# Executive Summary

The body of literature about tea tree (*Melaleuca alternifolia*) oil has grown dramatically over the last 10 years as a number of Australian and international researchers investigate tea tree oil. Collectively, their results represent a significant advance in our knowledge of tea tree oil and its properties. The inclusion of a literature review in this report is therefore a timely contribution to our understanding of tea tree oil.

The tea tree oil literature was reviewed focusing on the more recent literature but incorporating older publications for historical perspective. This review article will be published in a peer-review scientific journal and will be a significant benefit to the tea tree oil industry as it strives to establish tea tree oil as a bona fide alternative therapeutic agent.

The ecotoxicity of tea tree oil was reviewed. However, since very little data are available describing the ecotoxicity of tea tree oil, information from secondary related sources was sought. Data pertaining to the ecotoxicity of other essential oils and essential oil components against various aquatic and terrestrial vertebrates and invertebrates were compiled and reviewed. While these data may not substitute for tea tree oil data, they can guide and inform future ecotoxicity studies. This area of tea tree oil research has not received adequate attention.

The tea tree oil literature was compiled into a database designed to be accessible via the internet, potentially through the ATTIA web site. More than 500 tea tree oil publications were found, including research articles, reviews, conference abstracts or presentations, books and theses. Over 100 requests were made to publishers for copyright permissions to reproduce articles in full. In many cases this was granted or permission was granted to reproduce abstracts only. The availability of such a collection to industry stakeholders is unique and should facilitate greater appreciation of the work that has been done to date and the areas that require more attention.

A Material Safety Data Sheet (MSDS) was compiled from scientific publications, industry documents and various regulatory codes. This represents the most up to date and comprehensive MSDS available for tea tree oil. It is designed for universal application throughout the tea tree oil industry and will be of significant benefit to tea tree oil exporters. It may also enhance the standing of ATTIA to stakeholders, purchasers and regulatory agencies.

The collection and evaluation of all of this literature, and the construction of the MSDS made it possible to identify areas of research that have been overlooked or neglected, and to make recommendations regarding future tea tree oil studies. The two areas that require significant further work fall into two broad categories; (1) Safety and toxicity and (2) Clinical efficacy. Expansion of research in these two areas is an absolute requirement for further regulatory approvals for tea tree oil.

In conclusion, the contents of this report represent a unique collection and digest of the existing tea tree oil literature. This report should help industry stakeholders have a better understanding of the state of tea tree oil research and development.



# Chapter 1. Introduction

Compared to the early 1990's, there is now an extraordinary amount of literature available describing the properties of tea tree oil. In particular, ATTIA and industry participants have compiled an extensive collection of tea tree oil literature. However, the usefulness of these data collections could be significantly enhanced, as described below.

The existing scientific literature are somewhat incomplete and are not readily accessible to most industry stakeholders. A comprehensive collection of tea tree oil literature in the form of an electronic database would therefore be extremely valuable. Furthermore, the availability of the database to industry stakeholders would be a valuable resource for the industry.

As a natural extension of this, a collation and review of the safety, toxicity and eco-toxicology data is required. This could reduce or eliminate future duplication of effort, and highlight areas of research that have been overlooked. Since these areas of oversight are likely to be numerous, a review is unlikely to reduce research expenditures for the industry but will at least allow the industry to focus their limited resources on areas of priority.

Preparation of generic Material Safety Data Sheet (MSDS) for TTO suitable for multiple importing destinations will be of significant benefit to tea tree oil exporters. It could also enhance the standing of ATTIA to stakeholders, purchasers and regulatory agencies. The preparation of the MSDS may also highlight areas of research or inquiry that require further work.

In conclusion, despite the amount of literature available on tea tree oil, data have not been compiled into a readily accessible format for industry participants. The benefits of a review and compilation of tea tree oil literature to industry are numerous, and the preparation of an up-to-date, generic MSDS may simplify matters for both Australian exporters and overseas importers.

# Chapter 2. Objectives

The objectives of this work, in order of priority, are:

1. A review published in a peer-reviewed journal and for RIRDC of the following for TTO: safety and toxicity, clinical efficacy
2. An assessment and/or review of the eco-toxicology of TTO based on direct and indirect data. If sufficient data are available a review will be published in a peer-reviewed journal and RIRDC report.
3. Conversion of tea tree oil literature into an electronic resource for researchers, industry participants and stakeholders
4. Production of a Material Safety Data Sheet (MSDS) suitable for multiple importing destinations
5. Written recommendation for future TTO studies

# Chapter 3. Review of literature

## Tea tree oil

Many complementary and alternative medicines have enjoyed increased popularity in recent decades. Efforts to justify their use have seen their putative biological properties come under increasing scrutiny *in vitro* and, in some cases, *in vivo*. One such product is tea tree oil (TTO), the volatile essential oil derived mainly from the Australian native plant *Melaleuca alternifolia*. Employed largely for its antimicrobial properties, TTO is incorporated as the active ingredient in many topical formulations used to treat cutaneous infections. It is widely available over-the-counter in Australia, Europe and North America and is marketed as a remedy for various ailments.

## Composition and chemistry

TTO is composed of terpene hydrocarbons, mainly monoterpenes, sesquiterpenes and their associated alcohols. Terpenes are volatile, aromatic hydrocarbons and may be considered as polymers of isoprene which has the formula  $C_5H_8$  (Sharp, 1983). Early reports on the composition of TTO described 12 (Guenther, 1968), 21 (Laakso, 1965 cited in Altman, 1988) and 48 (Swords & Hunter, 1978) components. The seminal paper by Brophy and colleagues (1989) examined over 800 TTO samples by gas chromatography and gas chromatography mass spectrometry and reported approximately 100 components and their range of concentrations. Given the scope for variation, it is fortunate that the composition of oil sold as TTO is regulated by an international standard for “Oil of *Melaleuca* –terpinen-4-ol type” which sets maxima and/or minima for 14 components of the oil (International Organisation for Standardisation, 1996) (see Table 3.1). Notably the standard does not dictate the species of *Melaleuca* from which the TTO must be sourced. Instead, it sets out physical and chemical criteria for the desired chemotype. There are several varieties, or chemotypes, of *M. alternifolia* and each produces oil with a distinct chemical composition. Six chemotypes have been described as follows: terpinen-4-ol chemotype (1), terpinolene chemotype (2), and four 1,8-cineole chemotypes (3-6) (Homer *et al.*, 2000). The terpinen-4-ol chemotype typically contains levels of terpinen-4-ol of between 30-40% (Homer *et al.*, 2000) and is the chemotype used in commercial TTO production. This is the chemotype that will be discussed below. The components specified by the standard were selected for a variety of reasons including biological activity and provenance verification. For example, terpinen-4-ol is a major component of TTO and has long been considered the main antimicrobial component of the oil. Consequently, to optimise antimicrobial activity, a lower limit of 30% and no upper limit were set for terpinen-4-ol content. An upper limit of 15% and no lower limit were set for 1,8-cineole, although the rationale for this may not have been entirely sound; for many years cineole was erroneously considered to be a skin and mucous membrane irritant fuelling efforts to minimise its level in TTO. Recent work soundly refutes this notion but since cineole levels are usually inversely proportional to terpinen-4-ol levels, minimising cineole content in order to maximise terpinen-4-ol content remains an important consideration.

Despite the scope for batch to batch variation in TTO, no obvious differences in its bioactivity have been noted so far. The suggestion that oil from a particular *M. alternifolia* clone possesses enhanced cidal activity has been made (May *et al.*, 2000) but the evidence is not compelling.

TTO has a relative density of 0.885-0.906 (International Organisation for Standardisation, 1996), is only sparingly soluble in water and is miscible with non-polar solvents. Some of the chemical and physical properties of TTO components are shown in Table 3.2.

The composition of TTO may change considerably during storage with  $\rho$ -cymene levels increasing and  $\alpha$ - and  $\gamma$ -terpinene levels declining (Brophy *et al.*, 1989). Light, heat, exposure to air and

moisture all affect oil stability and TTO should be stored in dark, cool, dry conditions preferably in a vessel that contains little air.

## Provenance and nomenclature

The provenance of TTO is not always clear from its common name or those of its sources. It is known by a number of synonyms including “melaleuca oil” and “ti tree oil”, “ti tree” being a Maori and Samoan common name for plants in the genus *Cordyline* (Weiss, 1997). Even the term “melaleuca oil” is potentially ambiguous since several chemically distinct oils are distilled from other *Melaleuca* species such as cajuput oil (also cajeput or cajaput) from *M. cajuputi* and niaouli oil from *M. quinquenervia* (often misidentified as *M. viridiflora*) (Lassak and McCarthy, 1983; Southwell & Lowe, 1999). However, the term has been adopted by the Australian Therapeutic Goods Administration as the official name for TTO. The use of common plant names further confounds the issue. In Australia, “tea trees” are also known as “paperbark trees” and collectively these terms may refer to species in the *Melaleuca* or *Leptospermum* genera of which there are several hundred. For instance, common names for *M. cajuputi* include “swamp tea tree” and “paperbark tea tree” while those for *M. quinquenervia* include “broad-leaved tea tree” and “broad-leaved paperbark” (Lassak & McCarthy, 1983). Many *Leptospermum* species are cultivated as ornamental plants and are often mistakenly identified as the source of TTO. In addition, the essential oil kanuka and manuka derived from the New Zealand plants *Kunzea ericoides* and *Leptospermum scoparium*, respectively, are referred to as New Zealand TTOs (Christoph *et al.*, 2000) although they are very different in composition from Australian TTO (Perry *et al.*, 1997). In this review article, the term TTO will refer only to the oil of *M. alternifolia*.

As explained above, the international standard for TTO does not specify which *Melaleuca* species must be used to produce oil. Rather it sets out the requirements for an oil chemotype. Oils that meet the requirements of the standard have been distilled from *Melaleuca* species other than *M. alternifolia* including *M. dissitiflora*, *M. linariifolia* and *M. uncinata* (Murtagh, 1999). However, in practice commercial TTO is produced from *M. alternifolia* (Maiden and Betche) Cheel. The *Melaleuca* genus belongs to the Myrtaceae family and contains approximately 230 species almost all of which are native to Australia (Craven, 1999). When left to grow naturally, *M. alternifolia* grows to a tree reaching heights of approximately 5-8 metres (Colton & Murtagh, 1999). Trees older than three years flower typically in October and November (Lassak & McCarthy, 1983, Baker, 1999) and flowers are produced in loose, white to creamy coloured terminal spikes, which can give trees a “fluffy” appearance (Weiss, 1997).

## Commercial production

The commercial TTO industry was born after its medicinal properties were first reported by Penfold in the 1920s as part of a larger survey into Australian essential oils with economic potential. During that nascent stage, TTO was produced from natural bush stands of plants, ostensibly *M. alternifolia*, that produced oil with the appropriate chemotype. The native habitat of *M. alternifolia* is low-lying, swampy, sub-tropical, coastal ground around the Clarence and Richmond Rivers in north-eastern New South Wales and southern Queensland (Swords & Hunter, 1978) and, unlike several other *Melaleuca* species, it does not occur naturally outside Australia. The plant material was hand-cut and often distilled on the spot in make-shift, mobile, wood-fired bush stills. The industry continued in this fashion for several decades. Legend has it that the oil was considered so important for its medicinal uses that Australian soldiers were supplied oil as part of their military kits during World War II and that bush-cutters were exempt from national service (Carson & Riley, 1993). However, no evidence to corroborate these accounts could be found (A.-M Conde & M. Pollard, Australian War Memorial, Canberra, Australia, personal communication). Production ebbed after World War II as demand for the oil declined presumably due to the development of effective antibiotics and the waning image of natural products. Interest in the oil was rekindled in the 1970s as part of the general renaissance in natural products. Commercial plantations were established in the 1970s and 1980s allowing the industry to mechanise and produce large quantities of a consistent product (Brophy *et*

*al.*, 1989; Johns *et al.*, 1992). Today there are plantations in Western Australia, Queensland and New South Wales although the majority is in New South Wales around the Lismore region. Typically, plantations are established from seedlings sowed and raised in greenhouses prior to planting out in the field at high density. The time to first harvest varies from 1-3 years depending on the climate and rate of plant growth. Harvesting is by a coppicing process in which the whole plant is cut off close to ground level and chipped into smaller fragments prior to oil extraction.

### **Oil extraction**

TTO is produced by steam distillation of the leaves and terminal branches of *M. alternifolia*. Once condensed, the clear to pale yellow oil is separated from the aqueous distillate. The yield of oil is typically 1-2% of the wet weight of the plant material. Alternative extraction methods have been considered including those using microwave technology but none has been utilised on a commercial scale.

### **Antimicrobial activity**

Of all the properties claimed for TTO, it is those regarding antimicrobial activity that have received the most attention. The earliest reported use of the *M. alternifolia* plant that presumably exploited this property is the traditional use by the Bundjalung Aborigines of northern New South Wales. Crushed leaves of “tea trees” were inhaled to treat coughs and colds, or were sprinkled on wounds after which a poultice was applied (Shemesh & Mayo, 1991). In addition, tea tree leaves were soaked to make an infusion to treat sore throats or skin ailments (Low, 1990; Shemesh & Mayo, 1991). The oral history of Australian Aborigines also tells of healing lakes which were lagoons into which *M. alternifolia* leaves had fallen and decayed over time (Altman, 1988). Use of the oil itself, as opposed to the unextracted plant material, did not become common practice until Penfold published the first reports of its antimicrobial activity in a series of papers in the 1920s and 1930s. In evaluating the antimicrobial activity of *M. alternifolia* oil and other oils, he made comparisons with the disinfectant carbolic acid or phenol, the gold standard of the day, in a test known as the Rideal-Walker (RW) coefficient. TTO’s activity was compared directly with that of phenol and rated at 11 times as active (Penfold & Grant, 1925). The RW coefficient of several of the components of TTO were also reported including cineole (3.5) and cymene (8) (Penfold & Grant, 1923), linalool (13) (Penfold & Grant, 1924), terpinen-4-ol (13.5) and terpineol (16) (Penfold & Grant, 1925). As a result, TTO was promoted as a therapeutic agent (Anon., 1930; Anon., 1933a; Anon., 1933b). It must be mentioned that in terms of the evidence they provide for the medicinal properties of TTO, these and many other early publications (Humphery, 1930; MacDonald, 1930; Halford, 1936; Penfold & Morrison, 1946; Feinblatt, 1960; Peña, 1962) are of limited value since by today’s standards the data they provide are mostly anecdotal.

In contrast, contemporary data clearly show that the broad-spectrum antimicrobial activity of TTO includes antibacterial, antifungal, antiviral and anti-protozoal activity. Not all the activity has been characterised well in vitro and in the few cases where in vivo work has been done, data are promising but thus far inadequate. In vitro, methodological issues have plagued evaluation of the oil’s antimicrobial activity since the lipophilic oil does not lend itself to standard aqueous test systems. Despite this, considerable work has been done, particularly on the antibacterial activity of the oil.

### **Antibacterial activity**

Evaluation of the antimicrobial activity of TTO has been impeded by its physical properties; TTO is only sparingly soluble in water and this limits its miscibility in test media. The solubility of several components of TTO is shown in Table 3.2. Different strategies have been used to counteract this problem, the addition of surfactants to broth and agar test media being used most widely (Atkinson & Brice, 1955; Beylier, 1979; Carson *et al.*, 1995a,b; Griffin, Markham & Leach, 2000; Banes-Marshall *et al.*, 2001). Dispersion of TTO in liquid media usually results in a turbid suspension that makes determination of endpoints in susceptibility tests difficult. Occasionally dyes have been used as

visual indicators of the MIC with mixed success (Chand *et al.*, 1994; Carson *et al.*, 1995a,b Mann & Markham, 1998).

TTO has been tested *in vitro* against a wide variety of bacteria. Only a few reports of the antibacterial activity of TTO appear in the literature from 1940 to the 1980s. The earliest of these was published by Atkinson and Brice (1955), who assessed plants of the Myrtaceae family for antibacterial activity by both agar and broth dilution assays. Antibacterial titres (% v/v) as determined by agar and broth dilution assays were 0.63 and 0.31, respectively, for *Staphylococcus aureus*, 1.25 and 0.24 for *Salmonella typhi* and 0.31 and 0.10 for *Mycobacterium phlei* (Atkinson & Brice, 1955). Similarly, Low *et al.* (1974) described the antibacterial activity of a number of essential oils from the Myrtaceae family. They used the agar dilution method of Atkinson and Brice and found MICs (% v/v) of 0.062 for *S. aureus* and 0.031 for *Salm. typhi*. They also used an assay where test organisms were exposed to each neat essential oil for 10 minutes only, after which viable organisms were recovered. With *M. alternifolia* oil, *S. aureus* could not be recovered whereas viable *Pseudomonas aeruginosa* were recovered (Low *et al.*, 1974).

In the study by Beylier (1979), more than 100 oils were initially examined for antimicrobial activity, and 10 of these (including *M. alternifolia* oil) were selected for further investigation. The MIC (% v/v) ranges were 0.25 - 0.5 for *S. aureus*, 0.125 - 0.25 for *Escherichia coli* and 4 for *P. aeruginosa* (Beylier, 1979). MICs for *Candida albicans* and *Aspergillus niger* were also determined in this study and these will be discussed below.

Walsh and Longstaff (1987) used both broth and agar dilution methods to assess 'Melasol', a product containing 40% TTO, 13% isopropyl alcohol and 47% water, for activity against oral pathogens. MICs (% v/v) of Melasol were 0.08 for *S. aureus*, 0.16 for *Streptococcus faecalis*, 0.16 for *P. aeruginosa* and 0.08 for *E. coli*, by the agar method (Walsh & Longstaff, 1987). These MICs are low compared to those obtained in the previous studies, especially considering that Melasol contains only 40% TTO, however, the alcohol in the solution may have accounted for this activity. A range of oral microorganisms, such as *Actinomyces viscosus*, *Bacteroides gingivalis*, *Eikenella corrodens* and *Strep. mutans*, was tested also and MICs ranged from 0.02 - 0.08% (Walsh & Longstaff, 1987).

From the early 1990s onwards, many reports detailing the antimicrobial activity of TTO have appeared in the scientific literature. Although there was still a degree of discrepancy between the methods used in the different publications, often the MIC values reported were relatively similar. A summary of some of the published *in vitro* susceptibility data for bacteria is shown in Table 3.3. The majority of MICs and MBCs are in the range of 0.06% - 1.0%, however, MICs of more than 2% have been reported for some commensal skin staphylococci and micrococci, *Enterococcus faecalis* and *P. aeruginosa* (Hammer *et al.*, 1996; Banes-Marshall *et al.*, 2001).

The activity of TTO against antibiotic-resistant bacteria has attracted considerable attention with methicillin-resistant *S. aureus* (MRSA) receiving the most attention thus far. Since the potential to use TTO against MRSA was first hypothesised (Walsh & Longstaff, 1987), several groups have evaluated the activity of TTO against MRSA beginning with Carson *et al.* (1995a) who examined 64 MRSA from Australia and the United Kingdom, including 33 mupirocin-resistant isolates. The MIC and MBC of the Australian isolates were 0.25% and 0.5%, respectively, while those for the UK isolates were 0.312% and 0.625%, respectively. Subsequent reports on the susceptibility of MRSA to TTO have given similar results (Nelson, 1997; Chan & Loudon, 1998; Elsom & Hide, 1999; May *et al.*, 2000; Hada *et al.*, 2001).

### **Resistance to TTO**

Decreased susceptibility to TTO has been reported for a number of bacteria including *P. aeruginosa* (Hammer *et al.*, 1996; Griffin *et al.*, 2000, Banes-Marshall *et al.*, 2001). The mechanism by which *P. aeruginosa* tolerates higher concentrations of TTO has begun to be explored and appears to be

associated with the outer membrane (Mann, Cox & Markham, 2000; Griffin, Wyllie & Markham, 2001).

Resistance to TTO *per se* has not been reported despite medicinal use of the oil in Australia since the 1920s. However, the question of whether or not true resistance to TTO can be induced *in vitro* or may occur spontaneously *in vivo* remains unanswered. It is possible that the multi-component nature of TTO may reduce the potential for resistance to occur spontaneously since multiple simultaneous mutations may be required to overcome all the antimicrobial components of TTO. These are important issues if TTO is to be used more widely, particularly against antibiotic-resistant organisms. There has been one report of induced resistance to TTO in *S. aureus* (Nelson, 2000) where stepwise exposure of five MRSA isolates to increasing TTO concentrations yielded three isolates whose MIC had risen to 1% and one isolate each whose MIC had increased to 2% and 16% TTO. All isolates had initial MICs of 0.25%. There has also been one report suggesting that *E. coli* which harbour mutations in the multiple antibiotic resistance (*mar*) operon, so-called Mar mutants, may exhibit decreased susceptibility to TTO. However, the decrease in susceptibility seen in this work by time-kill and broth dilution methods was marginal and cannot be considered strong evidence of this phenomenon (Gustafson *et al.*, 2001), although it remains feasible and more data should be sought.

### ***Mechanism of antibacterial action***

The mechanism of action of TTO has now been partly elucidated. Prior to the availability of data, assumptions about its mechanism of action were made on the basis of its hydrocarbon structure and attendant lipophilicity. Hydrocarbons partition preferentially into biological membranes and disrupt their vital functions (Sikkema, deBont & Poolman, 1995) and TTO and its components were presumed to behave in this manner. This premise is further supported by data showing that TTO permeabilises model liposomal systems (Cox *et al.*, 2000). In previous work with hydrocarbons not found in TTO (Jackson & deMoss, 1965; Uribe *et al.*, 1990) and with terpenes found at low concentrations in TTO (Andrews, Parks & Spence, 1980; Uribe, Ramirez & Peña, 1985), lysis and the loss of membrane integrity and function manifested by the leakage of ions and the inhibition of respiration were demonstrated. Treatment of *S. aureus* with TTO precipitates the leakage of potassium ions (Cox *et al.*, 2000; Hada *et al.*, 2003) and 260 nm-absorbing materials (Carson, Mee & Riley, 2002) and inhibits respiration (Cox *et al.*, 2000). TTO also sensitizes previously tolerant cells to sodium chloride (Carson, Mee & Riley, 2002) and produces morphological changes apparent under electron microscopy (Reichling *et al.*, 2002). However, no significant lysis of whole cells was observed by electron microscopy (Reichling *et al.*, 2002) or spectrophotometrically (Carson, Mee & Riley, 2002), no cytoplasmic membrane damage as evidenced by lactate dehydrogenase release could be detected (Reichling *et al.*, 2002) and only modest uptake of propidium iodide was observed (Cox *et al.*, 2001b) after treatment with TTO.

In *E. coli*, detrimental effects on potassium homeostasis (Cox *et al.*, 1998), glucose-dependent respiration (Cox *et al.*, 1998), morphology (Gustafson *et al.*, 1998) and ability to exclude propidium iodide have been observed. A modest loss of 280 nm-absorbing material has also been reported (Cox *et al.*, 2001b). In contrast to the absence of whole cell lysis seen in *S. aureus* treated with TTO, lysis occurs in *E. coli* treated with TTO (Gustafson *et al.*, 1998) and this effect is exacerbated by co-treatment with EDTA (C Carson, unpublished data). All of these effects confirm that TTO compromises the structural and functional integrity of bacterial membranes.

When the effects on *S. aureus* of terpinen-4-ol and  $\alpha$ -terpineol, two of the main antibacterial components of TTO, and 1,8-cineole were examined, none was found to induce autolysis and all were found to cause the leakage of 260 nm-absorbing material and render cells susceptible to sodium chloride (Carson, Mee & Riley, 2002). Interestingly, the greatest effects were seen with 1,8-cineole, a component often considered to be marginally antimicrobial. This raises the possibility that while cineole may not be one of the primary antimicrobial components of TTO, it may permeabilise bacterial membranes and facilitate the entry of other more active components. Little work on the effects of TTO components on cell morphology has been reported. Electron microscopy of terpinen-

4-ol treated *S. aureus* cells (Carson, Mee & Riley, 2002) revealed lesions similar to those seen after TTO treatment (Reichling *et al.*, 2002), including mesosomes.

The loss of viability, inhibition of glucose-dependent respiration and induction of lysis seen after TTO treatment all occur to a greater degree with organisms in the exponential rather than stationary phase of growth (Cox *et al.*, 1997; Gustafson *et al.*, 1998). The increased vulnerability of actively growing cells was also apparent in the greater degree of morphological changes seen in these cells by electron microscopy (Cox *et al.*, 1997). The differences in susceptibility seen with bacteria in different phases of growth suggest that additional targets may be involved.

### *In vivo antibacterial activity*

Despite the increasing amount of in vitro data for bacteria, few in vivo (or clinical) investigations have been performed. Clinical studies investigating the effects of TTO treatment on acne, dental plaque formation and the elimination of MRSA colonisation have been published.

In an investigation of acne treatment, Bassett *et al.* (1990) compared the efficacy of 5% TTO and 5% benzoyl peroxide for therapy, with 58 and 61 evaluable patients in each treatment group, respectively (Bassett *et al.*, 1990). Patients were assessed at commencement, and at 1, 2, and 3 months. Parameters assessed were the numbers of inflamed and non-inflamed lesions, and a grade was given for oiliness, erythema, scaling, pruritis and dryness. The major findings of the study were that both treatments reduced the numbers of inflamed lesions, although benzoyl peroxide performed significantly better than TTO. The benzoyl peroxide group also showed significantly less oiliness than the tea tree group, however the tea tree group showed significantly less scaling, pruritis and dryness. Erythema did not differ between groups. Interestingly, significantly fewer overall side effects were reported by the TTO group (27 of 61 patients) than the benzoyl peroxide group (50 of 63 patients).

A study comparing the effects of mouthwashes containing either approximately 0.34% TTO, 0.1% chlorhexidine or placebo on plaque formation and vitality was performed using eight volunteers (Arweiler *et al.*, 2000). On day zero, volunteers had their teeth professionally cleaned, and for the next four days they rinsed twice daily with one of the treatments and did not clean their teeth in any other manner. Teeth were clinically evaluated on days 1, 2, 3 and 4. Each mouthwash was evaluated in this manner, with a wash-out period of 10 days between the end of one treatment and the beginning of the next. The plaque index and plaque vitality from the TTO mouthwash treatment did not differ from placebo mouthwash on any day, whereas the chlorhexidine mouthwash differed significantly on all days. Thus the TTO treatment was considered ineffective at reducing plaque regrowth or the vitality of plaque organisms (Arweiler *et al.*, 2000). In contrast, a small study evaluating the effect of a 0.2% TTO mouthwash on oral flora suggested that TTO could reduce the number of mutans streptococci, and the total number of oral bacteria and that residual activity maintained these reduced levels for two subsequent weeks (Groppo *et al.*, 2002).

A pilot study conducted by Caelli *et al.* (2000) examined the effectiveness of a 4% TTO nasal ointment and a 5% TTO body wash for the eradication of MRSA carriage, as compared to conventional treatment of mupirocin nasal ointment and Triclosan body wash. Of the 15 patients receiving conventional treatment, two were cleared and eight were chronic carriers at the end of therapy, compared to the tea tree group where five were cleared and three were chronic carriers. In addition, five patients from the conventional treatment group and seven from the TTO group did not complete therapy. Due to the low patient numbers, these differences were not statistically significant, although they indicate that TTO therapy may be effective in decolonising MRSA carriers.

In addition to these clinical studies, there is a single case report of a woman who treated herself successfully with a 5 day course of TTO pessaries after having been clinically diagnosed with bacterial vaginosis (Blackwell, 1991b). Of the three studies described above, two are limited by low

numbers of patients and all have some ambiguous or equivocal outcomes, indicating that much remains unknown about optimising TTO efficacy *in vivo*.

## Antifungal activity

Published studies investigating the antifungal activity of TTO have focussed on assessing either the *in vitro* activity of the oil against medically relevant fungi, or the use of TTO to treat human fungal infections. These studies will be discussed here.

The development of protocols for evaluating the susceptibility of fungi to antifungal agents has lagged behind similar methods that have been developed for bacteria and only recently have standard methods been published for evaluating the *in vitro* activity of antifungal agents (Rex *et al.*, 2001). Prior to the publication of these standard methods, researchers used a variety of different assays to assess *in vitro* activity, which means that data from these studies is often difficult to compare. Another limitation of some of these published studies is that very often only one isolate of a given species is tested in any particular investigation, meaning that generalisations about susceptibility are limited.

A range of yeasts from the genera *Candida*, *Malassezia* and *Trichosporon* are susceptible *in vitro* to concentrations of TTO of less than 1.0%. Since *Candida* yeasts (in particular *C. albicans*) are commonly chosen as test organisms, a moderate amount of susceptibility data are available for these organisms. Individual MICs and MIC<sub>90s</sub> that have been reported for *C. albicans*, by either the broth or agar dilution assay include (%) 0.04 (Beylier, 1979), 0.2 (Griffin, Markham & Leach, 2000), 0.25 (Vazquez *et al.*, 2000), 0.3 (Christoph *et al.*, 2000) and 0.44 (Nenoff *et al.*, 1996). Several other *Candida* species, such as *C. parapsilosis*, *C. glabrata*, *C. tropicalis*, *C. kefyr* and *C. krusei*, have been tested against TTO *in vitro* and MICs ranged from 0.25 to 0.5% and minimum fungicidal concentrations (MFCs) ranged from 0.5 to 1.0% (Vazquez *et al.*, 2000; Banes-Marshall *et al.*, 2001; D'Auria *et al.*, 2001). *Malassezia* yeasts also appear to be susceptible to TTO with MICs in the range of 0.06 – 0.44% (Nenoff *et al.*, 1996; Griffin & Markham, 2000). TTO has activity against single isolates of *T. cutaneatum*, *Schizosaccharomyces pombe* and *Debaromyces hansenii* with MICs of 0.22% (Nenoff *et al.*, 1996), 0.5% and 0.5%, respectively (D'Auria *et al.*, 2001).

Two studies have used the disc diffusion method to investigate the activity of TTO against dermatophytes. In both studies, zones of inhibition were seen adjacent to discs containing either 10 or 20 µl of neat TTO, using isolates of *Epidermophyton floccosum*, *M. audouinii*, *M. canis*, *T. mentagrophytes*, *T. rubrum* and *T. tonsurans* (Ånséhn, 1990; Concha *et al.*, 1998). The exception was one strain of *E. floccosum* which showed no zone of inhibition (Concha *et al.*, 1998). Several studies have investigated the activity of TTO against dermatophytes in more depth and have shown MICs of 0.7% for *E. floccosum* (Christoph *et al.*, 2000), 0.11 – 0.5% for *M. canis* (Nenoff *et al.*, 1996; D'Auria *et al.*, 2001), 0.25% for *M. gypseum* (D'Auria *et al.*, 2001) 0.12 – 0.75% for *T. mentagrophytes* (Bassett *et al.*, 1990; Nenoff *et al.*, 1996; Griffin & Markham, 2000; D'Auria *et al.*, 2001) and 0.12 – 1.0% for *T. rubrum* (Bassett *et al.*, 1990; Nenoff *et al.*, 1996; Griffin & Markham, 2000; D'Auria *et al.*, 2001). MFCs of TTO have been determined as follows; 0.25 – 0.5% for *M. canis* and *T. mentagrophytes*, 0.5% for *M. gypseum* and 0.25 – 1.0% for *T. rubrum* (D'Auria *et al.*, 2001).

Similar to studies performed with the dermatophytes, several methods have been used to investigate the activity of TTO against other filamentous fungi. With a few exceptions, these fungi are susceptible. All isolates of *Aspergillus niger*, *Rhizopus oligosporus* and *Penicillium* spp. showed zones of inhibition to either 20 µl or 35 µl oil on a paper disc (Concha *et al.*, 1998; Chao *et al.*, 2000). MICs for the filamentous fungi, mostly obtained by the agar dilution method, were in the range of 0.2 – 1.0% for isolates of *A. flavus*, *A. niger*, *Penicillium* spp., *Rhizopus* spp. and *Scopulariopsis* spp. (Beylier, 1979; Bassett *et al.*, 1990; Southwell, 1993; Rushton *et al.*, 1997; Christoph *et al.*, 2000; Griffin & Markham, 2000). However, isolates of *A. fumigatus* and *A. nidulans*

were not inhibited at 2% TTO in another study (Vazquez *et al.*, 2000). Fungicidal data for these organisms have not been published.

### *In vivo antifungal activity*

A small number of trials has been published investigating the efficacy of TTO for fungal infections. The earliest of these was by Walker (1972), who published a series of his observations of patients treated with a TTO solution for a range of foot problems, including tinea pedis and onychomycosis. More recently, two comparative trials investigating onychomycosis (Buck *et al.*, 1994; Syed *et al.*, 1999), two investigating tinea pedis (Tong *et al.*, 1992; Satchell *et al.*, 2002b) and one investigating dandruff (Satchell *et al.*, 2002a) have been published. In the first of the onychomycosis trials (Buck *et al.*, 1994), patients were treated twice daily with either neat TTO or 1% clotrimazole solution for a total of 6 months of treatment. After this time, of 64 patients treated with TTO, 18% were culture negative with a total of 60% of participants having full or partial resolution. This compared to the clotrimazole treatment group ( $n = 53$ ) of whom 11% were culture negative and 61% had full or partial resolution. Overall, there were no statistically significant differences between the two treatment groups. The second onychomycosis trial (Syed *et al.*, 1999) compared two creams, one containing 5% TTO alone and the other containing 5% TTO and 2% butenafine, both applied 3 times daily for 8 weeks. At completion of treatment the overall cure rate in patients treated with 5% TTO was 0%, compared to 80% for patients treated with both butenafine and TTO. The observation that TTO may be useful adjunct therapy for onychomycosis has also been made by Klimmek *et al.* (2002).

In the first trial investigating tinea pedis, patients were treated with 10% TTO in sorbolene, 1% tolnaftate or placebo, applied twice daily for 4 weeks (Tong *et al.*, 1992). At completion of treatment, patients treated with TTO had mycological cure and clinical improvement rates of 30% and 65%, respectively. This compares to mycological cure rates of 21% in patients receiving placebo and 85% in patients receiving tolnaftate. Similarly, clinical improvement was seen in 41% of patients receiving placebo and 68% of patients receiving tolnaftate. In the second trial, the efficacy of 25% and 50% TTO solutions in ethanol and polyethylene glycol solutions was evaluated by comparison to treatment with placebo (vehicle) (Satchell *et al.*, 2002b). Patients applied their randomly assigned treatment twice daily for four weeks and were assessed after 2 and 4 weeks of treatment. Marked clinical responses were seen in 72% and 68% of the 25% and 50% TTO treatment groups, respectively, compared to 39% in the placebo group. Similarly, there were mycological cures in 55% and 64% of the 25% and 50% TTO treatment groups, respectively, compared to 31% in the placebo group. Dermatitis occurred in one patient in the 25% TTO group and three patients in the 50% TTO group resulting in the recommendation that 25% TTO be considered an alternative treatment for tinea since it was associated with fewer adverse reactions and was as effective as 50% TTO. These studies highlight the importance of considering the formulation of the TTO product when conducting *in vivo* work, since it is likely that the sorbolene vehicle used in the first trial significantly compromised the antifungal activity of the oil.

The efficacy of TTO in the treatment of mild to moderate dandruff was evaluated in a large, randomised, single-blind, placebo-controlled trial in which patients used their allocated treatment daily for 4 weeks (Satchell *et al.*, 2002a). In this study, the 5% TTO group ( $n = 63$ ) showed statistically significant improvements in the investigator-assessed whole scalp lesion score, total area of involvement score and total severity score, as well as in the patient-assessed itchiness and greasiness scores compared to the placebo group ( $n = 62$ ). There were no serious adverse events in either treatment group and only three patients in the TTO group reported events compared to eight in the placebo group. The data from this trial show that 5% TTO is well-tolerated and appears effective in the treatment of mild to moderate dandruff.

Lastly, a case series of patients using TTO mouthwash for oropharyngeal candidiasis has been published (Jandourek *et al.*, 1998). The 13 patients included in the series were HIV positive patients who had already failed treatment with a 14 day course of oral fluconazole. Patients were treated with

15ml of tea tree solution four times a day for up to 28 days. After treatment of the 12 evaluable patients, two were cured, six were improved, four were unchanged and one patient had deteriorated. Overall, eight patients had a clinical response, and seven had a mycological response. In summarising the outcomes of these trials it seems apparent that treatment with TTO does not elicit a high rate of infection cure. This is most likely due to many factors such as length and frequency of treatment and the formulation of the trial product. In addition, it is believed that onychomycosis is unresponsive to topical treatment therefore a high rate of cure should not be expected (Weitzman & Summerbell, 1995).

### **Antiviral activity**

The few studies that have investigated the antiviral properties of TTO support the anecdotal notion that TTO has antiviral properties. The antiviral activity of TTO was first shown using tobacco mosaic virus and tobacco plants with agricultural applications in mind (Bishop, 1995). A field trial was conducted in which *Nicotiniana glutinosa* plants were sprayed with 100, 250 or 500 ppm TTO or control solutions, and all plants were then experimentally infected with tobacco mosaic virus. After 10 days, there were significantly fewer lesions per square centimetre of leaf of plants treated with TTO as compared to controls (Bishop, 1995).

Schnitzler *et al.* (2001) investigated the activity of tea tree and eucalyptus oils against herpes simplex virus (HSV). Briefly, the activity of TTO was determined by incubating virus with varying concentrations of TTO, and then using these treated viruses to infect cell monolayers. After 4 days, the numbers of plaques formed by virus treated with TTO, or untreated control virus, were determined and compared. The concentration of TTO inhibiting 50% of plaque formation, as compared to controls, was 0.0009% for HSV1 and 0.0008% for HSV2. These studies also showed that at the higher concentration of 0.003%, TTO reduced HSV1 titres by 98.2% and HSV2 titres by 93.0%. Also, by applying TTO at different stages in the virus replicative cycle, TTO was shown to have the greatest effect on free virus (prior to infecting cells) although when TTO was applied during the adsorption period a reduction in plaque formation was seen also.

Some activity against bacteriophages, or viruses that infect bacteria, has also been reported with exposure to 50% TTO at 4°C for 24 h reducing the number of plaques formed on a bacterial lawn (Chao *et al.*, 2000).

Further evidence for antiviral activity comes from a pilot study investigating the treatment of recurrent herpes labialis (cold sores) with a 6% TTO gel or a placebo gel without TTO (Carson *et al.*, 2001). Comparison of each patient group (both containing nine evaluable patients) at the end of the study showed that re-epithelialisation after treatment occurred after 9 days for the tea tree group and after 12.5 days for the placebo group. Other measures such as duration of virus positivity by culture or polymerase chain reaction, viral titres and time to crust formation were not significantly different, possibly due to small patient numbers. Interestingly, when TTO was evaluated for its protective efficacy in an in vivo mouse model of genital HSV type 2 infection it did not perform well (Bourne *et al.*, 1999). In contrast, 1,8-cineole, a component of TTO, performed well protecting 7 of 16 animals from disease.

The results of these studies indicate that TTO may act against viruses in several ways. In addition to lethal effects directly on virus particles, TTO can also affect the way virus adsorbs to tissue culture cells and can cause a reduced rate of infection in tobacco plants.

### **Anti-protozoal activity**

TTO also has anti-protozoal activity although the data on this are limited to two publications. TTO caused a 50% reduction in growth (as compared to controls) of the protozoa *Leishmania major* and *Trypanosoma brucei* at concentrations of 403 µg/ml and 0.5 µg/ml, respectively (Mikus *et al.*, 2000). Further investigation showed that terpinen-4-ol contributed significantly to this activity. In a different

study, TTO at 300 µg/ml killed all cells of *Trichomonas vaginalis* (Viollon *et al.*, 1996). This combined with anecdotal in vivo evidence that *Trichomonas vaginalis* infections may be successfully treated with TTO (Peña, 1962) suggest that further work is warranted.

### **Antimicrobial components of TTO**

Considerable attention has been paid to which components of TTO are responsible for the antimicrobial activity, mainly the antibacterial and antifungal activities. Early indications from RW coefficients were that much of the activity could be attributed to terpinen-4-ol and  $\alpha$ -terpineol (Penfold & Grant, 1925). Data available today confirm that these two components contribute substantially to the oil's activity (Carson & Riley, 1995; Raman, Weir & Bloomfield, 1995; Hammer *et al.*, 2003). However, of the components tested it seems that most possess at least some degree of antimicrobial activity (Carson & Riley, 1995; Raman, Weir & Bloomfield, 1995; Hammer *et al.*, 2003) and while some may be considered less active, none can be considered inactive.

The possibility that components in TTO may exert synergistic or antagonistic effects on the overall antimicrobial activity has been explored *in vitro* (Cox *et al.*, 2001a) as has the potential for interactions with other essential oils, such as lavender (Cassella *et al.*, 2002), and other essential oil components such as  $\beta$ -triketones from manuka oil (Christoph, Kaulfers & Stahl-Biskup, 2001; Christoph, Stahl-Biskup & Kaulfers, 2001). Given the numerous components of TTO, the scope for such effects is enormous and much more work is required to examine this question.

### **Anti-inflammatory activity**

Anti-inflammatory activity has also been attributed to TTO but for many years only anecdotal evidence was available. In vitro work over the last decade has demonstrated that terpinen-4-ol can inhibit the production of several inflammatory mediators (such as interleukins) by human peripheral blood monocytes (Hart *et al.*, 2000). This suggests a mechanism by which TTO may reduce the normal inflammatory response. Terpinen-4-ol also suppresses superoxide production by agonist-stimulated monocytes, but not neutrophils (Brand *et al.*, 2001). In vivo, topically applied TTO has been shown to modulate the oedema associated with the efferent phase of a contact hypersensitivity response (Brand *et al.*, 2002a). This activity was attributed primarily to terpinen-4-ol and  $\alpha$ -terpineol. Similarly, topical TTO reduced histamine-induced skin oedema of the type that is often associated with immediate type allergic hypersensitivities (Brand *et al.*, 2002b). This activity also appeared to be due mainly to terpinen-4-ol.

### **Agricultural applications**

The broad-spectrum antimicrobial activity of TTO lends itself to uses other than human and animal medicine. There has also been interest in exploiting its properties for disease protection in crops and produce. The greatest interest seems to have been in the antifungal properties of the oil and there are data from in vitro antifungal assays, greenhouse studies and field trials against many important agricultural pathogens. The plethora of methods used in this work preclude direct comparisons. However, of the in vitro data, Bishop & Thornton (1997) showed that the following organisms could be inhibited by exposure to TTO in a disc diffusion method or to TTO vapour: *Alternaria brassicicola*, *Alternaria solani*, *Botrytis cinerea*, *Fusarium solani*, *Myocentrospora acerina*, *Pythium ultimum*, *Rhizoctonia solani*, *Rhizopus sexualis*, *Rhizopus stolonifer*, *Sclerotinia sclerotiorum*, *Sclerotium cepivorum* and *Serpula lacrymans*. Further work on *B. cinerea* using a bioassay with *Brassica oleracea* var. *capitata* (Dutch White cabbage) demonstrated that a concentration of 3.2% TTO compared favourably with three commercial fungicides (Bishop & Reagan, 1998). Vapourised TTO also inhibited the germination of *B. cinerea* spores at 12.5% but not 6.25% TTO (Wilson *et al.*, 1997). Caolo-Tanski *et al.* (2002a,b) showed that TTO can inhibit a similar range of fungal pathogens *in vitro*, and in some cases in greenhouse studies and field trials. The fungi tested were *Alternaria alternata*, *A. solani*, *Cercospora beticola*, *Cochliobolus sativum*, *Fusarium graminearum*, *Phytophthora infestans*, *Pythium paroeandrum*, *Rhizoctonia solani* and *S. sclerotiorum*. Greenhouse

studies also confirmed the potential for 1% TTO to be used for the control of powdery mildew of cucurbits caused by *Sphaerotheca fuliginea* (Olsen *et al.*, 1988). The same concentration of oil proved effective in greenhouse trials in controlling false smut of palms caused by *Graphiola phoenicis* (Polizzi & Agosteo, 1995). Although the microbial pathogens were not identified, TTO vaporised at a concentration of 100 µl l<sup>-1</sup> reduced post-harvest decay in raspberries (*Rubus idaeus* L.) (Wang, 2003). Washington and colleagues (1999) showed in field trials on strawberries that TTO could control leather rot caused by *Phytophthora cactorum* and anthracnose (or blackspot) caused by *Colletotrichum acutatum*. Earlier work by this group had shown that a commercially available TTO crop treatment could reduce numbers of the predatory two spotted mites, *Typhlodromus occidentalis* (Washington *et al.*, 1991).

In one of the few investigations to examine bacterial disease in plants, TTO applied to soil infested with *Ralstonia solanacearum* failed to reduce the subsequent incidence of wilt in tomatoes (Pradhanang *et al.*, 2002). Similarly, TTO did not successfully control *Xanthomonas campestris* pv. *campestris* when applied to *Brassica oleracea* var. *capitata* (Dillard *et al.*, 2000). Antiviral activity has also attracted some attention and spray solutions containing TTO significantly decreased lesion numbers in tobacco plants when applied prior to inoculation with tobacco mosaic virus (Bishop 1995).

### **Insecticidal activity**

Anecdotally many essential oils have been mooted as insecticidal agents. Few have been investigated scientifically. TTO has been evaluated *in vitro* against *Pediculus humanus capitis* (head lice) (Veal, 1996; Downs *et al.*, 2000) and a shampoo containing several plant extracts including TTO performed well in a pilot study of lice treatment (McCage *et al.*, 2002). *Scabies sarcopti* (scabies) has also been tested *in vitro* and found to be susceptible to the oil (Walton, Myerscough & Currie, 2000). In contrast, in one *in vitro* test, a natural mosquito repellent product containing TTO provided almost no protection against *Aedes aegypti* (Chou *et al.*, 1997).

The activity of TTO against house dust mites has also been shown in two studies. In the first, the activity of several essential oils (including TTO) against house dust mites was compared to that of benzyl benzoate, a standard treatment. Oils of citronella and tea tree were as effective as 0.5% benzyl benzoate and TTO at a concentration of 0.8% killed 79% of mites after a 10 min exposure time (McDonald & Tovey, 1993). In the second study, TTO was the most effective at killing the house dust mite *Dermatophagoides pteronyssinus*, when compared to lavender and lemon essential oils (Priestley *et al.*, 1998). TTO at a concentration of 10% caused 100% immobility after 30 min and 100% mortality after 2 h.

### **Other properties**

It is likely that TTO possesses other properties common to the terpene family of chemicals. Many of the components in TTO have been shown to improve the percutaneous penetration of topically applied drugs. Most notable of these are cineole (Obata *et al.*, 1991; Yamane *et al.*, 1995; Gao & Singh, 1997;1998), and terpinen-4-ol and  $\alpha$ -terpineol (Magnusson *et al.*, 1997; Godwin & Michniak, 1999). By inference, it seems likely that TTO can also enhance the transdermal penetration of other compounds although it has not been reported to date. If TTO can penetrate the outer layers of the dermis this may help implementation of its antimicrobial properties; rather than inhibiting or killing microorganisms in the uppermost skin layers only, it may penetrate deeper eliminating underlying organisms and preventing relapses.

Anecdotally, TTO is also credited with anti-pruritic activity. No scientific data exist for this property although it may be linked to its anti-inflammatory activity since the pathophysiology of itch is thought to be related to the inflammatory response (Hägermark & Wahlgren, 1992).

Claims of analgesic properties have been made for TTO (Markham, 1999) but there are almost no data to support them and it is impossible to confirm or refute these claims. The exception is one paper describing reductions in the degree of pain and the total use of analgesics post-operatively after twice daily inhalation of tea tree and peppermint oils (Takahashi *et al.*, 2002).

## Other applications

Numerous other applications have been suggested for TTO. One for which several products have been developed but for which little research has been done is aerosolised TTO. There are anecdotal reports of aerosolised TTO reducing hospital acquired infections (Bowden, 2001) but no scientific data. Some preliminary in vitro work has been done with several researchers showing that vaporised TTO can inhibit bacteria including *Mycobacterium avium* ATCC 4676 (Maruzzella & Sicurella, 1960) and the respiratory pathogens *E. coli*, *Haemophilus influenzae*, *Streptococcus pyogenes* and *Strep. pneumoniae* (Inouye, Takizawa & Yamaguchi, 2001), and fungi (Inouye, Uchida & Yamaguchi, 2001). Related work on agricultural applications of TTO has made similar observations (Bishop & Thornton, 1997; Wilson *et al.*, 1997).

TTO products designed for application to burns have also been developed but scientific data on their suitability for use are lacking and their use has been questioned (Faoagali, George & Leditschke, 1997; Price, 1998). Some preliminary work has been done (Smith, 1995; Faoagali, George & Leditschke, 1997; Jandera *et al.*, 2000; Osti & Osti, 2002) but substantial additional research is required before informed conclusions about their role can possibly be made.

There has been some interest in using TTO in veterinary medicine and it has been suggested for the treatment of chronic dermatitis in dogs (Fitzi *et al.*, 2002).

Consideration has been given to using *M. alternifolia* in constructed wetlands for sewage treatment (Bolton & Greenway, 1997; 1999a,b). In addition to water treatment, this type of scheme offers the benefits of native habitat rehabilitation and TTO production.

TTO has been assessed as an alternative solvent for the gutta-percha solvents used in dentistry (Kaplowitz, 1990; Kaplowitz, 1991; Görduysus *et al.*, 1997).

## Product formulation issues

TTO's physical characteristics present certain difficulties for the formulation of products. Its lipophilicity leads to miscibility problems in aqueous based products while its volatility means that packaging must provide a suitable barrier to losses through volatilisation. Consideration must also be given to the properties of the finished product. Early suggestions that TTO's antimicrobial activity may be compromised by organic matter came from disc diffusion studies in which the addition of blood to agar medium decreased zone sizes (Ånséhn, 1990). This observation contrasts sharply with the old claim that the activity of TTO may be enhanced in the presence of organic matter such as blood and pus. Data from Hammer and colleagues comprehensively refuted this idea (Hammer, Carson & Riley, 1999) and also showed that product excipients may compromise activity.

Some work on the characteristics and behaviour of TTO within formulations has been conducted. Caboi *et al.* (2002) examined the potential of a monoolein/water system as a carrier for TTO and terpinen-4-ol. However, if stable, biologically-active formulations of TTO are going to be developed, much remains to be done.

## Safety and toxicity

Most TTO is used topically. Anecdotal evidence from almost 80 years of use suggests that topical use is safe, and that adverse events are minor and occasional. The toxicity of TTO can be considered in three major areas; toxicity from ingestion, from topical application and eco-toxicity. Topical or dermal toxicity can be further divided into allergic and irritant types of reaction.

### *Oral toxicity*

Tea tree is categorised as a Schedule 6 poison in Australia. According to the Drugs, Poisons and Controlled Substances Act 1981, substances classed within this category have “a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label”. To this end, neat TTO is labelled that it must be kept out of the reach of children, is packaged with a childproof cap and is labelled ‘not to be taken internally’.

TTO can be toxic if ingested, as evidenced by studies with animals and from cases of human poisoning. An established laboratory method for measuring the toxicity of a substance is to determine the LD<sub>50</sub>, which is the ingested dose that is lethal to 50% of a test population. This is expressed as units of toxic substance per kilogram of body weight. The LD<sub>50</sub> for TTO in a rat model is 1.9 – 2.6 ml/kg (Russell, 1999). Although values determined in animal models are not necessarily directly related to human toxicity, the animal model data indicate that TTO is orally toxic and therefore not suitable for internal use.

Several incidences of oral poisoning in humans have been reported in the literature. Such occurrences tend to be more dramatic in children because of their low body weight compared to an adult. One such case report involved a 23 month old child who drank approximately 10 ml of TTO. After a nap of approximately 30 min, the child was unsteady on his feet and appeared as if ‘drunk’. The child was taken to a hospital and treated with activated charcoal and sorbitol via a naso-gastric tube, and approximately 5 h later he appeared to be asymptomatic. All other signs (such as respiratory rate, oxygen saturation, pupil reactivity, electrolytes and blood glucose) were normal throughout (Jacobs & Hornfeldt, 1994). The authors attribute the clinical symptoms to a central nervous system depression caused by the ingested TTO.

A case of poisoning in an adult occurred when a patient drank approximately half a tea cup of TTO corresponding to a dose of approximately 0.5-1.0 ml/kg body weight (Seawright, 1993). The patient was comatose for 12 h, and semi-conscious and hallucinatory for the following 36 h. Symptoms of abdominal pain and diarrhoea continued for approximately 6 weeks after this. In another incident, a 60 year old man who swallowed one and a half teaspoonfuls of TTO as a preventative for a cold presented with a red rash which covered his feet, knees, upper body and arms including his palms and elbows (Elliott, 1993). His hands, feet and face were also swollen. The rash and other symptoms gradually disappeared and approximately one week later he had more or less recovered.

Apart from these reports, there are no data on the systemic toxicity of TTO in humans. However, the ingestion of TTO should not be recommended. Despite this, deliberate ingestion is occasionally suggested (Belaiche 1985; Blackwell, 1991a) or reported.

### *Dermal toxicity*

Systemic effects from topical TTO application in humans or other animals appear to be very rare, judging by published reports. The topical application of significant quantities of eucalyptus oil (containing approximately 80% 1,8-cineole) to a 6 year old girl caused systemic effects, including slurred speech, drowsiness, vomiting, ataxia and unconsciousness, although the girl recovered fully within approximately 6 h (Darben *et al.*, 1998). Severe systemic effects following dermal application of TTO to cats have been reported (Bischoff & Guale, 1998). Three cats with shaved but intact skin had approximately 120 ml of neat TTO applied to them topically as a flea repellent. Within 5 h all three cats were experiencing symptoms such as hypothermia, uncoordination, dehydration and trembling, and one was comatose (Bischoff & Guale, 1998). All cats were treated by a veterinarian and two recovered after 24 and 48 h, respectively, but the third cat was found dead 3 days after admission.

### *Irritant reactions*

Irritant reactions are an inflammatory type of response caused when an irritating substance comes into contact with a body surface, usually the skin. Importantly, these reactions are often concentration dependent, but are not dependent on previous exposure to the irritating agent. Irritant reactions may usually be avoided through the use of lower concentrations of the irritant and this bolsters the case for discouraging the use of neat oil and promoting the use of well-formulated products. The irritant capacity of TTO has been evaluated in both animal models and human trials, however, only the human data will be discussed below.

The irritant capacity of TTO has been investigated using an occlusive patch test method with Finn chambers (Southwell *et al.*, 1997). TTO was prepared in white soft paraffin at a concentration of 25% and this mixture was applied in patch tests on the backs or upper arms of volunteers. After 24 h, patches were removed and the skin was checked for any reactions. A new chamber was then applied to the same area, and checked again 24 h later. This was repeated at subsequent 24 h intervals for a total of 21 days. None of the 25 participants produced an irritant reaction from these tests. However, three of the original 28 participants showed distinct allergic reactions and were withdrawn from the trial. The TTO component 1,8-cineole, which has a reputation as a skin irritant, was also tested at concentrations up to and including 28% and did not produce any irritant reactions in the 25 (non-allergic) participants (Southwell *et al.*, 1997). Another study similarly found that of 20 patients patch-tested with 1% TTO, none had irritant reactions (Knight & Hausen, 1994). This study also showed that TTO was a 'weak sensitiser' after attempts were made to experimentally sensitise guinea pigs to TTO. Subsequent experiments have confirmed that newly distilled TTO has a relatively low sensitising capacity whereas TTO that had been exposed to light, oxygen, warmth and moisture, and was considered 'degraded', was a moderate to strong sensitiser (Hausen *et al.*, 1999).

### *Contact allergy*

Contact allergy is defined as a cutaneous reaction caused by direct contact with an allergen to which the patient has become sensitised (Hensyl, 1990). Once an allergic reaction to TTO has occurred it is likely that all subsequent exposures to TTO, no matter what concentration, will elicit further allergic reactions. A series of seven such patients were described in a report by Knight & Hausen (1994). All patients reacted to 1% TTO when tested by patch testing using Finn chambers. In addition, these patients also reacted to one or more of the components *d*-limonene,  $\alpha$ -terpinene, aromadendrene, terpinen-4-ol and  $\alpha$ -phellandrene at 1, 5 or 10%. In the study by Southwell discussed above, the three participants having allergic type reactions to 25% TTO were tested against TTO components and reacted mostly to the sesquiterpenoid fractions but not the pure monoterpenes (Southwell *et al.*, 1997). These studies indicate that contact allergy to TTO can occur, although the rate of occurrence is still not known.

### *Toxicity against cell lines in vitro*

The testing of human or animal cells *in vitro* is seen as a modern alternative to animal testing to determine toxicity. Several studies have investigated the toxic effects of TTO and/or components on (human) cell lines *in vitro*. The amounts of TTO that reduced the growth of cells by 50% as compared to controls (IC<sub>50</sub>) after 24 h, ranged from 20 to 2700  $\mu\text{g/ml}$  for HeLa, K562, CTVR-1, Molt-4 and Hep G2 cells (Hayes *et al.*, 1997). IC<sub>50</sub> values determined in other studies were 43.0  $\mu\text{g/ml}$  for human HL-60 cells (Mikus *et al.*, 2000), 0.006% for RC-37 cells (Schnitzler *et al.*, 2001), 575  $\mu\text{g/ml}$  for human fibroblasts and about 450  $\mu\text{g/ml}$  for human epithelial cells (Söderberg *et al.*, 1996). In addition, TTO produced toxic effects against human monocytes at concentrations of  $\geq 0.004\%$  (Hart *et al.*, 2000) or  $\geq 0.016\%$  (Brand *et al.*, 2001) and at  $\geq 0.016\%$  against human neutrophils (Brand *et al.*, 2001).

### *Eco-toxicity*

Literature on the ecotoxicity of TTO has been summarised and reviewed in Chapter 4.

**Table 3.1. Composition of *M. alternifolia* (tea tree) oil**

| Component     | Composition (%)             |                                  |
|---------------|-----------------------------|----------------------------------|
|               | ISO 4730 Range <sup>1</sup> | Typical composition <sup>2</sup> |
| terpinen-4-ol | ≥ 30 <sup>3</sup>           | 40.1                             |
| γ-terpinene   | 10 - 28                     | 23.0                             |
| α-terpinene   | 5 – 13                      | 10.4                             |
| 1,8-cineole   | ≤ 15 <sup>3</sup>           | 5.1                              |
| terpinolene   | 1.5 - 5                     | 3.1                              |
| p-cymene      | 0.5 - 12                    | 2.9                              |
| α-pinene      | 1 – 6                       | 2.6                              |
| α-terpineol   | 1.5 - 8                     | 2.4                              |
| aromadendrene | traces - 7                  | 1.5                              |
| δ-cadinene    | traces - 8                  | 1.3                              |
| limonene      | 0.5 - 4                     | 1.0                              |
| sabinene      | traces – 3.5                | 0.2                              |
| globulol      | traces - 3                  | 0.2                              |
| viridiflorol  | traces – 1.5                | 0.1                              |

<sup>1</sup> International Organisation for Standardisation

<sup>2</sup> Brophy et al., 1989

<sup>3</sup> no upper or lower limit set

**Table 3.2. Properties of TTO components**

| Component             | Type of compound           | Chemical formula                  | Solubility (ppm) <sup>1</sup> | log $K_{OW}$ <sup>2</sup> |
|-----------------------|----------------------------|-----------------------------------|-------------------------------|---------------------------|
| terpinen-4-ol         | monocyclic terpene alcohol | C <sub>10</sub> H <sub>18</sub> O | 1491                          | 3.26                      |
| $\gamma$ -terpinene   | monocyclic terpene         | C <sub>10</sub> H <sub>16</sub>   | 1.0                           | 4.36                      |
| $\alpha$ -terpinene   | monocyclic terpene         | C <sub>10</sub> H <sub>16</sub>   | 8.2                           | 4.25                      |
| 1,8-cineole           | monocyclic terpene alcohol | C <sub>10</sub> H <sub>18</sub> O | 907                           | 2.84                      |
| $\alpha$ -terpinolene | monocyclic terpene         | C <sub>10</sub> H <sub>16</sub>   | 4.3                           | 4.24                      |
| $p$ -cymene           | monocyclic terpene         | C <sub>10</sub> H <sub>14</sub>   | 6.2                           |                           |
| (+)- $\alpha$ -pinene | dicyclic terpene           | C <sub>10</sub> H <sub>16</sub>   | 0.57                          | 4.44                      |
| $\alpha$ -terpineol   | monocyclic terpene alcohol | C <sub>10</sub> H <sub>18</sub> O | 1827                          | 3.28                      |
| aromadendrene         | sesquiterpene              | C <sub>15</sub> H <sub>24</sub>   |                               |                           |
| $\delta$ -cadinene    | sesquiterpene              | C <sub>15</sub> H <sub>24</sub>   |                               |                           |
| (+)-limonene          | monocyclic terpene         | C <sub>10</sub> H <sub>16</sub>   | 1.0                           | 4.38                      |
| sabinene              | dicyclic monoterpene       | C <sub>10</sub> H <sub>16</sub>   |                               |                           |
| globulol              | sesquiterpene alcohol      | C <sub>15</sub> H <sub>26</sub> O |                               |                           |

<sup>1</sup> Griffin *et al.*, 1999b<sup>2</sup> Griffin *et al.*, 1999a

**Table 3.3 Susceptibility data for bacteria tested against *M. alternifolia* oil (% v/v)**

| Bacterial species                            | MIC, MIC <sub>range</sub><br>or MIC <sub>90</sub>          | MBC, MBC <sub>range</sub><br>or MBC <sub>90</sub> |
|--|--|---|
| <i>Acinetobacter baumannii</i>               | 1.0 <sup>8</sup>   | 1.0 <sup>8</sup>                                  |
| <i>Actinomyces viscosus</i>                  | 0.6 <sup>6</sup>   |   |
| <i>Actinomyces</i> spp.                      | 1.0 <sup>14</sup>  | 1.0 <sup>14</sup>                                 |
| <i>Bacillus cereus</i>                       | 0.3 <sup>2</sup>   |   |
| <i>Bacteroides</i> spp.                      | 0.06 <sup>1</sup> , 0.5 <sup>1</sup>                       | 0.06-0.12 <sup>1</sup>                            |
| <i>Corynebacterium</i> sp.                   | 0.2-0.3 <sup>2</sup> , 2.0 <sup>8</sup>                    | 2.0 <sup>8</sup>                                  |
| <i>Enterococcus faecalis</i>                 | 0.5-0.75 <sup>2</sup>                                      |   |
| <i>Enterococcus faecalis</i> (vancomycin R)  | 0.5-1 <sup>4</sup> , >8 <sup>10</sup>                      | 0.5-1 <sup>4</sup> , >8 <sup>10</sup>             |
| <i>Escherichia coli</i>                      | 0.25 <sup>3, 7</sup> , 0.08 <sup>11</sup>                  | 0.25 <sup>3, 7</sup>                              |
| <i>Fusobacterium nucleatum</i>               | >0.6 <sup>6</sup>  |   |
| <i>Klebsiella pneumoniae</i>                 | 0.25 <sup>8</sup> , 0.3 <sup>2</sup>                       | 0.25 <sup>8</sup>                                 |
| <i>Lactobacillus</i> spp.                    | 1.0 <sup>14</sup> , 2.0 <sup>1</sup>                       | 2.0 <sup>1, 14</sup>                              |
| <i>Micrococcus luteus</i>                    | 0.06-0.5 <sup>8</sup>                                      | 0.25-6.0 <sup>8</sup>                             |
| <i>Peptostreptococcus anaerobius</i>         | 0.2 <sup>6</sup> , 0.25 <sup>1</sup>                       | 0.03-0.12 <sup>1</sup>                            |
| <i>Porphyromonas endodontalis</i>            | 0.025-0.1 <sup>14</sup>                                    | 0.025-0.1 <sup>14</sup>                           |
| <i>Porphyromonas gingivalis</i>              | 0.11 <sup>6</sup>  |   |
| <i>Prevotella</i> spp.                       | 0.03 <sup>1</sup> , 0.25 <sup>1</sup>                      | 0.03 <sup>1</sup>                                 |
| <i>Prevotella intermedia</i>                 | 0.003-0.1 <sup>14</sup>                                    | 0.003-0.1 <sup>14</sup>                           |
| <i>Propionibacterium acnes</i>               | 0.05 <sup>2</sup> , 0.31-0.63 <sup>5</sup>                 | 0.5 <sup>13</sup>                                 |
| <i>Proteus vulgaris</i>                      | 0.08 <sup>11</sup> , 0.3 <sup>2</sup> , 2.0 <sup>10</sup>  | 4.0 <sup>10</sup>                                 |
| <i>Pseudomonas aeruginosa</i>                | 1->2.0 <sup>2</sup> , 1-8 <sup>10</sup> , 3.0 <sup>8</sup> | 2->8 <sup>10</sup> , 3.0 <sup>8</sup>             |
| <i>Staphylococcus aureus</i>                 | 0.63-1.25 <sup>5</sup> , 0.5 <sup>7, 10</sup>              | 1.0 <sup>10</sup> , 2.0 <sup>7</sup>              |
| <i>Staphylococcus aureus</i> (methicillin R) | 0.04 <sup>11</sup> , 0.25 <sup>4, 9</sup>                  | 0.5 <sup>4</sup> , 0.5 <sup>9</sup>               |
| <i>Staphylococcus epidermidis</i>            | 0.63-1.25 <sup>5</sup> , 1.0 <sup>8</sup>                  | 4.0 <sup>8</sup>                                  |
| <i>Staphylococcus hominis</i>                | 0.5 <sup>8</sup>   | 4.0 <sup>8</sup>                                  |
| <i>Streptococcus pyogenes</i>                | 0.12 <sup>12</sup>   | 0.25 <sup>12</sup>                                |
| <i>Veillonella</i> spp.                      | 0.016-1.0 <sup>14</sup>                                    | 0.03-1.0 <sup>14</sup>                            |

<sup>1</sup> Hammer *et al.*, 1999a; <sup>2</sup> Griffin *et al.*, 2000; <sup>3</sup> Gustafson *et al.*, 1998; <sup>4</sup> Nelson, 1997;<sup>5</sup> Raman *et al.*, 1995; <sup>6</sup> Shapiro *et al.*, 1994; <sup>7</sup> Carson *et al.*, 1995b; <sup>8</sup> Hammer *et al.*, 1996;<sup>9</sup> Carson *et al.*, 1995a; <sup>10</sup> Banes-Marshall *et al.*, 2001; <sup>11</sup> Mann & Markham, 1998;<sup>12</sup> Carson *et al.*, 1996; <sup>13</sup> Carson & Riley, 1994; <sup>14</sup> Hammer *et al.*, 2003

# Chapter 4. Review of tea tree oil ecotoxicity data

Ecotoxicology can be loosely defined as the effects of pollutants on natural ecosystems. Although data from acute toxicity testing of single animal or insect species may be regarded as overly simplistic, they are often the starting point for assessing ecotoxicity.

Data describing the ecotoxicity of tea tree oil are very limited. The toxicity of tea tree oil against fish, amphibians, insects, worms or other aquatic and terrestrial species, or ecosystems, has not been assessed to any great extent.

## 4.1 Acute toxicity of tea tree oil to aquatic organisms

Two publications have assessed the potential for tea tree oil to be used as an antifungal agent in fish aquaculture (Campbell *et al.*, 2001; Marking *et al.*, 1994). Whilst both studies tested the efficacy of tea tree oil against aquatic fungi, Marking *et al.* (1994) also assessed the toxicity of tea tree oil to rainbow trout eggs. They found that tea tree oil was non-toxic to rainbow trout eggs at a concentration of 1500 ppm.

Ecotoxicity data for two essential oils and some essential oil components are shown in Table 4.1. In addition, clove oil (containing ~ 90% eugenol) has been evaluated as an anaesthetic for fish. It has been shown to anaesthetise fish at concentrations of 6 - 200 mg/l (Afifi *et al.*, 2001; Sladky *et al.*, 2001) but data are not available describing lethal concentrations. The values shown in Table 4.1 show that thyme oil and eugenol are for the most part categorised as slightly toxic, having LC<sub>50</sub> values of between 10 and 100 mg/l (Kamrin, 1997). Lovage oil and its component ocimene are categorised as practically non-toxic (with LC<sub>50</sub> values of > 100 mg/l) whereas cumene is categorised as moderately toxic (with LC<sub>50</sub> values of 1 – 10 mg/l).

Ecotoxicity data for several components of tea tree oil are shown in Table 4.2.

Using the toxicity categories described above, and the limited data for tea tree oil components, limonene and cymene are classified as slightly toxic,  $\alpha$ -terpineol is moderately toxic,  $\alpha$ -pinene appears to be practically non-toxic and data for  $\beta$ -pinene are equivocal. Notably absent are any data for the tea tree oil components terpinen-4-ol or  $\gamma$ -terpinene, the two components present in the highest proportions in tea tree oil. Whilst ecotoxicity data for essential oils other than tea tree oil, or essential oil components, can only be used as a guide, they suggest that tea tree oil may fall into the 'slightly toxic' category, with LC<sub>50</sub> values of between 10 – 100  $\mu$ g/l.

**Table 4.1 Acute toxicity data for thyme oil, eugenol, lovage oil, ocimene and cumene**

| Volatile oil | Aquatic species            | Data                                      | Reference                                 |
|--------------|----------------------------|---|---|
| Thyme oil    | Rainbow trout <sup>1</sup> | LC <sub>50</sub> = 16.1 mg/l <sup>a</sup> | Bull Env Contam Toxicol 1998; 60: 923-930 |
|              | Coho salmon <sup>2</sup>   | LC <sub>50</sub> = 21.1 mg/l <sup>a</sup> | Bull Env Contam Toxicol 1998; 60: 923-930 |
| Eugenol      | Coho salmon <sup>2</sup>   | LC <sub>50</sub> = 67.6 mg/l <sup>a</sup> | Bull Env Contam Toxicol 1998; 60: 923-930 |
|              | Rainbow trout <sup>1</sup> | LC <sub>50</sub> = 61.5 mg/l <sup>a</sup> | Bull Env Contam Toxicol 1998; 60: 923-930 |
|              | Rainbow trout <sup>1</sup> | LC <sub>50</sub> = 9 mg/l <sup>c</sup>    | Aqua Res 1998; 29: 89-101                 |
|              | Rainbow trout <sup>1</sup> | LC <sub>50</sub> = 125 mg/l <sup>b</sup>  | J Aquatic Animal Health 2000; 12: 224-229 |
|              | Cherry salmon <sup>5</sup> | LC <sub>50</sub> = 63 mg/l <sup>b</sup>   | J Aquatic Animal Health 2000; 12: 224-229 |
|              | Goldfish <sup>6</sup>      | LC <sub>50</sub> = 250 mg/l <sup>b</sup>  | J Aquatic Animal Health 2000; 12: 224-229 |
| Lovage oil   | Brine shrimp <sup>3</sup>  | LD <sub>50</sub> = 228 ppm                | Int J Aromather 2001; 11: 145-151         |
| Ocimene      | Brine shrimp <sup>3</sup>  | LD <sub>50</sub> = 697 ppm                | Int J Aromather 2001; 11: 145-151         |
| Cumene       | Sheepshead minnow          | LC <sub>50</sub> = 8.1 mg/l <sup>a</sup>  | Ecotoxicol Env Saf 1995; 31: 287-289      |
|              | Rainbow trout <sup>1</sup> | LC <sub>50</sub> = 6.4 mg/l <sup>a</sup>  | Ecotoxicol Env Saf 1995; 31: 287-289      |
|              | Water flea <sup>4</sup>    | LC <sub>50</sub> = 4.8 mg/l <sup>a</sup>  | Ecotoxicol Env Saf 1995; 31: 287-289      |

<sup>1</sup>*Onchorhynchus mykiss*

<sup>2</sup>*Onchorhynchus kisutch*

<sup>3</sup>*Artemia salina*

<sup>4</sup>*Daphnia magna*

<sup>5</sup>*Onchorhynchus masou*

<sup>6</sup>*Carassius aurantus*

<sup>a</sup>24 h exposure time

<sup>b</sup>60 min exposure time

<sup>c</sup>estimated over 8 – 96 h

**Table 4.2 Acute toxicity of components of tea tree oil to aquatic species**

| Component           | Aquatic species<br>(life stage)  | Data   | Reference   |
|---------------------|----------------------------------|--|---|
| $\alpha$ -Pinene    | Water flea <sup>4</sup>          | LC <sub>50</sub> = 68 mg/l <sup>a</sup>  | Bull Env Contam Toxicol 1980; 24: 684-691         |
|                     | Brine shrimp <sup>3</sup>        | LD <sub>50</sub> = 494 ppm   | Int J Aromather 2001; 11: 145-151                 |
| $\beta$ -Pinene     | Brine shrimp <sup>3</sup>        | LD <sub>50</sub> = 491 ppm   | Int J Aromather 2001; 11: 145-151                 |
|                     | Rainbow trout (fry) <sup>1</sup> | LC <sub>50</sub> = 1.2 mg/l <sup>d</sup>   | J Great Lakes Res 1995; 21: 373-383               |
| Limonene            | Carp <sup>7</sup>                | LC <sub>0</sub> = 26 mg/l<br>LC <sub>50</sub> = 34 mg/l<br>LC <sub>100</sub> = 43 mg/l | Z. Wasser-Abwasser Forsch 1978; 11(5):<br>161-164 |
|                     | Brine shrimp                     | LD <sub>50</sub> = 706 ppm   | Int J Aromather 2001; 11: 145-151                 |
| $\alpha$ -Terpineol | Rainbow trout<br>(fingerlings)   | Toxic dose range:<br>10 – 100 mg/l <sup>e</sup>  | Water Res. 1976; 10: 303-306                      |
|                     | Coho salmon                      | LC <sub>50</sub> = 6.8 mg/l <sup>a</sup>   | Bull Env Contam Toxicol 1998; 60: 923-930         |
|                     | Rainbow trout                    | LC <sub>50</sub> = 6.7 mg/l <sup>a</sup>   | Bull Env Contam Toxicol 1998; 60: 923-930         |
| p-Cymene            | Water flea                       | LC <sub>50</sub> = 9.4 mg/l <sup>a</sup>   | Bull Env Contam Toxicol 1980; 24: 684-691         |
|                     | Sheepshead minnow                | LC <sub>50</sub> = 56 ppm <sup>a</sup>   | Bull Env Contam Toxicol 1981; 27: 596-604         |

<sup>1</sup> *Onchorhynchus mykiss*; <sup>2</sup> *Onchorhynchus kisutch*; <sup>3</sup> *Artemia salina*; <sup>4</sup> *Daphnia magna*; <sup>5</sup> *Onchorhynchus masou*;

<sup>6</sup> *Carassius aurantus*; <sup>7</sup> *Leuciscus idius melanotus*

<sup>a</sup>24 h exposure time; <sup>b</sup>60 min exposure time; <sup>c</sup>estimated over 8 – 96 h; <sup>d</sup>60 day exposure time;

<sup>e</sup>96 exposure time

## 4.2 Acute toxicity of tea tree oil to terrestrial insects

The acute toxicity of essential oils and components has most commonly been evaluated in the context of using essential oils as crop fumigants and protectants. Data describing the toxic effects of tea tree oil on insects are limited. However, the LD<sub>50</sub> of tea tree oil against the rice weevil *Sitophilus oryzae* (L.) has been determined as >150 µl/l of air (Lee *et al.*, 2001). In addition, varroa mites, which are parasitic to honey bees, have been shown to be susceptible to tea tree oil. After 6 h treatment, 59.4% of mites exposed to tea tree oil in air had died, compared to only 20% of control mites (Sammataro *et al.*, 1998). The toxicity of several essential oils to insects is shown in Table 4.3. Whilst these data are a useful indication of which concentrations of essential oil are toxic, it remains to be determined whether tea tree oil has similar toxicity.

**Table 4.3 Selected acute toxicity data for essential oils and terrestrial insects**

| Oil or Component   | Insect species<br>(life stage) | Data                                 | Reference                             |
|--|--------------------------------|--------------------------------------|---------------------------------------|
| Citronella oil   | Rice weevil <sup>3</sup>       | LD <sub>50</sub> = > 150 µl/l of air | Crop Prot 2001; 20: 317-320           |
| Lavender oil   | Rice weevil <sup>3</sup>       | LD <sub>50</sub> = 54 µl/l of air    | Crop Prot 2001; 20: 317-320           |
| Oregano ( <i>Oreganum vulgare</i> subsp. <i>hirtum</i> ) | Fruit fly <sup>2</sup>         | LD <sub>50</sub> = 5.6 µl/fly        | J Agric Food Chem 1998; 46: 1111-1115 |
| Pennyroyal ( <i>Mentha pulegium</i> )                    | Fruit fly <sup>2</sup>         | LD <sub>50</sub> = 2.09              | J Agric Food Chem 1997; 45: 2690-2694 |
| Rosemary oil   | Rice weevil <sup>3</sup>       | LD <sub>50</sub> = 30.5 µl/l of air  | Crop Prot 2001; 20: 317-320           |
| Savory ( <i>Satureja thymbra</i> )                       | Fruit fly <sup>2</sup>         | LD <sub>50</sub> = 3.3 µl/fly        | J Agric Food Chem 1998; 46: 1111-1115 |
| Spearmint ( <i>Mentha spicata</i> )                      | Fruit fly <sup>2</sup>         | LD <sub>50</sub> = 1.12              | J Agric Food Chem 1997; 45: 2690-2694 |
| Tea tree oil   | Rice weevil <sup>3</sup>       | LD <sub>50</sub> = > 150 µl/l of air | Crop Prot 2001; 20: 317-320           |
| Thyme oil  | Rice weevil <sup>3</sup>       | LD <sub>50</sub> = 63.9 µl/l of air  | Crop Prot 2001; 20: 317-320           |
|  | <i>Spodoptera litura</i>       | LD <sub>50</sub> = 43.7 µg/larva     | J Agric Food Chem 2001; 49: 715-720   |
|  | Fruit fly <sup>2</sup>         | LD <sub>50</sub> = 6.78 µl/fly       | J Agric Food Chem 1998; 46: 1111-1115 |

<sup>a</sup>24 h exposure time; <sup>1</sup>*Musca domestica*; <sup>2</sup>*Drosophila melanogaster*; <sup>3</sup>*Sitophilus oryzae*

In addition to toxicity tests with whole oils, several studies have determined the toxicity of essential oil components. These data may give a general indication of the likely toxicity of tea tree oil to insects. Data are shown in Table 4.4.

**Table 4.4 Selected acute toxicity data for essential oil components and terrestrial insects**

| Component              | Insect species           | Data  | Reference                             |
|------------------------|--------------------------|---|---------------------------------------|
| Carvacrol <sup>†</sup> | <i>Spodoptera litura</i> | LD <sub>50</sub> = 1.6 µg/larva               | J Agric Food Chem 2001; 49: 715-720   |
|                        | Fruit fly <sup>2</sup>   | LD <sub>50</sub> = 42.7 µg/larva              | J Agric Food Chem 1998; 46: 1111-1115 |
| 1,8-Cineole            | Rice weevil <sup>3</sup> | LD <sub>50</sub> = 23.5 µl/l of air           | Crop Prot 2001; 20: 317-320           |
| p-Cymene               | Rice weevil <sup>3</sup> | LD <sub>50</sub> = 25.0 µl/l of air           | Crop Prot 2001; 20: 317-320           |
| Limonene               | <i>Spodoptera litura</i> | LD <sub>50</sub> = 273.7 µg/larva             | J Agric Food Chem 2001; 49: 715-720   |
|                        | Rice weevil <sup>3</sup> | LD <sub>50</sub> = 61.5 µl/l of air           | Crop Prot 2001; 20: 317-320           |
|                        | Cockroach <sup>4</sup>   | LD <sub>50</sub> = 700 µg/insect <sup>a</sup> | J Pest Sci 1988; 13: 287-290          |
|                        | House fly <sup>1</sup>   | LD <sub>50</sub> = 90 µg/insect <sup>a</sup>  | J Pest Sci 1988; 13: 287-290          |
|                        | House fly <sup>1</sup>   | LD <sub>50</sub> = 50.4 µg/fly <sup>a</sup>   | J Agric Food Chem 2002; 50: 4576-4580 |
| Linalool               | Rice weevil <sup>3</sup> | LD <sub>50</sub> = 39.2 µl/l of air           | Crop Prot 2001; 20: 317-320           |
| α-Pinene               | House fly <sup>1</sup>   | LD <sub>50</sub> = 111.5 µg/fly <sup>a</sup>  | J Agric Food Chem 2002; 50: 4576-4580 |
| α-Terpinene            | House fly <sup>1</sup>   | LD <sub>50</sub> = 117.2 µg/fly <sup>a</sup>  | J Agric Food Chem 2002; 50: 4576-4580 |
|                        | Rice weevil <sup>3</sup> | LD <sub>50</sub> = 71.2 µl/l of air           | Crop Prot 2001; 20: 317-320           |
| Terpinen-4-ol          | Rice weevil <sup>3</sup> | LD <sub>50</sub> = 25.6 µl/l of air           | Crop Prot 2001; 20: 317-320           |
|                        | <i>Spodoptera litura</i> | LD <sub>50</sub> = 130.4 µg/larva             | J Agric Food Chem 2001; 49: 715-720   |
| α-Terpineol            | Rice weevil <sup>3</sup> | LD <sub>50</sub> = 69.1 µl/l of air           | Crop Prot 2001; 20: 317-320           |
|                        | House fly <sup>1</sup>   | LD <sub>50</sub> = 175.7 µg/fly <sup>a</sup>  | J Agric Food Chem 2002; 50: 4576-4580 |
|                        | <i>Spodoptera litura</i> | LD <sub>50</sub> = 141.3 µg/larva             | J Agric Food Chem 2001; 49: 715-720   |
| Thymol <sup>†</sup>    | <i>Spodoptera litura</i> | LD <sub>50</sub> = 25.4 µg/larva              | J Agric Food Chem 2001; 49: 715-720   |
|                        | Fruit fly <sup>2</sup>   | LD <sub>50</sub> = 2.6 µg/larva               | J Agric Food Chem 1998; 46: 1111-1115 |

<sup>a</sup>24 h exposure time; <sup>†</sup>component not found in tea tree oil

<sup>1</sup>*Musca domestica*; <sup>2</sup>*Drosophila melanogaster*; <sup>3</sup>*Sitophilus oryzae*; <sup>4</sup>*Blatella germanica*

In addition, another study showed that the treatment of insects for 14 h with several compounds at a concentration 0.05 µg/l of air resulted in varying mortalities. Treatment with linalool resulted in 100% mortality in house flies, German cockroaches and saw-toothed grain beetles, 10% mortality in red flour beetles and 0% in rice weevils. Terpineol resulted in 100% mortality in saw-toothed grain beetles, no mortality in German cockroaches, red flour beetles or rice weevils and 20% in house flies. Treatment with cineole resulted in 100% mortality in all insects. Similarly, treatment with limonene resulted in 100% mortality for all insects except red flour beetles, which had a mortality rate of 60% (Lee *et al.*, 2003).

In addition to acute toxicity data, several studies have indicated that essential oils can have other effects, such as inhibition of larval growth (Hummerbrunner & Isman, 2001), inhibition of

reproduction (Regnault-Roger & Hamraoui, 1995) and deterrence of feeding (Hummerbrunner & Isman, 2001).

The above studies with both whole oils and components indicate that tea tree oil is likely to be toxic to insects. However, it has been stated that the acute toxicity of monoterpenes to insects is relatively low, compared to conventional insecticides (Lee *et al.*, 1997). Whether this is also true for tea tree oil remains unknown.

### **4.3 Other acute toxicity data**

One study has shown that d-limonene is toxic to the earthworm *Eisenia fetida* (Savigny) (Karr *et al.*, 1990). The LD<sub>50</sub> by topical application was 60 ppm, and when earthworms were exposed to 12.6 ppm it took 4.9 h for 50% of the organisms to die. Chronic exposure to limonene also resulted in weight loss.

### **4.4 Conclusions**

Although very limited data are available regarding the ecotoxicity of tea tree oil, it can be extrapolated from data for other essential oils and components that tea tree oil should be considered slightly to moderately toxic, as a conservative estimate of overall ecotoxicity.

# Chapter 5. Literature Database

The existing scientific literature on TTO are not readily accessible to most industry stakeholders. A comprehensive collection of TTO literature in the form of an electronic database available through the ATTIA web site would be a valuable resource for the industry.

## 5.1 Methods

The following electronic databases were searched for publications that include data on TTO, TTO components, *Melaleuca alternifolia* and other *Melaleuca* species of relevance to the TTO industry: Agricola (1979 to current), Biological Abstracts (1995 to current), CAB Abstracts (1973 to current), Current Contents (1993 week 27 to current), EMBASE (1988 to current) and Medline (1966 to current). Articles up to and including those indexed on these databases by June 2003 were included. Information on popular press books was primarily found from general internet searches, including searches of websites specifically dealing with books. Additional articles were sourced from the extensive literature collections of C. Carson and K. Hammer. Publications containing any of the above keywords were manually scrutinised to identify additional papers. Publications containing substantial reference to tea tree oil, in the form of one or more paragraphs, were included in the database.

The journal articles cited in the database came from approximately 200 different publications, from approximately 100 different publishers. Wherever possible, the contact details for each publisher were obtained. A request was sent to each publisher requesting permission to reproduce the relevant article(s) in full in the tea tree oil database. The majority of publishers were contacted by May 31, 2003. Articles that were written entirely in a language other than english were not contacted. In addition, journals for which no contact details could be found, despite extensive searching, were not contacted.

Where permission was granted to include the full text of articles, they were either obtained in the form of PDF files from journal websites or authors, or each page of the article was scanned to create an image and a PDF file was constructed.

## **5.2 Results**

### **Citations**

More than 500 tea tree oil publications were found, including research articles, reviews, conference abstracts or presentations, books and theses. Several citations were omitted from the database, usually because they had been made redundant by subsequent publication, were never officially published, or because of insufficient quality.

### **Obtaining permission for reproduction of material**

Results of permission requests to publishers are shown in Appendix 2. Due to the modest budget for the project the decision was made to not pay fees if payment was required in order to reproduce articles. Permission to reproduce the full text of articles was requested on the basis that the articles would be available through the ATTIA web site, to ATTIA members only and that the database would be password protected.

### **Database construction and delivery**

The database was structured as an introductory page, a list of citations (Appendix 1), with links to either the abstract or full text or both, and a list of abstracts. The list of abstracts is not included in an appendix because copyright permission to reproduce them in this report was not granted. It is intended that the database will be available through the ATTIA web site (<http://www.teatree.org.au/>). ATTIA bears responsibility for making the database available through its web site, for ensuring that it is available only to members and that it is password protected. It should be noted that permission has been granted for the use of the articles and abstracts within this database for ATTIA members for personal educational purposes only. Permission has not been granted for ATTIA members to reproduce or distribute this information. To do so would be an infringement of copyright.

## Chapter 6. Material safety data sheet

A material safety data sheet (MSDS) was created for tea tree oil (Appendix 3), following the guidelines set out in the National Code of Practice for the Preparation of Material Safety Data Sheets (National Occupational Safety and Health Commission, 2003).

Industry personnel, scientific literature and the following data sources were consulted to obtain correct, up to date information for tea tree oil:

1. International Standards Organisation (1996) Oil of Melaleuca, terpinen-4-ol type (tea tree oil). International Standard ISO 4730:1996(E), International Standards Organisation, Geneva
2. Sweet DV. (Editor) (1997) Registry of toxic effects of chemical substances (RTECS), comprehensive guide. U.S. Department of Health and Human Services, Cincinnati, Ohio.
3. Standard for the uniform scheduling of drugs and poisons (2002) Commonwealth Department of Health Published Canberra: Australian Government Publishing Service. March 2002, 16.
4. Australian code for the transport of dangerous goods by road and rail (ADG code) (1999). Commonwealth Department of Transport and Regional Services, Canberra, 6th Edition.
5. Approved criteria for classifying hazardous substances (NOHSC: 1008(1994)) National Occupational Health and Safety Commission. Australian Govt. Pub. Service, Canberra, 1994.
6. The Australian inventory of chemical substances (1992). Department of the Arts, Sport, the Environment and Territories, Commonwealth Environment Protection Agency, AGPS Press, Canberra.
7. National Occupational Health and Safety Commission (2003) National Code of Practice for the Preparation of Material Safety Data Sheets [NOHSC:2011 (2003)]. Australian Government Publishing Service, Canberra, April 2003.

# Chapter 7. Recommendations for further studies

The recommendations for further studies listed below represent the opinions of the authors of this report. It is quite plausible that other experts, such as toxicologists, dermatologists or medical doctors may arrive at a different set of conclusions regarding what further tea tree oil research needs to be conducted. As such, this list must not be regarded as exhaustive, definitive or in order of priority.

The recommendations as to further research that should be conducted into tea tree oil can be subdivided into two broad categories, shown below.

## 1) Safety and toxicity

- a. Toxicity studies, using an animal model
  - Safety of inhaled tea tree oil
  - Absorption through broken skin and/or wounds
  - Reproductive toxicity, including mutagenicity and teratology studies
  - Chronic toxicity
- b. Toxicity studies, using human volunteers
  - Absorption through skin, looking for oil or metabolites in blood and urine
  - Repeat application studies
  - Mucous membrane irritation studies
- c. Ecotoxicity studies
  - Aquatic and terrestrial insects
  - Fish species
  - Plant species

## 2) Clinical efficacy (pilot studies and full clinical trials)

- Wounds (diabetic ulcers, chronic wounds)
- Head lice
- Impetigo
- Vaginal candidiasis
- Mouthrinse for gingivitis
- Pre and post-operative wound infections

In addition, the work investigating the anti-inflammatory properties of tea tree oil must be continued and expanded. Corroboration of existing clinical data for infections or conditions such as tinea, dandruff, acne, MRSA carriage, onychomycosis and oral candidiasis is imperative.

There are several other potential clinical applications for tea tree oil that first require significant preliminary in vitro work.

- Tea tree oil has great potential as an intra-vaginal microbicide
- The activity of tea tree oil against microbial biofilms needs to be determined, with a view to using it to impregnate indwelling medical devices such as catheters.
- The efficacy of aerosolised tea tree oil against bacteria and microbial biofilms requires attention, as inhaled tea tree oil may be a potential therapy for lung infections such as cystic fibrosis

# References

- Affi, S. H., Al-Thobaiti, S. & Rasem, B. M. 2001. Multiple exposure of Asian sea bass (*Lates calcarifer*, Centropomidae) to clove oil: a histopathological study. *Journal of Aquaculture in the Tropics* **16**:131-138.
- Altman, P. M. 1988. Australian tea tree oil. *Australian Journal of Pharmacy* **69**:276-278.
- Andrews, R. E., L. W. Parks, and K. D. Spence. 1980. Some effects of Douglas fir terpenes on certain microorganisms. *Applied and Environmental Microbiology* **40**:301-304.
- Anon. 1930. A retrospect. *Medical Journal of Australia* **i**:85-89.
- Anon. 1933a. An Australian antiseptic oil. *British Medical Journal* **i**:966.
- Anon. 1933b. Ti-trol oil. *British Medical Journal* **ii**:927.
- Ånséhn, S. 1990. The effect of tea tree oil on human pathogenic bacteria and fungi in a laboratory study. *Swedish Journal of Biological Medicine* **2**:5-8.
- Arweiler, N. B., N. Donos, L. Netuschil, E. Reich, and A. Sculean. 2000. Clinical and antibacterial effect of tea tree oil--a pilot study. *Clinical Oral Investigations* **4**:70-73.
- Atkinson, N., and H. E. Brice. 1955. Antibacterial substances produced by flowering plants. 2. The antibacterial action of essential oils from some Australian plants. *Australian Journal of Experimental Biology* **33**:547-554.
- Baker, G. 1999. Tea tree breeding, pp. 135-154. In: Tea tree: the genus *Melaleuca*. Eds: Southwell, I., and R. Lowe. Harwood Academic Publishers, Amsterdam, Netherlands.
- Bassett, I. B., D. L. Pannowitz, and R. S. C. Barnetson. 1990. A comparative study of tea-tree oil versus benzoylperoxide in the treatment of acne. *Medical Journal of Australia* **153**:455-458.
- Banes-Marshall, L., P. Cawley, and C. A. Phillips. 2001. *In vitro* activity of *Melaleuca alternifolia* (tea tree) oil against bacterial and *Candida* spp. isolates from clinical specimens. *British Journal of Biomedical Science* **58**:139-145.
- Belaiche, P. 1985. Propriétés germicides de l'huile essentielle de *Melaleuca alternifolia* (Cheel.) dans les infections urinaires colibacillaires chroniques idiopathiques. *Phytotherapy* **15**:9-11.
- Beylier, M. F. 1979. Bacteriostatic activity of some Australian essential oils. *Perfumer and Flavourist* **4**:23-25.
- Bischoff, K., and F. Guale. 1998. Australian tea tree (*Melaleuca alternifolia*) oil poisoning in three purebred cats. *Journal of Veterinary Diagnostic Investigation* **10**:208-210.
- Bishop, C. D. 1995. Antiviral activity of the essential oil of *Melaleuca alternifolia* (Maiden & Betche) Cheel (Tea Tree) against tobacco mosaic virus. *Journal of Essential Oil Research* **7**:641-644.
- Bishop, C. D., and J. Reagan. 1998. Control of the storage pathogen *Botrytis cinerea* on Dutch White cabbage (*Brassica oleracea* var. *capitata*) by the essential oil of *Melaleuca alternifolia*. *Journal of Essential Oil Research* **10**:57-60.
- Bishop, C. D., and I. B. Thornton. 1997. Evaluation of the antifungal activity of the essential oils of *Monarda citriodora* var. *citriodora* and *Melaleuca alternifolia* on post-harvest pathogens. *Journal of Essential Oil Research* **9**:77-82.
- Blackwell, R. 1991a. An insight into aromatic oils: Lavender and tea tree. *British Journal of Phytotherapy* **2**:5-30.
- Blackwell, A. L. 1991b. Tea tree oil and anaerobic (bacterial) vaginosis [letter]. *Lancet* **337**:300.
- Bolton, K. G. E., and M. Greenway. 1997. A feasibility study of *Melaleuca* trees for use in constructed wetlands in subtropical Australia. *Water Science and Technology* **35**:247-254.
- Bolton, K. G. E., and M. Greenway. 1999a. Nutrient sinks in a constructed *Melaleuca* wetland receiving secondary treated effluent. *Water Science & Technology* **40**:341-347.
- Bolton, K. G. E., and M. Greenway. 1999b. Pollutant removal capability of a constructed *Melaleuca* wetland receiving primary settled sewage. *Water Science & Technology* **39**:199-206.
- Brophy, J. J., N. W. Davies, I. A. Southwell, I. A. Stiff, and L. R. Williams. 1989. Gas chromatographic quality control for oil of *Melaleuca* terpinen-4-ol type (Australian tea tree). *Journal of Agriculture and Food Chemistry* **37**:1330-1335.

- Bourne, K. Z., N. Bourne, S. F. Reising, and L. R. Stanberry.** 1999. Plant products as topical microbicide candidates: assessment of in vitro and in vivo activity against herpes simplex virus type 2. *Antiviral Research* **42**:219-226.
- Bowden, L.** 2001. The effectiveness of tea tree oil in reducing hospital acquired infections in care of the elderly ward. (abstract) Infection Control Nurses Association Annual Infection Control Conference. 24-28 September 2001. Blackpool, United Kingdom p. 23.
- Brand, C., A. Ferrante, R. H. Prager, T. V. Riley, C. F. Carson, J. J. Finlay-Jones, and P. H. Hart.** 2001. The water soluble components of the essential oil of *Melaleuca alternifolia* (tea tree oil), suppress the production of superoxide by human monocytes, but not neutrophils, activated in vitro. *Inflammation Research* **50**:213-219.
- Brand, C., M. A. Grimbaldeston, J. R. Gamble, J. Drew, J. J. Finlay-Jones, and P. H. Hart.** 2002a. Tea tree oil reduces the swelling associated with the efferent phase of a contact hypersensitivity response. *Inflammation Research* **51**:236-44.
- Brand, C., S. L. Townley, J. J. Finlay-Jones, and P. H. Hart.** 2002b. Tea tree oil reduces histamine-induced oedema in murine ears. *Inflammation Research* **51**:283-9.
- Buck, D. S., D. M. Nidorf, and J. G. Addino.** 1994. Comparison of two topical preparations for the treatment of onychomycosis: *Melaleuca alternifolia* (tea tree) oil and clotrimazole. *Journal of Family Practice* **38**:601-605.
- Caboi, F., S. Murgia, M. Monduzzi, and P. Lazzari.** 2002. NMR investigation on *Melaleuca alternifolia* essential oil dispersed in the monoolein aqueous system: Phase behavior and dynamics. *Langmuir* **18**:7916-7922.
- Caelli, M., J. Porteous, C. F. Carson, R. Heller, and T. V. Riley.** 2000. Tea tree oil as an alternative topical decolonization agent for methicillin-resistant *Staphylococcus aureus*. *Journal of Hospital Infection* **46**:236-237.
- Campbell, R. E., Lilley, J. H., Taukhid, Panyawachira, V. & Kanchanakhan, S.** 2001. *In vitro* screening of novel treatments for *Aphanomyces invadans*. *Aquaculture Research* **32**:223-233
- Caolo-Tanski, J. M., , L. E. Hanson, A. L. Hill, and J. P. Hill.** 2002. Use of *Melaleuca alternifolia* oil for plant disease control. (abstract) presented at the American Phytopathological Society's annual meeting in Milwaukee, Wisconsin, July 27-31, 2002.
- Caolo-Tanski, J. M., , L. E. Hanson, A. L. Hill, and J. P. Hill.** 2002. The potential use of Australian "tea tree oil" (*Melaleuca alternifolia*) as a method of control for several plant pathogens. (abstract) Proceedings of the 6th annual Rocky Mountain Plant Biotechnology and Molecular Biology Symposium. pg. 22. 2002. (poster) at Colorado State University, Ft.Collins April 17, 2002.
- Carson, C. F., L. Ashton, L. Dry, D. W. Smith, and T. V. Riley.** 2001. *Melaleuca alternifolia* (tea tree) oil gel (6%) for the treatment of recurrent herpes labialis. *Journal of Antimicrobial Chemotherapy* **48**:450-1.
- Carson, C. F., B. D. Cookson, H. D. Farrelly, and T. V. Riley.** 1995a. Susceptibility of methicillin-resistant *Staphylococcus aureus* to the essential oil of *Melaleuca alternifolia*. *Journal of Antimicrobial Chemotherapy* **35**:421-4.
- Carson, C. F., K. A. Hammer, and T. V. Riley.** 1995b. Broth micro-dilution method for determining the susceptibility of *Escherichia coli* and *Staphylococcus aureus* to the essential oil of *Melaleuca alternifolia* (tea tree oil). *Microbios* **82**:181-5.
- Carson, C. F., K. A. Hammer, and T. V. Riley.** 1996. In-vitro activity of the essential oil of *Melaleuca alternifolia* against *Streptococcus* spp. *Journal of Antimicrobial Chemotherapy* **37**:1177-1178.
- Carson, C. F., B. J. Mee, and T. V. Riley.** 2002. Mechanism of action of *Melaleuca alternifolia* (tea tree) oil on *Staphylococcus aureus* determined by time-kill, lysis, leakage, and salt tolerance assays and electron microscopy. *Antimicrobial Agents & Chemotherapy* **46**:1914-1920.
- Carson, C. F., and T. V. Riley.** 1993. Antimicrobial activity of the essential oil of *Melaleuca alternifolia* [review]. *Letters in Applied Microbiology* **16**:49-55.
- Carson, C. F., and T. V. Riley.** 1995. Antimicrobial activity of the major components of the essential oil of *Melaleuca alternifolia*. *Journal of Applied Bacteriology* **78**:264-269.
- Carson, C. F., and T. V. Riley.** 1994. Susceptibility of *Propionibacterium acnes* to the essential oil of *Melaleuca alternifolia*. *Letters in Applied Microbiology* **19**:24-25.

- Cassella, S., J. P. Cassella, and I. Smith.** 2002. Synergistic antifungal activity of tea tree (*Melaleuca alternifolia*) and lavender (*Lavandula angustifolia*) essential oils against dermatophyte infection. *International Journal of Aromatherapy* **12**:2-15.
- Chan, C. H., and K. W. Loudon.** 1998. Activity of tea tree oil on methicillin-resistant *Staphylococcus aureus* (MRSA). *Journal of Hospital Infection* **39**:244-245.
- Chand, S., P. Karuso, I. Lusunzi, D. A. Veal, and L. R. Williams.** 1994. Rapid screening of the antimicrobial activity of extracts and natural products. *Journal of Antibiotics* **47**:751-760.
- Chao, S. C., D. G. Young, and C. J. Oberg.** 2000. Screening for inhibitory activity of essential oils on selected bacteria, fungi and viruses. *Journal of Essential Oil Research* **12**:639-649.
- Chou J. T., P. A. Rossignol, J. W. Ayres.** 1997. Evaluation of commercial insect repellents on human skin against *Aedes aegypti* (Diptera: Culicidae). *Journal of Medical Entomology* **34**:624-630.
- Christoph, F., P. M. Kaulfers, and E. Stahl-Biskup.** 2000. A comparative study of the in vitro antimicrobial activity of tea tree oils s.l. with special reference to the activity of beta-triketones. *Planta Medica* **66**:556-560.
- Christoph, F., P. M. Kaulfers, and E. Stahl-Biskup.** 2001. In vitro evaluation of the antibacterial activity of beta-triketones admixed to Melaleuca oils. *Planta Medica* **67**:768-71.
- Christoph, F., E. Stahl-Biskup, and P. M. Kaulfers.** 2001. Death kinetics of *Staphylococcus aureus* exposed to commercial tea tree oils s.l. *Journal of Essential Oil Research* **13**:98-102.
- Colton, R. T., and G. J. Murtagh.** 1999. Cultivation of tea tree, pp. 63-78. *In: Tea tree: the genus Melaleuca*. Eds: Southwell, I., and R. Lowe. Harwood Academic Publishers, Amsterdam, Netherlands.
- Concha, J. M., L. S. Moore, and W. J. Holloway.** 1998. Antifungal activity of *Melaleuca alternifolia* (tea tree) oil against various pathogenic organisms. *Journal of the American Podiatric Medical Association* **88**:489-492.
- Cox, S. D., J. E. Gustafson, C. M. Mann, J. L. Markham, Y. C. Liew, R. P. Hartland, H. C. Bell, J. R. Warmington, and S. G. Wyllie.** 1998. Tea tree oil causes K<sup>+</sup> leakage and inhibits respiration in *Escherichia coli*. *Letters in Applied Microbiology* **26**:355-358.
- Cox, S. D., C. M. Mann, and J. L. Markham.** 2001a. Interactions between components of the essential oil of *Melaleuca alternifolia*. *Journal of Applied Microbiology* **91**:492-497.
- Cox, S. D., C. M. Mann, J. L. Markham, H. C. Bell, J. E. Gustafson, J. R. Warmington, and S. G. Wyllie.** 2000. The mode of antimicrobial action of the essential oil of *Melaleuca alternifolia* (tea tree oil). *Journal of Applied Microbiology* **88**:170-175.
- Cox, S. D., C. M. Mann, J. L. Markham, J. E. Gustafson, J. R. Warmington, and S. G. Wyllie.** 2001b. Determining the antimicrobial actions of tea tree oil. *Molecules* **6**:87-91.
- Cox, S. D., J. L. Markham, C. M. Mann, S. G. Wyllie, J. E. Gustafson, and J. R. Warmington.** 1997. The effect of the essential oil of *Melaleuca alternifolia* on *Escherichia coli*. *In: Progress in Essential Oil Research* Eds: Baser, K. H. C. & Kirmer, N., Proceedings of the 28<sup>th</sup> International Symposium on Essential Oils, 1-3 September, 1997, Eskisehir, Turkey.
- Craven, L. A.** 1999. Behind the names: the botany of tea tree, cajput and niaouli, pp. 11-28. *In: Tea tree: the genus Melaleuca*. Eds: Southwell, I., and R. Lowe. Harwood Academic Publishers, Amsterdam, Netherlands.
- Darben, T., B. Cominos, and C. T. Lee.** 1998. Topical eucalyptus oil poisoning. *Australasian Journal of Dermatology* **39**:265-267.
- D'Auria, F. D., L. Laino, V. Strippoli, M. Tecca, G. Salvatore, L. Battinelli, and G. Mazzanti.** 2001. In vitro activity of tea tree oil against *Candida albicans* mycelial conversion and other pathogenic fungi. *Journal of Chemotherapy* **13**:377-383.
- Dillard, H. R., A. C. Cobb, K. E. McCormick, G. A. Straight, S. J. Walker, and A. T. Burr.** 2000. Evaluation of fungicides for control of alternaria leaf spot in cabbage. *Fungicide and Nematicide Tests* **56**:V1.
- Downs, A. M. R., K. A. Stafford, and G. C. Coles.** 2000. Monoterpenoids and tetralin as pediculocides. *Acta Dermato Venereologica* **80**: 69-70.
- Elliott, C.** 1993. Tea tree oil poisoning [letter] [see comments]. *Medical Journal of Australia* **159**:830-831.

- Elsom, G. K. F., and D. Hide.** 1999. Susceptibility of methicillin-resistant *Staphylococcus aureus* to tea tree oil and mupirocin. *Journal of Antimicrobial Chemotherapy* **43**:427-428.
- Faoagali, J., N. George, and J. F. Leditschke.** 1997. Does tea tree oil have a place in the topical treatment of burns? *Burns* **23**:349-351.
- Feinblatt, H. M.** 1960. Cajeput\* oil for the treatment of furunculosis. *Journal of the National Medical Association* **52**:32-33.
- Fitzi, J., J. Furst-Jucker, T. Wegener, R. Saller, and J. Reichling.** 2002. Phytotherapy of chronic dermatitis and pruritus of dogs with a topical preparation containing tea tree oil (Bogaskin (R)). *Schweizer Archiv fur Tierheilkunde* **144**:223-231.
- Franzios, G., Mirotsoy, M., Hatziapostolou, E., Kral, J., Scouras, Z. G. & Mavragani-Tsipidou, P.** 1997. Insecticidal and genotoxic activities of mint essential oils *Journal of Agricultural and Food Chemistry* **45**: 2690 - 2694
- Gao, S., and J. Singh.** 1997. Mechanism of transdermal transport of 5-fluorouracil by terpenes: carvone, 1,8-cineole and thymol. *International Journal of Pharmaceutics* **154**:67-77.
- Gao, S., and J. Singh.** 1998. In vitro percutaneous absorption enhancement of a lipophilic drug tamoxifen by terpenes. *Journal of Controlled Release* **51**:193-199.
- Glickman, A. H., Alexander, H. C., Buccafusco, R. J., Morris, C. R., Francis, B. O., Surprenant, D. C. & Ward, T. J.** 1995 An evaluation of the aquatic hazard of cumene (isopropyl benzene). *Ecotoxicology & Environmental Safety* **31**(3):287-289.
- Godwin, D. A., and B. B. Michniak.** 1999. Influence of drug lipophilicity on terpenes as transdermal penetration enhancers. *Drug Development and Industrial Pharmacy* **25**:905-915.
- Görduysus, M. O., F. Tasman, S. Tuncer, and I. Etikan.** 1997. Solubilizing efficiency of different gutta-percha solvents: a comparative study. *Journal of Nihon University School of Dentistry* **39**:133-135.
- Griffin, S. G., J. L. Markham, and D. N. Leach.** 2000. An agar dilution method for the determination of the minimum inhibitory concentration of essential oils. *Journal of Essential Oil Research* **12**:249-255.
- Griffin, S. G., S. G. Wyllie, and J. L. Markham.** 1999. Determination of octanol-water partition coefficients for terpenoids using reversed-phase high-performance liquid chromatography. *Journal of Chromatography A* **864**:221-228.
- Griffin, S. G., S. G. Wyllie, and J. L. Markham.** 2001. Role of the outer membrane of *Escherichia coli* AG100 and *Pseudomonas aeruginosa* NCTC 6749 and resistance/susceptibility to monoterpenes of similar chemical structure. *Journal of Essential Oil Research* **13**:380-386.
- Griffin, S. G., S. G. Wyllie, J. L. Markham, and D. N. Leach.** 1999b. The role of structure and molecular properties of terpenoids in determining their antimicrobial activity. *Flavour and Fragrance Journal* **14**:322-332.
- Grodniczky, J. A. & Coats, J. R.** 2002. QSAR evaluation of monoterpenoids' insecticidal activity. *Journal of Agricultural and Food Chemistry* **50**:4576-4580.
- Groppo, F. C., J. C. Ramacciato, R. P. Simoes, F. M. Florio, and A. Sartoratto.** 2002. Antimicrobial activity of garlic, tea tree oil, and chlorhexidine against oral microorganisms. *International Dental Journal* **52**:433-437.
- Guenther, E.** 1968. Australian tea tree oils. Report of a field survey. *Perfumery and Essential Oil Records* **59**:642-644.
- Gustafson, J. E., S. D. Cox, Y. C. Liew, S. G. Wyllie, and J. R. Warmington.** 2001. The bacterial multiple antibiotic resistant (Mar) phenotype leads to increased tolerance to tea tree oil. *Pathology* **33**:211-215.
- Gustafson, J. E., Y. C. Liew, S. Chew, J. Markham, H. C. Bell, S. G. Wyllie, and J. R. Warmington.** 1998. Effects of tea tree oil on *Escherichia coli*. *Letters in Applied Microbiology* **26**:194-198.
- Hada, T., S. Furuse, Y. Matsumoto, H. Hamashima, K. Masuda, K. Shiojima, T. Arai, and M. Sasatsu.** 2001. Comparison of the effects in vitro of tea tree oil and plaunotol on methicillin-susceptible and methicillin-resistant strains of *Staphylococcus aureus*. *Microbios* **106 S2**:133-141.
- Hada, T., Y. Inoue, A. Shiraishi, and H. Hamashima.** 2003. Leakage of K<sup>+</sup> ions from *Staphylococcus aureus* in response to tea tree oil. *Journal of Microbiological Methods* **53**:309-312.

- Hägermark, Ö., and C.-F Wahlgren.** 1992. Some methods for evaluating itch and their application for studying pathophysiological mechanisms. *Journal of Dermatological Science* **4**:55-62.
- Hales, J.** 1999. The antimicrobial activity of oil of *Melaleuca alternifolia* (Australian tea tree oil) against selected oral pathogens and periodontitis plaque samples [poster presentation]. *Journal of Dental Research* **78**: 344.
- Halford, A. C. F.** 1936. Diabetic gangrene. *Medical Journal of Australia* **ii**:121-122.
- Hammer, K. A., C. F. Carson, and T. V. Riley.** 1996. Susceptibility of transient and commensal skin flora to the essential oil of *Melaleuca alternifolia* (tea tree oil). *American Journal of Infection Control* **24**:186-189.
- Hammer, K. A., C. F. Carson, and T. V. Riley.** 1999a. In vitro susceptibilities of lactobacilli and organisms associated with bacterial vaginosis to *Melaleuca alternifolia* (tea tree) oil. *Antimicrobial Agents & Chemotherapy* **43**:196.
- Hammer, K. A., C. F. Carson, and T. V. Riley.** 2003. Antifungal activity of the components of *Melaleuca alternifolia* (tea tree) oil. *Journal of Applied Microbiology* **95**:853-860.
- Hammer, K. A., L. Dry, M. Johnson, E. M. Michalak, C. F. Carson, and T. V. Riley.** 2003. Susceptibility of oral bacteria to *Melaleuca alternifolia* (tea tree) oil in vitro. *Oral Microbiology and Immunology* **18**:389-392.
- Harkenthal, M., G. Layh-Schmitt, and J. Reichling.** 2000. Effect of Australian tea tree oil on the viability of the wall-less bacterium *Mycoplasma pneumoniae*. *Pharmazie* **55**:380-384.
- Hart, P. H., C. Brand, C. F. Carson, T. V. Riley, R. H. Prager, and J. J. Finlay-Jones.** 2000. Terpinen-4-ol, the main component of the essential oil of *Melaleuca alternifolia* (tea tree oil), suppresses inflammatory mediator production by activated human monocytes. *Inflammation Research* **49**:619-626.
- Hausen, B. M., J. Reichling, and M. Harkenthal.** 1999. Degradation products of monoterpenes are the sensitizing agents in tea tree oil. *American Journal of Contact Dermatitis* **10**:68-77.
- Hayes, A. J., D. N. Leach, and J. L. Markham.** 1997. In vitro cytotoxicity of Australian tea tree oil using human cell lines. *Journal of Essential Oil Research* **9**:575-582.
- Heitmuller, P. T., Hollister, T. A. & Parrish, P. R.** 1981. Acute toxicity of 54 industrial chemicals to sheepshead minnows (*Cyprinodon variegatus*). *Bull Environ Contam Toxicol* **27(5)**: 596-604.
- Hensyl, W. R.,** Stedman's medical dictionary. 25<sup>th</sup> edn. Williams & Wilkins, Baltimore. USA.
- Hogg, C. L., Svoboda, K. P., Hampson, J. B. & Brocklehurst, S.** 2001. Investigation into the composition and bioactivity of essential oil from lovage (*Levisticum officinale* W. D. J. Koch). *International Journal of Aromatherapy* **11**:144-151.
- Homer, L. E., D. N. Leach, D. Lea, L. S. Lee, R. J. Henry, and P. R. Baverstock.** 2000. Natural variation in the essential oil content of *Melaleuca alternifolia* Cheel (Myrtaceae). *Biochemical Systematics & Ecology* **28**:367-82.
- Hummelbrunner, L. A. & Isman, M. B.** 2001. Acute, sublethal, antifeedant, and synergistic effects of monoterpenoid essential oil compounds on the tobacco cutworm, *Spodoptera litura* (Lep., Noctuidae) *Journal of Agricultural and Food Chemistry* **49**:715 – 720.
- Humphery, E. M.** 1930. A new Australian germicide. *The Medical Journal of Australia* **1**:417-418.
- Hussein, M. M. A., Wada, S., Hatai, K. & Yamamoto, A.** 2000. Antimycotic activity of eugenol against selected water molds. *Journal of Aquatic Animal Health* **12(3)**:224-229.
- Inouye, S., T. Takizawa, and H. Yamaguchi.** 2001. Antibacterial activity of essential oils and their major constituents against respiratory tract pathogens by gaseous contact. *Journal of Antimicrobial Chemotherapy* **47**:565-573.
- Inouye, S., K. Uchida, and H. Yamaguchi.** 2001. In-vitro and in-vivo anti-*Trichophyton* activity of essential oils by vapour contact. *Mycoses* **44**:99-107.
- International Organisation or Standardisation.** 1996. ISO 4730:1996, Oil of *Melaleuca*, terpinen-4-ol type (tea tree oil). International Organisation for Standardisation, Geneva, Switzerland.
- Jackson, R. W., and J. A. DeMoss.** 1965. Effects of toluene on *Escherichia coli*. *Journal of Bacteriology* **90**:1420-1424.
- Jacobs, M. R., and C. S. Hornfeldt.** 1994. Melaleuca oil poisoning. *Journal of Toxicology - Clinical Toxicology* **32**:461-464.

- Jandera, V., D. A. Hudson, P. M. de Wet, P. M. Innes, and H. Rode.** 2000. Cooling the burn wound: evaluation of different modalities. *Burns* **26**:265-270.
- Jandourek, A., J. K. Vaishampayan, and J. A. Vazquez.** 1998. Efficacy of melaleuca oral solution for the treatment of fluconazole refractory oral candidiasis in AIDS patients. *Aids* **12**:1033-1037.
- Johns, M. R., J. E. Johns, and V. Rudolph.** 1992. Steam distillation of tea tree (*Melaleuca alternifolia*) oil. *Journal of Science and Food Agriculture* **58**:49-53.
- Juhnke, I. & Luedemann, D.** 1978. Results of the investigation of 200 chemical compounds for acute fish toxicity with the golden orfe test. *Z. Wasser-Abwasser-Forsch.* **11(5)**:161-164.
- Kamrin, M. A.** 1997. Pesticide profiles: toxicity, environmental impact and fate. Lewis publishers, Boca Raton, Florida USA.
- Kaplowitz, G. J.** 1990. Evaluation of Gutta-percha solvents. *Journal of Endodontics* **16**:539-540.
- Kaplowitz, G. L.** 1991. The effect of essential oil type on the setting time of Grossman's sealer and Roth root canal cement. *Journal of Endodontics* **17**:280-281.
- Karpouhtsis, I., Pardali, E., Feggou, E., Kokkini, S., Scouras, Z. G. & Mavragani-Tsipidou, P.** 1998. Insecticidal and genotoxic activities of oregano essential oils *Journal of Agricultural and Food Chemistry* **46**:1111-1115.
- Karr, L. L., Drewes, C. D. & Coats, J. R.** 1990. Toxic effects of d-limonene in the earthworm *Eisenia foetida* (Savigny). *Pesticide Biochemistry & Physiology.* **36(2)**:175-186.
- Karr, L. L. & Coats, J. R.** 1988. Insecticidal properties of d-limonene. *Journal of Pesticide Science.* **13(2)**:287-290.
- Keene, J. L., Noakes, D. L. G., Moccia, R. D. & Soto, C. G.** 1998. The efficacy of clove oil as an anaesthetic for rainbow trout, *Oncorhynchus mykiss* (Walbaum). *Aquaculture Research* **29**:89-101.
- Klimmek, J. K., R. Nowicki, K. Szendzielorz, M. Kunicka, R. Rosentrit, G. Honisz, and W. Krol.** 2002. Application of tea tree oil and its preparations in combined treatment of dermatomycoses. *Mikologia Lekarska* **9**:93-96.
- Knight, T. E., and B. M. Hausen.** 1994. Melaleuca oil (tea tree oil) dermatitis. *Journal of the American Academy of Dermatology* **30**:423-427.
- Lassak, E. V., and T. McCarthy.** 1983. Antiseptics and bactericides - treatment of wounds and inflammations, p. 93-99, 115, Australian Medicinal Plants. Methuen Australia, North Ryde.
- LeBlanc, G. A.** 1980. Acute toxicity of priority pollutants to water flea (*Daphnia magna*). *Bulletin of Environmental Contamination and Toxicology* **24**:684-691.
- Lee, S., Tsao, R., Peterson, C. & Coats, J. R.** 1997. Insecticidal activity of monoterpenoids to western corn rootworm (Coleoptera: Chrysomelidae), twospotted spider mite (Acari: Tetranychidae), and house fly (Diptera: Muscidae). *Journal of Economic Entomology* **90(4)**:883-892.
- Lee, B. H., Choi, W. S., Lee, S. E. & Park, B. S.** 2001. Fumigant toxicity of essential oils and their constituent compounds towards the rice weevil, *Sitophilus oryzae* (L.). *Crop Protection* **20**:317-320.
- Lee, S., Peterson, C. J. & Coats, J. R.** 2003. Fumigation toxicity of monoterpenoids to several stored product insects. *Journal of Stored Products Research* **39**:77-85.
- Low, D., B. D. Rawal, and W. J. Griffin.** 1974. Antibacterial action of the essential oils of some Australian Myrtaceae with special references to the activity of chromatographic fractions of oil of *Eucalyptus citriodora*. *Planta Medica* **26**:184-189.
- Low, T.** 1990. *Bush Medicine. A Pharmacopoeia of Natural Remedies.* Collins/Angus and Robertson Publishers. Sydney, New South Wales, Australia
- McCage, C. M., S. M. Ward, C. A. Paling, D. A. Fisher, P. J. Flynn, and J. L. McLaughlin.** 2002. Development of a paw paw herbal shampoo for the removal of head lice. *Phytomedicine* **9**:743-8.
- MacDonald, V.** 1930. The rationale of treatment. *Australian Journal of Dentistry* **34**:281-282.
- McDonald, L. G., and E. Tovey.** 1993. The effectiveness of benzyl benzoate and some essential plant oils as laundry additives for killing house dust mites. *Journal of Allergy and Clinical Immunology* **92**:771-772.
- Magnusson, B. M., P. Runn, and L.-O. D. Koskinen.** 1997. Terpene-enhanced transdermal permeation of water and ethanol in human epidermis. *Acta Dermato Venereologica (Stockholm)* **77**:264-267.

- Mann, C. M., S. D. Cox, and J. L. Markham.** 2000. The outer membrane of *Pseudomonas aeruginosa* NCTC 6749 contributes to its tolerance to the essential oil of *Melaleuca alternifolia* (tea tree oil). *Letters in Applied Microbiology* **30**:294-297.
- Mann, C. M., and J. L. Markham.** 1998. A new method for determining the minimum inhibitory concentration of essential oils. *Journal of Applied Microbiology* **84**:538-44.
- Markham, J. L.** 1999. Biological activity of tea tree oil, pp. 169-190. *In: Tea tree: the genus Melaleuca*. Eds: Southwell, I., and R. Lowe. Harwood Academic Publishers, Amsterdam, Netherlands.
- Marking, L. L., Rach, J. J. & Schreier, T. M.** 1994. Evaluation of antifungal agents for fish culture. *Progressive Fish-Culturist* **56**:225-231.
- May, J., C. H. Chan, A. King, L. Williams, and G. L. French.** 2000. Time-kill studies of tea tree oils on clinical isolates. *Journal of Antimicrobial Chemotherapy* **45**:639-643.
- Maruzzella, J. C., and N. A. Sicurella.** 1960. Antibacterial activity of essential oil vapors. *Journal of American Pharmaceutical Association* **49**:692-694.
- Mikus, J., M. Harkenthal, D. Steverding, and J. Reichling.** 2000. In vitro effect of essential oils and isolated mono- and sesquiterpenes on *Leishmania major* and *Trypanosoma brucei*. *Planta Medica* **66**:366-368.
- Murtagh, J. G.** 1999. Biomass and oil production of tea tree, pp. 109-133. *In: Tea tree: the genus Melaleuca*. Eds: Southwell, I., and R. Lowe. Harwood Academic Publishers, Amsterdam, Netherlands.
- Nelson, R. R. S.** 1997. In-vitro activities of five plant essential oils against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecium* [letter]. *Journal of Antimicrobial Chemotherapy* **40**:305-306.
- Nelson, R. R.** 2000. Selection of resistance to the essential oil of *Melaleuca alternifolia* in *Staphylococcus aureus*. *Journal of Antimicrobial Chemotherapy* **45**:549-550.
- Nenoff, P., U. F. Haustein, and W. Brandt.** 1996. Antifungal activity of the essential oil of *Melaleuca alternifolia* (tea tree oil) against pathogenic fungi in vitro. *Skin Pharmacology* **9**:388-94.
- Obata, Y., K. Takayama, Y. Machida, and T. Nagai.** 1991. Combined effect of cyclic monoterpenes and ethanol on percutaneous absorption of diclofenac sodium. *Drug Design and Delivery* **8**:137-144.
- Olsen, M. W., J. Cassells, and D. Cross.** 1988. Presented at the Annual Meeting of the American Phytopathology Society and the Pacific Division, San Diego, USA. 13-17 November.
- Osti, E., and F. Osti.** 2002. Cutaneous burns of various degrees. Our experience with Burnshield®. Preliminary data. *Annals of Burns and Fire Disasters* **15**(4): 187-190.
- Passino-Reader, D. R., Berlin, W. H. & Hickey, J. P.** 1995. Chronic bioassays of rainbow trout fry with compounds representative of contaminants in Great Lakes fish. *Journal of Great Lakes Research* **21**(3):373-383.
- Peña, E. F.** 1962. *Melaleuca alternifolia* oil - its use for trichomonal vaginitis and other vaginal infections. *Obstetrics and Gynecology* **19**:793-795.
- Penfold, A. R., and R. Grant.** 1923. The germicidal values of the principal commercial Eucalyptus oils and their pure constituents, with observations on the value of concentrated disinfectants. *Journal and Proceedings of the Royal Society of New South Wales* **57**:80-89.
- Penfold, A. R., and R. Grant.** 1924. The germicidal values of the pure constituents of Australian essential oils, together with those for some essential oil isolates and synthetics. Part II. *Journal and Proceedings of the Royal Society of New South Wales* **58**: 117-123.
- Penfold, A. R., and R. Grant.** 1925. The germicidal values of the pure constituents of Australian essential oils, together with those for some essential oil isolates and synthetics. Part III. *Journal and Proceedings of the Royal Society of New South Wales* **59**:346-350
- Penfold, A. R., and F. R. Morrison.** 1937. Some notes on the essential oil of *Melaleuca alternifolia*. *The Australasian Journal of Pharmacy* **18**:274-275.
- Penfold, A. R., and F. R. Morrison.** 1946. Bulletin No. 14. Australian tea trees of economic value. Part 1 (Third edition). Thomas Henry Tennant, Government printer, Sydney, Australia.

- Perry, N. B., N. J. Brennan, J. W. Van Klink, W. Harris, M. H. Douglas, J. A. McGimpsey, B. M. Smallfield, and R. E. Andersen.** 1997. Essential oils from New Zealand manuka and kanuka: chemotaxonomy of *Leptospermum*. *Phytochemistry* 44:1485-1494.
- Polizzi, G., and G. E. Agosteo.** 1995. Efficacy of natural fungicides and chemicals in controlling *graphiola phoenicis* causal agent of false smut of palms. *La Difesa delle Piante* 18:122-126.
- Pradhanang, P. M., M. T. Momol, S. M. Olson, and J. B. Jones.** 2002. Effects of plant essential oils on *Ralstonia solanacearum* population density and bacterial wilt incidence in tomato. *Plant Disease* 87(4):423-427.
- Price, J.** 1998. Burnaid [letter; comment]. *Burns* 24:80-82.
- Priestley, C. M., I. Burgess, and E. M. Williamson.** 1998. Effects of essential oils on house dust mites. *Journal of Pharmacy and Pharmacology* 50 (Suppl):193.
- Ramacciato, J. C., R. P. Simões, F. M. Flório, R. Cecanho, F. C. Groppo, and T. R. M. Mattos-Filho.** 2000. Antimicrobial activity of *Melaleuca alternifolia* against streptococci and *S. aureus*. *Journal of Dental Research* 79:1071.
- Raman, A., U. Weir, and S. F. Bloomfield.** 1995. Antimicrobial effects of tea-tree oil and its major components on *Staphylococcus aureus*, *Staph. epidermidis* and *Propionibacterium acnes*. *Letters in Applied Microbiology* 21:242-245.
- Regnault-Roger, C. & Hamraoui, A.** 1995. Fumigant toxic activity and reproductive inhibition induced by monoterpenes on *Acanthoscelides obtectus* (Say) (Coleoptera), a bruchid of kidney bean (*Phaseolus vulgaris* L.), *Journal of Stored Products Research* 31:291-299.
- Reichling, J., Weseler, A., Landvatter, U., and Saller, R.** 2002. Bioactive essential oils used in phytomedicine as antiinfective agents: Australian tea tree oil and manuka oil. *Acta Phytotherapeutica* 1:26-32.
- Rex, J. H., M. A. Pfaller, T. J. Walsh, V. Chaturvedi, A. Espinel-Ingroff, M. Ghannoum, L. L. Gosey, F. C. Odds, M. G. Rinaldi, D. J. Sheehan, and D. W. Warnock.** 2001. Antifungal susceptibility testing: practical aspects and current challenges. *Clinical Microbiology Reviews* 14:643-658.
- Rushton, R. T., N. W. Davis, J. C. Page, and C. A. Durkin.** 1997. The effect of tea tree oil extract on the growth of fungi. *The Lower Extremity* 4:113-116.
- Russell, M.** 1999. Toxicology of tea tree oil, pp. 191-201. In: Tea tree: the genus *Melaleuca*. Eds: Southwell, I., and R. Lowe. Harwood Academic Publishers, Amsterdam, Netherlands.
- Satchell, A. C., A. Saurajen, C. Bell, and R. S. Barnetson.** 2002a. Treatment of dandruff with 5% tea tree oil shampoo. *Journal of the American Academy of Dermatology* 47:852-5.
- Satchell, A. C., A. Saurajen, C. Bell, and R. S. Barnetson.** 2002b. Treatment of interdigital tinea pedis with 25% and 50% tea tree oil solution: a randomized, placebo-controlled, blinded study. *Australasian Journal of Dermatology* 43:175-178.
- Schnitzler, P., K. Schon, and J. Reichling.** 2001. Antiviral activity of Australian tea tree oil and eucalyptus oil against herpes simplex virus in cell culture. *Pharmazie* 56:343-347.
- Seawright, A.** 1993. Tea tree oil poisoning - comment. *Medical Journal of Australia* 159:831.
- Shapiro, S., A. Meier, and B. Guggenheim.** 1994. The antimicrobial activity of essential oils and essential oil components towards oral bacteria. *Oral Microbiology & Immunology* 9:202-208.
- Sharp, D. W. A., Ed.** 1983. The penguin dictionary of chemistry. Penguin Books Ltd., Middlesex, United Kingdom.
- Shemesh, A., and W. L. Mayo.** 1991. Australian tea tree oil: a natural antiseptic and fungicidal agent. *The Australian Journal of Pharmacy* 72:802-803.
- Sikkema, J., J. A. M. de Bont, and B. Poolman.** 1995. Mechanisms of membrane toxicity of hydrocarbons. *Microbiological Reviews* 59:201-222.
- Sladky, K. K., Swanson, C. R., Stoskopf, M. K., Loomis, M. R. & Lewbart, G. A.** 2001. Comparative efficacy of tricaine methanesulfonate and clove oil for use as anesthetics in red pacu (*Piaractus brachypomus*). *American Journal of Veterinary Research* 62:337-342.
- Smith, K. E.** 1995. Stopping the burn. *Occupational Health & Safety* 64:159-160.
- Soderberg, T. A., A. Johansson, and R. Gref.** 1996. Toxic effects of some conifer resin acids and tea tree oil on human epithelial and fibroblast cells. *Toxicology* 107:99-109.

- Southwell, I. A.** 1993. The search for optimally bioactive Australian tea tree oil. *Acta Horticulture* **344**:256-265.
- Southwell, I. A., S. Freeman, and D. Rubel.** 1997. Skin irritancy of tea tree oil. *Journal of Essential Oil Research* **9**:47-52.
- Southwell, I., and R. Lowe, (Eds.).** 1999. Tea tree - the genus *Melaleuca*. Harwood Academic Publishers, Amsterdam, Netherlands.
- Stroh, J., Wan, M. T., Isman, M. B., Moul, D. J.** 1998. Evaluation of acute toxicity to juvenile pacific coho salmon and rainbow trout of some plant essential oils, a formulated product, and the carrier. *Bulletin of Environmental Contamination & Toxicology* **60(6)**:923-930.
- Swords, G., and G. L. K. Hunter.** 1978. Composition of Australian tea tree oil (*Melaleuca alternifolia*). *Journal of Agricultural and Food Chemistry* **26**:734-737.
- Syed, T. A., Z. A. Qureshi, S. M. Ali, S. Ahmad, and S. A. Ahmad.** 1999. Treatment of toenail onychomycosis with 2% butenafine and 5% *Melaleuca alternifolia* (tea tree) oil in cream. *Tropical Medicine & International Health* **4**:284-287.
- Takahashi, N., A. Kida, Y. Ishizuka, and M. Hiraishi.** 2002. Aromatic oil inhalation the reduction of pain after tonsillectomy. *Oto Rhino Laryngology Tokyo* **45**:5-7.
- Tong, M. M., P. M. Altman, and R. S. Barnetson.** 1992. Tea tree oil in the treatment of tinea pedis. *Australasian Journal of Dermatology* **33**:145-149.
- Uribe, S., J. Ramirez, and A. Peña.** 1985. Effects of  $\beta$ -pinene on yeast membrane functions. *Journal of Bacteriology* **161**:1195-1200.
- Uribe, S., P. Rangel, G. Espínola, and G. Aguirre.** 1990. Effects of cyclohexane, an industrial solvent, on the yeast *Saccharomyces cerevisiae* and on isolated yeast mitochondria. *Applied and Environmental Microbiology* **56**:2114-2119.
- Vazquez, J. A., M. T. Arganoza, D. Boikov, J. K. Vaishampayan, and R. A. Akins.** 2000. In vitro susceptibilities of *Candida* and *Aspergillus* species to *Melaleuca alternifolia* (tea tree) oil. *Revista Iberoamericana de Micología* **17**:60-63.
- Veal, L.** 1996. The potential effectiveness of essential oils as a treatment for headlice, *Pediculus humanus capitis*. *Complementary Therapies in Nursing & Midwifery* **2**:97-101.
- Viollon, C., D. Mandin, and J. P. Chaumont.** 1996. Activities antagonistes, in vitro, de quelques huiles essentielles et de composés naturels volatils vis à vis de la croissance de *Trichomonas vaginalis*. *Fitoterapia* **63**:279-281.
- Walker, M.** 1972. Clinical investigation of Australian *Melaleuca alternifolia* oil for a variety of common foot problems. *Current Podiatry* April, pp.7-15.
- Walsh, L. J., and J. Longstaff.** 1987. The antimicrobial effects of an essential oil on selected oral pathogens. *Periodontology* **8**:11-15.
- Walton, S. F., M. R. Myerscough, and B. J. Currie.** 2000. Studies in vitro on the relative efficacy of current acaricides for *Sarcoptes scabiei* var. *hominis*. *Transactions of the Royal Society of Tropical Medicine & Hygiene* **94**:92-96.
- Wang, C. Y.** 2003. Maintaining postharvest quality of raspberries with natural volatile compounds. *International Journal of Food Science and Technology* **38**:869-875.
- Washington, W. S., S. Engleitner, G. Boontjes, and N. Shanmuganathan.** 1999. Effect of fungicides, seaweed extracts, tea tree oil, and fungal agents on fruit rot and yield in strawberry. *Australian Journal of Experimental Agriculture* **39**:487-494.
- Washington, W. S., S. Engleitner, and J. MacFarlane.** 1991. Effect of fungicides and biological treatments on the control of two-spotted mite of strawberry, 1989. *Fungicide and Nematicide Tests* **46**:106.
- Webb, M., Ruber, H. & Leduc, G.** 1976. The toxicity of various mining flotation reagents to rainbow trout (*Salmo gairdneri*). *Water Research* **10**:303-306.
- Weiss, E. A.** 1997. Myrtaceae. In: *Essential Oil Crops*. pp.235-341. CAB International, Wallingford, United Kingdom.
- Weitzman, I., and R. C. Summerbell.** 1995. The dermatophytes. *Clinical Microbiology Reviews* **8**:240-259.
- Wilson, C. L., J. M. Solar, A. El Ghaouth, and M. E. Wisniewski.** 1997. Rapid evaluation of plant extracts and essential oils for antifungal activity against *Botrytis cinerea*. *Plant Disease* **81**:204-210.

**Yamane, M. A., A. C. Williams, and B. W. Barry.** 1995. Effects of terpenes and oleic acid as skin penetration enhancers towards 5-fluorouracil as assessed with time; permeation, partitioning and differential scanning calorimetry. *International Journal of Pharmaceutics* **116**:237-251.

# Appendix 1 – Literature database

The following is a list of published documents that relate to tea tree oil. This is the most exhaustive and comprehensive bibliography of tea tree oil literature published to date. The abstracts and full text of many of the documents are available on the database. The remainder may be available through document delivery services such as Infotrieve, Ingenta, Loansome Doc on Public Medline or Science Direct. Visit these web sites for further information.

- Adamson S.** (1997) Infection Control. *Hospital & Healthcare* **28(6)**: 24. [News]
- Ahmad AW, Mansor P, Abdul Malek, Y & Jaafar H.** (1998) Distillation of tea-tree (*Melaleuca alternifolia*) oil. I. Establishment of basic parameters and standard conditions for a test distiller and evaluation of two prototype distillers. *Journal of Tropical Agriculture & Food Science* **26**: 175-187. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission.*
- Ahmad AW, Mansor P & Tunku Kassim TAR.** (1998) Distillation of tea-tree (*Melaleuca alternifolia*) oil. II. Comparison of different fuels for steam generation using a prototype distiller. *Journal of Tropical Agriculture & Food Science* **26**: 189-194. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission.*
- Ahmed S & Tsang M.** (2001) A study of the anti-bacterial activity of a number of constituents of 'tea tree' oil against *E. coli* and the effect of varying the constituent ratio. *British Pharmaceutical Conference Abstract Book*. p. 113 [Conference abstract]
- Allen P.** (2001) Tea tree oil: the science behind the antimicrobial hype. *Lancet*. **358**: 1245. [News] No abstract.
- Altman PM.** (1988) Australian tea tree oil. *The Australian Journal of Pharmacy* **69**: 276-278. [Review] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission.*
- Altman PM.** (1988) Potential use of essential oils in cosmetics. *Cosmetics, Aerosols and Toiletries in Australia* **2**: 13-14,22. [Review] No abstract.
- Altman PM.** (1989) Australian tea tree oil - a natural antiseptic. *Australian Journal of Biotechnology* **3**: 247-248. [Review] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission.*
- Altman PM.** (1991) Australian tea tree oil - an update. *Cosmetics, Aerosols and Toiletries in Australia* **5**: 27-29. [Review]
- Anderson JN & Fennessy PA.** (2000) Can tea tree (*Melaleuca alternifolia*) oil prevent MRSA? *Medical Journal of Australia*. 173: 489. [Letter] [Full text \(PDF\)](#) *Copyright 2000, The Medical Journal of Australia. Reproduced with permission.*
- Anon** (1930) A retrospect. *Medical Journal of Australia* **i**: 85-89. [Letter] [Full text \(PDF\)](#) *Copyright 1930, The Medical Journal of Australia. Reproduced with permission.*
- Anon** (1936) Revised medical and dental data of ti-trol (antiseptic oil) and melasol (antiseptic solution). Australian Essential Oils Ltd., Sydney, NSW. [Booklet]
- Anon** (1933) An Australian antiseptic oil. *British Medical Journal* **i**: 966. [Letter]
- Anon** (1933) Ti-trol oil. *British Medical Journal* **ii**: 927. [Letter]
- Anon** (1990) Tea-tree oil and acne. *Lancet* **Dec 8**: 1438. [Letter]
- Anon** (1995) Special takeout feature: Tea tree oil. *CAJ* **111**: 19-21.
- Anon** (1997) Tea tree oil – skin reactions. Bulletin from Swedish Adverse Drug Reactions Advisory Committee (SADRAC) **66**: 4. [Letter]
- Anon** (1997) Tea tree oil – universal agent? *Soap, Perfumery and Cosmetics* **May 1997**: 50-52 [News]
- Anon** (1997) Lessons I've learned. *Complementary Therapies in Medicine* **5**: 241-242. [News]
- Anon** (2002) Tea tree oil, latest alternative medicine. *Journal of the National Medical Association* **92(8)**: A14 [News] | [Full text \(PDF\)](#) *Reproduced with permission*
- Anon** (2002) Aussie tea tree oil wins international recognition – export boost to follow. News release from Standards Australia. [News]
- Ånséhn S.** (1990) The effect of tea tree oil on human pathogenic bacteria and fungi in a laboratory study [Swedish]. *Swedish Journal of Biological Medicine* **2**: 5-8. [Research article] [View abstract in Pubmed](#)
- Apted JH.** (1991) Contact dermatitis associated with the use of tea-tree oil. *Australasian Journal of Dermatology*. **32**: 177. [Letter] | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Arweiler NB, Donos N, Netuschil L, Reich E & Sculean A.** (2000) Clinical and antibacterial effect of tea tree oil - a pilot study. *Clinical Oral Investigations* **4**: 70-73. [Research article] [View abstract in Pubmed](#)
- Atkinson N & Brice HE.** (1955) Antibacterial substances produced by flowering plants. *Australian Journal of Experimental Biology and Medicine* **33**: 547-554. [Research article] No abstract.

- Austin N.** (1987) Tea-tree oil may become megabuck earner. *The Bulletin* **109** (November 10): 38. [News]
- Bailey PCE, Watkins SC, Morris KL, Boon PI.** (2003) Do *Melaleuca ericifolia* Sm. leaves suppress organic matter decay in freshwater wetlands? *Archiv fur Hydrobiologie* **156**: 225-240. [Research article] [Abstract](#)
- Baker GR, Lowe RF & Southwell IA.** (2000) Comparison of oil recovered from tea tree leaf by ethanol extraction and steam distillation. *Journal of Agricultural & Food Chemistry* **48**: 4041-4043. [Research article] [Abstract](#)
- Banes-Marshall L, Cawley P & Phillips Carol A.** (2001) In vitro activity of *Melaleuca alternifolia* (tea tree) oil against bacterial and *Candida* spp. isolates from clinical specimens. *British Journal of Biomedical Science* **58**: 139-145. [Research article] [View abstract in Pubmed](#)
- Bang B & Agner T.** (2000) Picture of the month. Allergic contact dermatitis. [Swedish] *Ugeskrift for Laeger* **162**: 3867. [Case report] No abstract.
- Bassett IB, Pannowitz DL & Barnetson RStC.** (1990) A comparative study of tea-tree oil versus benzoylperoxide in the treatment of acne. *Medical Journal of Australia*. **153**: 455-458. [Research article] [Abstract](#) | [Full text \(PDF\)](#) Copyright 1990, The Medical Journal of Australia. Reproduced with permission.
- Baumann LS.** (2002) Cosmeceutical critique - tea tree oil. *eSkin and Allergy News* **33**: 14. [News]
- Becker D.** (2001) Sensitizations to tea tree oil and propolis are increasing. *Tw Dermatologie*. **5**: 30. [Letter]
- Beckman B & Ippen H.** (1998) Tea tree oil [German]. *Dermatosen* **46**: 120-124. [Research article]
- Bedi MK & Shenefelt PD.** (2002) Herbal therapy in dermatology. *Archives of Dermatology* **138**: 232-242. [Review] [View abstract in Pubmed](#)
- Beer C.** (1986) Tea tree oil loves skin. *Nature and Health* **7**: 16-17. [News]
- Beer C.** (1987) Australian tea tree oil. *Nature and Health* **8**: 3-7. [News]
- Belaiche P.** (1985) Germicidal properties of the essential oil of *Melaleuca alternifolia* (Cheel) for the idiopathic, chronic urinary tract infections caused by coliforms [French]. *Phytotherapy* **15**: 9-11. [Research article] French abstract only.
- Belaiche P.** (1985) Treatment of cutaneous infections with the essential oil of *Melaleuca alternifolia* Cheel [French]. *Phytotherapy* **15**: 15-17. [Research article] French abstract only.
- Belaiche P.** (1985) Treatment of vaginal infections of *Candida albicans* with the essential oil of *Melaleuca alternifolia* (Cheel) [French]. *Phytotherapy* **15**: 13-14. [Research article] French abstract only.
- Betts TJ, Moir CM & Tassone AI.** (1991) Use of a liquid crystal stationary phase at temperatures below its melting point for the gas chromatographic study of some volatile oil constituents. *Journal of Chromatography A*. **547**: 335-344. [Research article] [View abstract in Pubmed](#)
- Beylier MF.** (1979) Bacteriostatic activity of some Australian essential oils. *Perfumer and Flavourist* **4**: 23-25. [Research article] No abstract.
- Bhushan M & Beck MH.** (1997) Allergic contact dermatitis from tea tree oil in a wart paint. *Contact Dermatitis* **36**: 117-118. [Case report] | [Full text \(PDF\)](#) Reproduced with permission from Blackwell Publishers
- Bischoff K & Guale F.** (1998) Australian tea tree (*Melaleuca alternifolia*) oil poisoning in three purebred cats. *Journal of Veterinary Diagnostic Investigation* **10**: 208-210. [Research article] [Full text \(PDF\)](#) Reproduced with permission.
- Bishop CD.** (1995) Antiviral activity of the essential oil of *Melaleuca alternifolia* (Maiden & Betche) Cheel (tea tree) against tobacco mosaic virus. *Journal of Essential Oil Research* **7**: 641-644. [Research article] <http://perfumerflavorist.com/ME2/Audiences/default.asp>
- Bishop CD & Reagan J.** (1998) Control of the storage pathogen *Botrytis cinerea* on Dutch White cabbage (*Brassica oleracea* var. *capitata*) by the essential oil of *Melaleuca alternifolia*. *Journal of Essential Oil Research* **10**: 57-60. [Research article]
- Bishop CD & Thornton IB.** (1997) Evaluation of the antifungal activity of the essential oils of *Monarda citriodora* var. *citriodora* and *Melaleuca alternifolia* on post-harvest pathogens. *Journal of Essential Oil Research* **9**: 77-82. [Research article]
- Blackwell AL.** (1991) Tea tree oil and anaerobic (bacterial) vaginosis. *Lancet*. **337**: 300. [Letter]

- Blackwell R.** (1991) An insight into aromatic oils: lavender and tea tree. *British Journal of Phytotherapy* **2**: 26-30.
- Blamey C.** (2001) Case history of infected eczema treated with essential oils. *Grand Rounds* **5**: 11-14. [Case report]
- Bolton KGE & Greenway M.** (1997) A feasibility study of *Melaleuca* trees for use in constructed wetlands in subtropical Australia. *Water Science & Technology* **35**: 247-254. [Research article] [View abstract in Pubmed](#)
- Bolton KGE & Greenway M.** (1999) Nutrient sinks in a constructed *Melaleuca* wetland receiving secondary treated effluent. *Water Science & Technology* **40**: 341-347. [Research article] [View abstract in Pubmed](#)
- Bolton KGE & Greenway M.** (1999) Pollutant removal capability of a constructed *Melaleuca* wetland receiving primary settled sewage. *Water Science & Technology* **39**: 199-206. [Research article] [View abstract in Pubmed](#)
- Boon PI & Johnstone L.** (1997) Organic matter decay in coastal wetlands: an inhibitory role for essential oil from *Melaleuca alternifolia* leaves? *Archiv Fur Hydrobiologie* **138**: 433-449. [Research article] [Abstract](#)
- Bouic F.** (2000) Use of tea tree oil in the treatment of head lice. *British Medical Journal* **2000**: [Letter - electronic publication only] [Free full text at journal webpage](#)
- Bourne KZ, Bourne N, Reising SF & Stanberry LR.** (1999) Plant products as topical microbicide candidates: assessment of in vitro and in vivo activity against herpes simplex virus type 2. *Antiviral Research* **42**: 219-226. [Research article] [View abstract in Pubmed](#)
- Bowden L.** (2001) The effectiveness of tea tree oil in reducing hospital acquired infections in care of the elderly ward. Infection Control Nurses Association Annual Infection Control Conference. 24-28 September 2001. Blackpool, UK p. 23. [Conference abstract]
- Brand C, Ferrante A, Prager RH, Riley TV, Carson CF, Finlay-Jones JJ & Hart PH.** (2001) The water-soluble components of the essential oil of *Melaleuca alternifolia* (tea tree oil) suppress the production of superoxide by human monocytes, but not neutrophils, activated in vitro. *Inflammation Research* **50**: 213-219. [Research article] [View abstract in Pubmed](#)
- Brand C, Grimbaldston MA, Gamble JR, Drew J, Finlay-Jones JJ & Hart PH.** (2002) Tea tree oil reduces the swelling associated with the efferent phase of a contact hypersensitivity response. *Inflammation Research* **51**: 236-244. [Research article] [View abstract in Pubmed](#)
- Brand C, Townley SL, Finlay-Jones JJ & Hart PH.** (2002) Tea tree oil reduces histamine-induced oedema in murine ears. *Inflammation Research* **51**: 283-289. [Research article] [View abstract in Pubmed](#)
- Brenan JA, Dennerstein GJ, Sfamini SF, Drinkwater P, Marin G & Scurry JP.** (1996) Evaluation of patch testing in patients with chronic vulvar symptoms. *Australasian Journal of Dermatology* **37**: 40-43. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Brophy JJ, Davies NW, Southwell IA, Stiff IA & Williams LR.** (1989) Gas chromatographic quality control for oil of *Melaleuca* terpinen-4-ol type (Australian tea tree). *Journal of Agricultural & Food Chemistry* **37**: 1330-1335. [Research article] [Abstract](#)
- Bruynzeel DP.** (1999) Contact dermatitis due to tea tree oil. *Tropical Medicine & International Health* **4**: 630. [Letter] | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Buchbauer G.** (1997) About tea tree oil [German]. *Eurocosmetics* **i**: 21-24. [News]
- Buchness MR.** (1998) Alternative medicine and dermatology. *Seminars in Cutaneous Medicine & Surgery* **17**: 284-290. [Review] [View abstract in Pubmed](#)
- Buck DS, Nidorf DM & Addino JG.** (1994) Comparison of two topical preparations for the treatment of onychomycosis: *Melaleuca alternifolia* (tea tree) oil and clotrimazole. *Journal of Family Practice* **38**: 601-605. [Research article] [Abstract](#)
- Budhiraja SS, Cullum ME, Sioutis SS, Evangelista L & Habanova ST.** (1999) Biological activity of *Melaleuca alternifolia* (tea tree) oil component, terpinen-4-ol, in human myelocytic cell line HL-60. *Journal of Manipulative & Physiological Therapeutics* **22**: 447-453. [Research article] [View abstract in Pubmed](#)

- Bunnell T.** (2000) Tea tree oil antiseptic cream: a new treatment for ringworm and sarcoptic mange in the hedgehog (*Erinaceus europaeus*). *Journal of the American Holistic Veterinary Association* **19**: 29-31 [Research article] No abstract.
- Burdzenia O.** (2002) The use of volatile oils in sports [Polish]. *Medycyna sportowa* **18**: 33-38 [Review]
- Burfield T. & Sheppard-Hanger S.** (2000) Super clone “88” *Melaleuca alternifolia* – what is its value? First International Phyto-Aromatic Conference, Nice France, March 24-26, 2000. [Conference abstract]
- Butcher PA.** (1995) Genetic diversity in *Melaleuca alternifolia*: implications for breeding to improve production of Australian tea tree oil. Australian National University [PhD Thesis]
- Butcher PA, Bell JC & Moran GF.** (1992) Patterns of genetic diversity and nature of the breeding system in *Melaleuca alternifolia* (Myrtaceae). *Australian Journal of Botany* **40**: 365-375. [Research article] [Abstract](#)
- Butcher PA, Byrne M & Moran GF.** (1995) Variation within and among the chloroplast genomes of *Melaleuca alternifolia* and *M. linariifolia* (Myrtaceae). *Plant Systematics & Evolution* **194**: 69-81. [Research article] [Abstract](#)
- Butcher PA, Doran JC & Slee MU.** (1994) Intraspecific variation in leaf oils of *Melaleuca alternifolia* (Myrtaceae). *Biochemical Systematics & Ecology* **22**: 419-430. [Research article] [View abstract in Pubmed](#)
- Butcher PA, Matheson AC & Slee MU.** (1996) Potential for genetic improvement of oil production in *Melaleuca alternifolia* and *M. linariifolia*. *New Forests* **11**: 31-51. [Research article] [Abstract](#)
- Byrne W.** (1996) Tea tree oil for thrush. *Australian Pharmacist* **15**: 104,109. [News] [Full text \(PDF\)](#) *Reprinted with permission.*
- Byrnes NB.** (1986) A revision of *Melaleuca* Myrtaceae in northern and eastern Australia 3. *Austrobaileya* **2**: 254-273. [Research article] [Abstract](#)
- Caboi F, Murgia S, Monduzzi M & Lazzari P.** (2002) NMR investigation on *Melaleuca alternifolia* essential oil dispersed in the monoolein aqueous system: phase behaviour and dynamics. *Langmuir* **18**: 7916-7922. [Research article] [Abstract](#)
- Caelli M, Riley TV, Heller R & Carson CF.** (1998) Tea tree oil - an alternative topical decolonisation agent for adult inpatients with methicillin-resistant *Staphylococcus aureus* (MRSA) – a pilot study. *Journal of Hospital Infection* **40(Suppl A)**: P.9.2.20. [Conference abstract]
- Caelli M, Porteous J, Carson CF, Heller R & Riley TV.** (2000) Tea tree oil as an alternative topical decolonization agent for methicillin-resistant *Staphylococcus aureus*. *Journal of Hospital Infection* **46**: 236-237. [Research note] [View abstract in Pubmed](#)
- Campbell RE, Lilley JH, Taukhid, Panyawachira V & Kanchanakhan S.** (2001) In vitro screening of novel treatments for *Aphanomyces invadans*. *Aquaculture Research* **32**: 223-233. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Campbell AJ & Maddox CDA.** (1997) Controlling insect pests in tea tree using pyrgo beetle as the basis. RIRDC project DAN-91A, RIRDC publication R97/062, 64pp. [Government publication]
- Caolo-Tanski JM, Hanson LE, Hill AL & Hill JP.** (2002) Use of *Melaleuca alternifolia* oil for plant disease control. Presented at the American Phytopathological Society's annual meeting in Milwaukee, Wisconsin, July 27-31, 2002 [Conference abstract]
- Caolo-Tanski JM, Hanson LE, Hill AL & Hill JP.** (2002) The potential use of Australian tea tree oil (*Melaleuca alternifolia*) as a method of control for several plant pathogens. Proceedings of the 6th Annual Rocky Mountain Plant Biotechnology and Molecular Biology Symposium at Colorado State University, Ft. Collins April 17, 2002, pg. 22. [Conference abstract]
- Carr A.** (1998) Therapeutic properties of New Zealand and Australian tea trees (*Leptospermum* and *Melaleuca*). *New Zealand Pharmacy* **18**: 29-31. [Review] No abstract.
- Carson CF.** (1998) Tea tree oil – applications and implications. *Cosmetics & Toiletries Manufacture Worldwide* **1998**: 17-21. [News]
- Carson CF.** (1999) Antimicrobial activity of the essential oil of *Melaleuca alternifolia* (tea tree oil) The University of Western Australia. [PhD Thesis]
- Carson CF.** (1999) Tea tree essential oil – fact and fiction. *Aromatherapy Today* **10**: 6-10. [News] [Full text \(PDF\)](#) *Reproduced with permission*

- Carson CF, Ashton L, Dry L, Smith DW & Riley TV.** (2001) *Melaleuca alternifolia* (tea tree) oil gel (6%) for the treatment of recurrent herpes labialis. *Journal of Antimicrobial Chemotherapy* **48**: 450-451. [Letter] **No abstract.**
- Carson CF, Cookson BD, Farrelly HD & Riley TV.** (1995) Susceptibility of methicillin-resistant *Staphylococcus aureus* to the essential oil of *Melaleuca alternifolia*. *Journal of Antimicrobial Chemotherapy* **35**: 421-424. [Research article] [View abstract in Pubmed](#)
- Carson CF, Hammer KA & Riley TV.** (1995) Broth micro-dilution method for determining the susceptibility of *Escherichia coli* and *Staphylococcus aureus* to the essential oil of *Melaleuca alternifolia* (tea tree oil). *Microbios* **82**: 181-185. [Research article] [View abstract in Pubmed](#)
- Carson CF, Hammer KA & Riley TV.** (1997) In-vitro activity of the essential oil of *Melaleuca alternifolia* against *Streptococcus* spp. *Journal of Antimicrobial Chemotherapy* **37**: 1177-1178. [Letter] **No abstract.**
- Carson CF, Hammer KA & Riley TV.** (1997) Use of the essential oil of *Melaleuca alternifolia* (tea tree oil) in cutaneous fungal infections. *Journal of British Podiatric Medicine* **52**: iv-v. [Letter] **No abstract.**
- Carson CF, Hammer KA & Riley TV.** (1998) Antimicrobial activity of *Melaleuca alternifolia* (tea tree) oil against wound organisms. In Program and Abstracts of the 4th International Conference of the Hospital Infection Society, 13-17 September 1998, Edinburgh. Abstr. P.9.2.16. [Conference abstract]
- Carson CF, Hammer KA & Riley TV.** (1998) A brief review of antifungal activity of the essential oil of *Melaleuca alternifolia* (tea tree oil). *Mikologia Lekarska* **5**: 205-207. [Review]
- Carson CF, Mee BJ & Riley TV.** (2002) Mechanism of action of *Melaleuca alternifolia* (tea tree) oil on *Staphylococcus aureus* determined by time-kill, lysis, leakage, and salt tolerance assays and electron microscopy. *Antimicrobial Agents & Chemotherapy* **46**: 1914-20. [Research article] [Abstract](#) | [Free full text at journal webpage](#)
- Carson CF & Riley TV.** (1993) Antimicrobial activity of the essential oil of *Melaleuca alternifolia*. *Letters in Applied Microbiology* **16**: 49-55. [Review] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Carson CF & Riley TV.** (1994) The antimicrobial activity of tea tree oil. *Medical Journal of Australia* **160**: 236. [Letter] [Full text \(PDF\)](#) *Copyright 1994, The Medical Journal of Australia. Reproduced with permission.*
- Carson CF & Riley TV.** (1994) Susceptibility of *Propionibacterium acnes* to the essential oil of *Melaleuca alternifolia*. *Letters in Applied Microbiology*. **19**: 24-25. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Carson CF & Riley TV.** (1995) Antimicrobial activity of the major components of the essential oil of *Melaleuca alternifolia*. *Journal of Applied Bacteriology* **78**: 264-269. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Carson CF & Riley TV.** (1995) Toxicity of the essential oil of *Melaleuca alternifolia* or tea tree oil. *Journal of Toxicology - Clinical Toxicology* **33**: 193-194. [Letter] **No abstract.**
- Carson CF & Riley TV.** (1996) Working with and against tea tree oil - issues of synergy and antagonism. In Program and Abstracts of the 19th International Federation of the Societies of Cosmetic Chemists Congress. Sydney, Australia, Oct 22 - 25 1996. [Conference abstract]
- Carson CF & Riley TV.** (1997) Investigations into the mechanism of action of *Melaleuca alternifolia* (tea tree) oil. In Program and Abstracts of the Australian Society for Microbiology Annual Scientific Meeting and Exhibition. Australian Society for Microbiology, Adelaide. Abstr. P02.38, p. A109. [Conference abstract]
- Carson CF & Riley TV.** (1998) Antimicrobial activity of tea tree oil. RIRDC Project No UWA-24A, RIRDC Publication No 98/070, 63pp. [Government publication]
- Carson CF & Riley TV.** (2001) Safety, efficacy and provenance of tea tree (*Melaleuca alternifolia*) oil. *Contact Dermatitis* **45**: 65-67. [Review] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Carson CF & Riley TV.** (2003) Non-antibiotic therapies for infectious diseases. *Communicable Diseases Intelligence* **27(Suppl)**: S143-146. [Journal Article]

- Carson CF, Riley TV & Cookson BD.** (1998) Efficacy and safety of tea tree oil as a topical antimicrobial agent. *Journal of Hospital Infection* **40**: 175-178. [Review] No abstract.
- Cassella S, Cassella JP & Smith I.** (2002) Synergistic antifungal activity of tea tree (*Melaleuca alternifolia*) and lavender (*Lavandula angustifolia*) essential oils against dermatophyte infection. *International Journal of Aromatherapy* **12**: 2-15. [Research article]
- Cassella JP, Cassella S.** (2000) Onychomycosis: barking up the wrong tea tree. *Podiatry Now* **2000(November)**: 477. [Letter] {comment on article by Goodwin & Hardiman}
- Chan CH & Loudon KW.** (1998) Activity of tea tree oil on methicillin-resistant *Staphylococcus aureus* (MRSA). *Journal of Hospital Infection* **39**: 244-245. [Letter]
- Chan CH, Stockley J & Williams LR.** (1999) The antimicrobial efficacy of tea tree oils on a range of bacteria. Abstracts of the ASM Tri-State Meeting, 25-28 April, 1999, Alice Springs, NT, Australia. Abstract S2.8. [Conference abstract]
- Chao SC, Young DG & Oberg CJ.** (2000) Screening for inhibitory activity of essential oils on selected bacteria, fungi and viruses. *Journal of Essential Oil Research* **12**: 639-649. [Research article]
- Cheng-Fan M, Williams RR.** (1997) Factors affecting pH changes of *in vitro* media. *Acta Botanica Sinica* **39**: 347-352. [Research article] [View abstract in Pubmed](#)
- Christoph F, Kaulfers PM & Stahl-Biskup E.** (2000) A comparative study of the *in vitro* antimicrobial activity of tea tree oils s.l. with special reference to the activity of beta-triketones. *Planta Medica* **66**: 556-560. [Research article] [View abstract in Pubmed](#)
- Christoph F, Kaulfers PM & Stahl-Biskup E.** (2001) *In vitro* evaluation of the antibacterial activity of beta-triketones admixed to Melaleuca oils. *Planta Medica* **67**: 768-771. [Research article] [View abstract in Pubmed](#)
- Christoph F, Stahl-Biskup E & Kaulfers PM.** (2001) Death kinetics of *Staphylococcus aureus* exposed to commercial tea tree oils s.l. *Journal of Essential Oil Research* **13**: 98-102. [Research article]
- Clark ST.** (1998) The great Melaleuca fact book. Gaughan Fisch Inc., St Paul, MN, USA. ASIN: 0963952102 (124 pages) [Book]
- Concha JM, Moore LS & Holloway WJ.** (1998) Antifungal activity of *Melaleuca alternifolia* (tea-tree) oil against various pathogenic organisms. *Journal of the American Podiatric Medical Association* **88**: 489-92. [Research article] [Abstract](#)
- Combest W.** (1999) Alternative therapies: tea tree. *U.S. Pharmacist* **24(4)**: 35 [News]
- Cornwell CP, Reddy N, Leach DN & Wyllie SG.** (2000) Origin of (+)-delta-cadinene and the cubenols in the essential oils of the Myrtaceae. *Flavour & Fragrance Journal* **15**: 352-361. [Research article]
- Cornwell CP, Leach DN & Wyllie SG.** (1995) Incorporation of oxygen-18 into terpinen-4-ol from the H218O steam distillates of *Melaleuca alternifolia* (tea tree). *Journal of Essential Oil Research* **7**: 613-620. [Research article]
- Cousens RD, Murtagh GJ, Sutton BG, Virtue JG.** (2000) Weed interference reduces yield of coppiced tea tree (*Melaleuca alternifolia*). *Australian Journal of Experimental Agriculture* **40**: 1157-1164. [Research article] [Abstract](#)
- Coutts I, Shaw S & Orton D.** (2002) Patch testing with pure tea tree oil - 12 months experience. *British Journal of Dermatology* **147(suppl 62)**: 70 [Conference abstract] | [Full text \(PDF\)](#)  
*Reproduced with permission from Blackwell Publishers*
- Cox SD, Gustafson JE, Mann CM, Markham JL, Liew YC, Hartland RP, Bell HC, Warmington JR & Wyllie SG.** (1998) Tea tree oil causes K<sup>+</sup> leakage and inhibits respiration in *Escherichia coli*. *Letters in Applied Microbiology* **26**: 355-358. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Cox SD, Mann CM & Markham JL.** (2001) Interactions between components of the essential oil of *Melaleuca alternifolia*. *Journal of Applied Microbiology* **91**: 492-497. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Cox SD, Mann CM, Markham JL, Bell HC, Gustafson JE, Warmington JR & Wyllie SG.** (2000) The mode of antimicrobial action of the essential oil of *Melaleuca alternifolia* (tea tree oil).

- Journal of Applied Microbiology* **88**: 170-175. [Research article] [Abstract](#) | [Full text \(PDF\)](#)  
 Reproduced with permission from Blackwell Publishers
- Cox SD, Mann CM, Markham JL, Gustafson JE, Warmington JR & Wyllie SG.** (2001) Determining the antimicrobial actions of tea tree oil. *Molecules* **6**: 87-91. [Research article] [Abstract](#) | [Full text \(PDF\)](#) Reproduced with permission
- Cox S & Markham J.** (2002) Tolerance of *Pseudomonas aeruginosa* to essential oil components. In Program and Abstracts of the Australian Society for Microbiology Annual Scientific Meeting and Exhibition, 29 Sept - 3 Oct 2002, Melbourne, Australia. Abstract P07.7 [Conference abstract]
- Cox S, Markham JL, Mann CM, Wyllie SG, Gustafson JE & Warmington JR.** (1997) The effect of the essential oil of *Melaleuca alternifolia* on *Escherichia coli*. Proceedings of the 28th International Symposium on Essential Oils, 1-3 September, 1997, Eskisehir, Turkey. In: *Progress in Essential Oil Research* (Eds: Baser KHC & Kirmer N.) [Conference paper]
- Cullum ME, Budhiraja S, Lucio E & Habanova S.** (1998) Biological activity of *Melaleuca alternifolia* (tea tree) oil in human HL-60 myelocytic cell line treated with retinoic acid. *Federation of American Societies for Experimental Biology (FASEB) Journal* **12**: A3667. [Conference abstract]
- Curtis A.** (1996) Growth and essential oil production of Australian tea tree (*Melaleuca alternifolia*) (Maiden and Betche (Cheel)). University of Queensland. [Masters Ag. Sc. Thesis]
- D'Auria FD, Laino L, Strippoli V, Tecca M, Salvatore G, Battinelli L & Mazzanti G** (2001) In vitro activity of tea tree oil against *Candida albicans* mycelial conversion and other pathogenic fungi. *Journal of Chemotherapy* **13**: 377-383. [Research article] [Abstract](#)
- de Groot AC.** (1996) Airborne allergic contact dermatitis from tea tree oil. *Contact Dermatitis* **35**: 304-305. [Case report] [Abstract](#) | [Full text \(PDF\)](#) Reproduced with permission from Blackwell Publishers
- de Groot AC & Weyland JW.** (1992) Systemic contact dermatitis from tea tree oil. *Contact Dermatitis* **27**: 279-280. [Case report] | [Full text \(PDF\)](#) Reproduced with permission from Blackwell Publishers
- de Groot AC & Weyland JW.** (1993) Contact allergy to tea tree oil. *Contact Dermatitis* **28**: 309. [Case report] | [Full text \(PDF\)](#) Reproduced with permission from Blackwell Publishers
- del Beccaro MA.** (1995) Melaleuca oil poisoning in a 17-month-old. *Veterinary & Human Toxicology* **37**: 557-558. [Research article] [Abstract](#) | [Full text \(PDF\)](#) Reproduced with permission
- Dharmagunawardena B, Takwale A, Sanders KJ, Cannan S, Rodger A, Ilchyshyn A.** (2002) Gas chromatography: an investigative tool in multiple allergies to essential oils. *Contact Dermatitis* **47**: 288-292 [Research article] [Abstract](#) | [Full text \(PDF\)](#) Reproduced with permission from Blackwell Publishers
- Dillard HR, Cobb AC, McKormick KE, Straight GA, Walker SJ, Burr AT.** (2000) Evaluation of fungicides for control of Alternaria leaf spot in cabbage. *Fungicide and Nematicide Tests* **56**: V1 [Research note]
- Dillard HR, Cobb AC, McKormick KE, Straight GA, Walker SJ, Burr AT.** (2000) Evaluation of materials for control of black rot in cabbage. *Fungicide and Nematicide Tests* **56**: V2 [Research note]
- Doran JC, Baker GR, Murtagh GJ & Southwell IA.** (1996) Improving tea tree yield and quality through breeding and selection. RIRDC project DAN-87A, RIRDC publication R97-053, 52pp. [Government publication]
- Doran JC, Baker GR, Williams ER & Southwell IA.** (2002) Improving Australian tea tree through selection and breeding-1996–2001. RIRDC Project DAN-151A, RIRDC Publication No. 02/017, 105pp. [Government publication]
- Dorman HJD & Deans SG.** (2000) Antimicrobial agents from plants: antibacterial activity of plant volatile oils. *Journal of Applied Microbiology* **88**: 308-316. [Research article] [Abstract](#) | [Full text \(PDF\)](#) Reproduced with permission from Blackwell Publishers
- Downs AMR, Stafford KA & Coles GC.** (2000) Monoterpenoids and tetralin as pediculocides. *Acta Dermato Venereologica* **80**: 69-70. [Research article] No abstract.
- Drinnan JE.** (1998) Development of the north Queensland tea tree industry. RIRDC project DAQ-184A, RIRDC publication R98/006, 40pp. [Government publication]
- Drinnan JE.** (2000) Australian tea tree oil plant nutritional survey. RIRDC Project No. DAQ-252A, RIRDC Publication No. R00/107, 36pp. [Government publication]

- Drury S.** (1991) Tea tree oil: a medicine kit in a bottle. The C.W. Daniel Company Ltd; Saffron Walden, Essex, ISBN: 0852072384 (86pp) [Book]
- Eedy DJ.** (2002) Updates from the British Association of Dermatologists 82nd annual meeting, 9-12 July 2002, Edinburgh, UK. *British Journal of Dermatology* **147**: 1080-1095. [News] | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Ellercamp P.** (1987) Tea-tree oil set for a comeback. *Business Review Weekly* **October 2**: 110-111. [News]
- Elliott C.** (1993) Tea tree oil poisoning. *Medical Journal of Australia* **159**: 830-831. [Letter] [Full text \(PDF\)](#) *Copyright 1993, The Medical Journal of Australia. Reproduced with permission.*
- Elsom GK & Hide D.** (1999) Susceptibility of methicillin-resistant *Staphylococcus aureus* to tea tree oil and mupirocin. *Journal of Antimicrobial Chemotherapy* **43**: 427-428. [Letter] No abstract.
- Elvis A, George G, Selim N, Patel D, Vegotsky K.** (1999) The tea tree oil bible: your essential guide for health and home uses, your first aid kit in a bottle. Adi Gaia Esalen Publications. Niagara Falls, NY, USA. ISBN: 1886508100 (246 pages) [Book]
- Elvis A.** (Editor) (2002) The all-in one guide to tea tree oil (2nd edition). Adi Gaia Esalen Publications, Niagara Falls, NY, USA. ISBN: 1886508348 (256 pages) [Book]
- Ergin A & Arikian S.** (2002) Comparison of microdilution and disc diffusion methods in assessing the in vitro activity of fluconazole and *Melaleuca alternifolia* (tea tree) oil against vaginal *Candida* isolates. *Journal of Chemotherapy* **14**: 465-472. [Research article] [Abstract](#)
- Ernst E.** (1991) Oil of the Australian tea tree and dermatitis [German]. *Fortschritte der Medizin* **109**: 13. [Letter]
- Ernst E.** (2000) Tea tree oil - household remedy of Australian aborigines [German]. *MMW Fortschritte der Medizin* **142**: 35. [News] No abstract.
- Ernst E.** (2001) Herbal medicinal products: an overview of systematic reviews and meta-analyses. *Perfusion* **14**: 398-404 [Review] [Abstract](#)
- Ernst E & Huntley A.** (2000) Tea tree oil: a systematic review of randomized clinical trials. *Forschende Komplementarmedizin und Klassische Naturheilkunde* **7**: 17-20. [Review]
- Ernst E, Pittler MH & Stevinson C.** (2002) Complementary/alternative medicine in dermatology: evidence-assessed efficacy of two diseases and two treatments. *American Journal of Clinical Dermatology* **3**: 341-348. [Review] [View abstract in Pubmed](#)
- Faoagali J, George N & Leditschke JF.** (1997) Does tea tree oil have a place in the topical treatment of burns? *Burns* **23**: 349-351. [Research article] [View abstract in Pubmed](#)
- Faoagali JL, George N & Leditschke JF.** (1998) Antimicrobial effects of melaleuca oil. *Burns* **24**: 383. [Letter]
- Farag RS, Daw ZY, Mahassen MAS & Saffaa HM.** (1998) Biochemical and biological studies on some tea trees (*Melaleuca* spp.) essential oils. *Advances in Food Sciences* **20**: 153-162. [Research article] [View abstract in Pubmed](#)
- Feinblatt HM.** (1960) Cajepu\* oil for the treatment of furunculosis. *Journal of the National Medical Association* **52**: 32-33. [Research article] No abstract.
- Fergeus J.** (2000) What will be the next big oils from Australia? *Perfumer and Flavorist* **25**: 6,8-19. [News]
- Fitzi J, Furst-Jucker J, Wegener T, Saller R & Reichling J.** (2002) Phytotherapy of chronic dermatitis and pruritus of dogs with a topical preparation containing tea tree oil (Bogaskin). *Schweizer Archiv fur Tierheilkunde* **144**: 223-231. [Research article] [View abstract in Pubmed](#)
- Finlay-Jones, JJ, Hart P, Riley TV & Carson CF.** (2001) Anti-inflammatory activity of tea tree oil. RIRDC Project No UF-5A, RIRDC Publication No 01/10. [Government publication]
- Finlay-Jones JJ, Hart P, Carson CF & Riley TV.** (2002) The anti-inflammatory activity and anti-itch properties of tea tree oil RIRDC Project UF-6A, RIRDC publication R02/053, 31pp. [Government publication]
- Fleckman P.** (2002) Onychomycosis: diagnosis and topical therapy. *Dermatologic Therapy* **15**: 71-77. [Review] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Ford RA.** (1988) Fragrance raw materials monographs (tea tree oil). *Food and Chemical Toxicology* **26**: 405. [Letter]

- Friedman M, Henika PR & Mandrell RE. (2002)** Bactericidal activities of plant essential oils and some of their constituents against *Campylobacter jejuni*, *Escherichia coli*, *Listeria monocytogenes*, and *Salmonella enterica*. *Journal of Food Protection* **65**: 1545-1560. [Research article] [View abstract in Pubmed](#)
- Fritz TM & Elsner P. (1998)** Allergic contact eczema to tea tree oil in a patient with psoriasis [German]. *Aktuelle Dermatologie* **24**: 7-10. [Case report]
- Fritz TM, Burg G & Krasovec M. (2001)** Allergic contact dermatitis to cosmetics containing *Melaleuca alternifolia* (tea tree oil) [French]. *Annales de Dermatologie et de Venereologie* **128**: 123-126. [Research article] [Abstract](#)
- Galle-Hoffman U & König WA. (1999)** Tea tree oil from *Melaleuca alternifolia*. Part 2 [German]. *Deutsche Apotheker Zeitung* **139(3)**: 64-72 [Research article]
- Galle-Hoffman U & König WA. (1999)** More tea tree oils from the genus *Melaleuca* [German]. *Deutsche Apotheker Zeitung* **139(50)**: 53-62. [Research article]
- Gershenson J, Murtagh GJ & Croteau R. (1993)** Absence of rapid terpene turnover in several diverse species of terpene-accumulating plants. *Oecologia* **96**: 583-592. [Research article] [View abstract in Pubmed](#)
- Gobert JF. (2001)** Terpinen-4-ol (melaleucol) - a novel raw material obtained by fractional distillation of tea tree oil. *Chemical Weekly* **47(3)**: 137-144 [News] **Full text (PDF)** *Reproduced with permission*
- Goodwin G & Hardiman S. (2000)** Tea tree oil as a therapeutic agent. *Podiatry Now* **3**: 234-237. [Research article] No abstract.
- Gorduysus MO, Tasman F, Tuncer S & Etikan I. (1997)** Solubilizing efficiency of different gutta-percha solvents: a comparative study. *Journal of Nihon University School of Dentistry* **39**: 133-135. [Research article] [View abstract in Pubmed](#)
- Grandi M, Numico GM & Joanni F. (1993)** Essential oil of *Melaleuca alternifolia* for oral or vaginal candidiasis in immunosuppressed patients [Italian]. Natural Medicine Conference, 23-24 October, Milan, Italy. [Conference abstract]
- Gray SG, Clair AA. (2002)** Influence of aromatherapy on medication administration to residential-care residents with dementia and behavioral challenges. *American Journal of Alzheimers Disease and Other Dementias* **17**: 169-174. [Research article] [Abstract](#)
- Green M. (1997)** NT/3M national nursing awards. *Nursing Times* **93(47)**: 26-29 [News]
- Greig JE, Thoo SL, Carson CF & Riley TV. (1999)** Allergic contact dermatitis following use of a tea tree oil hand-wash not due to tea tree oil. *Contact Dermatitis* **41**: 354-355. [Letter] | **Full text (PDF)** *Reproduced with permission from Blackwell Publishers*
- Greig JE, Carson CF, Stuckey MS, Riley TV. (1999)** Skin sensitivity testing for tea tree oil. RIRDC project UWA-42A, RIRDC publication R99/076, 54pp. [Government publication]
- Greig JE, Carson CF, Stuckey MS, Riley TV. (2002)** Safety of tea tree oil - second stage. RIRDC project UWA-51A, RIRDC publication 02/036, 32pp. [Government publication]
- Griffin SG, Markham JL & Leach DN. (2000)** An agar dilution method for the determination of the minimum inhibitory concentration of essential oils. *Journal of Essential Oil Research* **12**: 249-255. [Research article]
- Griffin SG, Wyllie SG, Markham JL & Leach DN. (1999)** The role of structure and molecular properties of terpenoids in determining their antimicrobial activity. *Flavour and Fragrance Journal* **14**: 322-332. [Research article]
- Griffin SG, Wyllie SG & Markham JL. (1999)** Determination of octanol-water partition coefficient for terpenoids using reversed-phase high-performance liquid chromatography. *Journal of Chromatography A* **864**: 221-228. [Research article] [View abstract in Pubmed](#)
- Griffin SG, Wyllie SG & Markham JL. (2001)** Role of the outer membrane of *Escherichia coli* AG100 and *Pseudomonas aeruginosa* NCTC 6749 and resistance/susceptibility to monoterpenes of similar chemical structure. *Journal of Essential Oil Research* **13**: 380-386. [Research article]
- Grosso FC, Ramacciato JC, Simoes RP, Florio FM, Sartoratto A. (2002)** Antimicrobial activity of garlic, tea tree oil, and chlorhexidine against oral microorganisms. *International Dental Journal* **52**: 433-437. [Research article] [Abstract](#) | **Full text (PDF)** *Reproduced with permission*

- Guenther E.** (1968) Australian tea tree oils, report of a field survey. *Perfumery and Essential Oil Records* **59**: 642-644. [Review] No abstract.
- Guin JD & Kincannon J.** (1997) Medication-induced contact reactions. *Clinics in Dermatology* **15**: 511-525. [Review] No abstract.
- Gustafson JE, Cox SD, Liew YC, Wyllie SG & Warmington JR.** (2001) The bacterial multiple antibiotic resistant (Mar) phenotype leads to increased tolerance to tea tree oil. *Pathology* **33**: 211-215. [Research article] [View abstract in Pubmed](#)
- Gustafson JE, Liew YC, Chew S, Markham J, Bell HC, Wyllie SG & Warmington JR.** (1998) Effects of tea tree oil on *Escherichia coli*. *Letters in Applied Microbiology* **26**: 194-198. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Gustafson JE, Liew YC, Hartland RP, Cox SD, Mann CM, Markham JL, Bell CE, Wyllie SG & Warmington JR.** (1998) Multiple antibiotic resistant (Mar) mutants of *Escherichia coli* show increased levels of resistance to tea tree oil and terpenes. Abstracts of the 98th General Meeting of the American Society for Microbiology, May 17-21, 1998. Abstract I-96. [Conference abstract]
- Hackzell-Bradley M, Bradley T & Fischer T.** (1997) A case report - contact allergy caused by tea tree oil [Swedish]. *Lakartidningen* **94**: 4359-4361. [Case report] No abstract.
- Hada T, Furuse S, Matsumoto Y, Hamashima H, Masuda K, Shiojima K, Arai T & Sasatsu M.** (2001) Comparison of the effects in vitro of tea tree oil and plaunotol on methicillin-susceptible and methicillin-resistant strains of *Staphylococcus aureus*. *Microbios* **106**: 133-141. [Research article] [View abstract in Pubmed](#)
- Hada T, Inoue Y, Shiraishi A, Hamashima H.** (2003) Leakage of K(+) ions from *Staphylococcus aureus* in response to tea tree oil. *Journal of Microbiological Methods* **53(3)**: 309-312. [View abstract in Pubmed](#)
- Hales J.** (1999) The antimicrobial activity of oil of *Melaleuca alternifolia* (Australian tea tree oil) against selected oral pathogens and periodontitis plaque samples. *Journal of Dental Research* **78**: 344 (Abstract #1908). [Conference abstract] [Abstract \(PDF\)](#) *Reprinted with permission from Journal of Dental Research.*
- Halford ACF.** (1936) Diabetic gangrene. *Medical Journal of Australia* **ii**: 121-122. [Case report] [Full text \(PDF\)](#) *Copyright 1936, The Medical Journal of Australia. Reproduced with permission.*
- Haller CA, Anderson IB, Kim SY, Blanc PD.** (2002) An evaluation of selected herbal reference texts and comparison to published reports of adverse herbal events. *Adverse Drug Reactions & Toxicological Reviews* **21**: 143-150. [Review] [View abstract in Pubmed](#)
- 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**: 186-189. [Research article] [View abstract in Pubmed](#)
- Hammer KA, Carson, CF & Riley TV.** (1996) The in-vitro susceptibility of *Malassezia furfur* to tea tree oil. In Program and Abstracts of the 19th International Federation of the Societies of Cosmetic Chemists Congress. Sydney, Australia, Oct 1996. Abstract 37. [Conference abstract]
- Hammer KA, Carson CF & Riley TV.** (1997) In vitro susceptibility of *Malassezia furfur* to the essential oil of *Melaleuca alternifolia*. *Journal of Medical & Veterinary Mycology* **35**: 375-377. [Research article] [View abstract in Pubmed](#)
- Hammer KA, Carson CF & Riley TV.** (1997) Effect of organic matter, surfactants and cations on the antimicrobial activity of *Melaleuca alternifolia* (tea tree) oil. In Program and Abstracts of the Australian Society for Microbiology Annual Scientific Meeting and Exhibition. Australian Society for Microbiology, 28 September - 3 October 1997, Adelaide, SA. Abstr. P02.49, p. A111. [Conference abstract]
- Hammer KA, Carson CF & Riley TV.** (1998) In-vitro activity of essential oils, in particular *Melaleuca alternifolia* (tea tree) oil and tea tree oil products, against *Candida* spp. *Journal of Antimicrobial Chemotherapy* **42**: 591-595. [Research article] [View abstract in Pubmed](#)
- Hammer KA, Carson CF & Riley TV.** (1998) Effect of organic matter on the antimicrobial activity of *Melaleuca alternifolia* (tea tree) oil. In Program and Abstracts of the 4th International Conference of the Hospital Infection Society. 13-17 September 1998, Edinburgh. Abstr. P.9.2.18. [Conference abstract]

- Hammer KA, Carson CF & Riley TV.** (1999) Antimicrobial activity of essential oils and other plant extracts. *Journal of Applied Microbiology* **86**: 985-990. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Hammer KA, Carson CF & Riley TV.** (1999) In vitro susceptibility of yeasts to *Melaleuca alternifolia* (tea tree) oil. In Program and Abstracts of the IXth International Congress of Bacteriology and Applied Microbiology and IXth International Congress of Mycology (International Union of Microbiological Societies), 16-20 August, Sydney, Australia. Abstr. MP3.08, p. 227. [Conference abstract]
- Hammer KA, Carson CF & Riley TV.** (1999) In vitro susceptibilities of lactobacilli and organisms associated with bacterial vaginosis to *Melaleuca alternifolia* (tea tree) oil. *Antimicrobial Agents & Chemotherapy* **43**: 196. [Letter] [Free full text at journal website](#)
- Hammer KA, Carson CF & Riley TV.** (1999) Influence of organic matter, cations and surfactants on the antimicrobial activity of *Melaleuca alternifolia* (tea tree) oil in vitro. *Journal of Applied Microbiology* **86**: 446-452. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Hammer KA, Carson CF & Riley TV.** (2000) Activity of *Melaleuca alternifolia* (tea tree) oil against dermatophytes in vitro. In Program and Abstracts of the Joint Annual Meeting and Exhibition of ASM, NZMS and FAPMS, 8 - 13 July, 2000, Cairns, Australia. Abstr. P1.03, p. A109. [Conference abstract]
- Hammer KA, Carson CF & Riley TV.** (2000) In vitro activities of ketoconazole, econazole, miconazole, and *Melaleuca alternifolia* (tea tree) oil against *Malassezia* species. *Antimicrobial Agents & Chemotherapy* **44**: 467-469. [Research note] [Abstract](#) | [Free full text at journal website](#)
- Hammer KA, Carson CF & Riley TV.** (2000) *Melaleuca alternifolia* (tea tree) oil inhibits germ tube formation by *Candida albicans*. *Medical Mycology* **38**: 355-362. [Research article] [View abstract in Pubmed](#)
- Hammer KA, Carson CF & Riley TV.** (2001) Anti-fungal activity of tea tree oil. RIRDC project UWA 50A, RIRDC publication R01/11, 32pp. [Government publication]
- Hammer KA, Carson CF & Riley TV.** (2001) *Melaleuca alternifolia* (tea tree) oil and components alter the permeability of *Candida albicans*. In Program and Abstracts of the Australian Society for Microbiology Annual Scientific Meeting and Exhibition, 30 Sept - 5 Oct 2001, Perth, Australia. Abstr. PP4.1, p. A75. [Conference abstract]
- Hammer KA, Carson CF & Riley TV.** (2001) In vitro activity of *Melaleuca alternifolia* (tea tree) oil against filamentous fungi. In Program and Abstracts of the Australian Society for Antimicrobials, 5-7 April, 2001 Melbourne, Australia. Abstr. 07 [Conference abstract]
- Hammer KA, Carson CF & Riley TV.** (2002) In vitro activity of *Melaleuca alternifolia* (tea tree) oil against dermatophytes and other filamentous fungi. *Journal of Antimicrobial Chemotherapy* **50**: 195-199. [Research article] [View abstract in Pubmed](#)
- Hammer KA, Carson CF & Riley TV.** (2002) Antimicrobial activity of tea tree oil against oral microorganisms. RIRDC Project UWA-55A, RIRDC publication #R03/019 [Government publication]
- Hammer KA, Carson CF & Riley TV.** (2002) The antifungal activity of tea tree oil in vitro. RIRDC Project UWA-58A, RIRDC publication #R03/020 [Government publication]
- Hammer KA, Carson CF & Riley TV.** (2002) Effects of sub-inhibitory concentrations of *Melaleuca alternifolia* (tea tree) oil on *Candida albicans*. In Program and Abstracts of the Australian Society for Microbiology Annual Scientific Meeting and Exhibition, 29 Sept - 3 Oct 2002, Melbourne, Australia. Abstr. PP03.4. [Conference abstract]
- Haney L, Pippin MA, Tipton DA, Babu J & Dabbous MKH. (1994) Anticollagenolytic activity of tea tree oil. *Journal of Dental Research* **73**: 259. [Conference abstract] [Abstract \(PDF\)](#) *Reprinted with permission from Journal of Dental Research.*
- Harkenthal M, Hausen BM & Reichling J.** (2000) 1,2,4-Trihydroxy menthane, a contact allergen from oxidized Australian tea tree oil. *Pharmazie* **55**: 153-154. [Research note]
- Harkenthal M, Layh-Schmitt G & Reichling J.** (2000) Effect of Australian tea tree oil on the viability of the wall-less bacterium *Mycoplasma pneumoniae*. *Pharmazie* **55**: 380-384. [Research article] [Abstract](#)

- Harkenthal M, Reichling J, Geiss HK & Saller R.** (1998) Australian tea tree oil - oxidation products as the possible cause of contact dermatitis [German]. *Pharmazie PZ* **143**: 26-28. [Research article] German abstract.
- Harkenthal M, Reichling J, Geiss HK & Saller R.** (1999) Comparative study on the in vitro antibacterial activity of Australian tea tree oil, cajuput oil, niaouli oil, manuka oil, kanuka oil, and eucalyptus oil. *Pharmazie* **54**: 460-463. [Research article] [Abstract](#)
- Hart PH, Brand C, Carson CF, Riley TV, Prager RH & Finlay-Jones JJ.** (2000) Terpinen-4-ol, the main component of the essential oil of *Melaleuca alternifolia* (tea tree oil), suppresses inflammatory mediator production by activated human monocytes. *Inflammation Research* **49**: 619-626. [Research article] [View abstract in Pubmed](#)
- Hausen BM.** (1999) Wonder drug with hidden danger: Tea tree oil [German]. *Tw Dermatologie*. **9-10**: 27. [Letter]
- Hausen BM, Reichling J & Harkenthal M.** (1999) Degradation products of monoterpenes are the sensitizing agents in tea tree oil. *American Journal of Contact Dermatitis* **10**: 68-77. [Research article] [Abstract](#)
- Hay IC, Jamieson M & Ormerod AD.** (1998) Randomized trial of aromatherapy - successful treatment for alopecia areata. *Archives of Dermatology* **134**: 1349-1352. [Research article] [View abstract in Pubmed](#)
- Hayes AJ, Markham JL, Leach DN & Southwell IA.** (1993) Relationship between chemical composition and antimicrobial activity of Australian tea tree oil. In Program and Abstracts of the Annual Scientific Meeting of the Australian Society for Microbiology, Perth, Western Australia, 1993. Abstract P2.2, p. A-4. [Conference abstract]
- Hayes AJ, Leach DN, Markham JL & Markovic B.** (1997) In vitro cytotoxicity of Australian tea tree oil using human cell lines. *Journal of Essential Oil Research* **9**: 575-582. [Research article]
- Hayes A & Markovic B.** (1999) Alternatives to animal testing for determining the safety of cosmetics. *Cosmetics Aerosols and Toiletries in Australia* **12**: 24-28 [Review] No abstract.
- Hayes A & Markovic B.** (2002) In vitro methods for assessing the safety and toxicity of Australian essential oils. Abstract E13. Fourth World Congress of the Alternatives Congress Trust, Aug 11-15 2002, New Orleans, Louisiana, USA. [Conference abstract]
- Hili P, Evans CS, Veness RG.** (1997) Antimicrobial action of essential oils: the effect of dimethylsulfoxide on the activity of cinnamon oil. *Letters in Applied Microbiology* **24**: 269-275. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Hill N, Cameron M, Samah M.** (2001) An evaluation of Neem oil, tea tree oil and conventional insecticides to control house dust mites, the major indoor trigger of atopic allergies. Program and Abstracts of The science & application of neem. Glasgow, UK, April 2001. pp 47-49. [Conference paper]
- Hoffman AF & Driver VR.** (1996) Onychomycosis. *Clinics in Podiatric Medicine and Surgery* **13**: 13-29. [Review] No abstract.
- Hohlmaier K & Hausen BM.** (2000) Type IV allergy to tea tree oil in cosmetics combined with allergy to zimaldehyde and cypress spurge [German]. *Zeitschrift für Hautkrankheiten* **75**: 471. abstract P8. [Conference abstract]
- Homer LE, Leach DN, Lea D, Lee LS, Henry RJ & Baverstock PR.** (2000) Natural variation in the essential oil content of *Melaleuca alternifolia* Cheel (Myrtaceae). *Biochemical Systematics & Ecology* **28**: 367-382. [Research article] [View abstract in Pubmed](#)
- Horne D, Holm M, Oberg C, Chao S & Young DG.** (2001) Antimicrobial effects of essential oils on *Streptococcus pneumoniae*. *Journal of Essential Oil Research* **13**: 387-392. [Research article]
- Horowitz S.** (1999) Aromatherapy - modern applications of essential oils. *Alternative and Complementary Therapies* **5**: 199-203. [Review] [Full text \(PDF\)](#) *(Reproduced with permission)*
- Humphery EM.** (1930) A new Australian germicide. *The Medical Journal of Australia* **1**: 417-418. [News] [Full text \(PDF\)](#) Copyright 1930, The Medical Journal of Australia. Reproduced with permission.
- Ingram C.** (1999) Tea tree oil: the natural antiseptic. Knowledge House, Cedar Rapids, Iowa, USA. ISBN: 0911119248 (123 pages) [Book]

- Inouye S.** (2002) Recent progress in tea tree oil from its production to clinical application (Part 1) [Japanese]. *Aroma Research* **3**: 222-232. [Review] [Abstract](#)
- Inouye S.** (2002) Recent progress in tea tree oil from its production to clinical application (Part 2) [Japanese]. *Aroma Research* **3**: 335-341. [Review] [Abstract](#)
- Inouye S, Tsuruoka T, Uchida K & Yamaguchi H.** (2001) Effect of sealing and Tween 80 on the antifungal susceptibility testing of essential oils. *Microbiology & Immunology* **45**: 201-208. [Research article] [View abstract in Pubmed](#)
- Inouye S, Tsuruoka T, Watanabe M, Takeo K, Akao M, Nishiyama Y & Yamaguchi H.** (2000) Inhibitory effect of essential oils on apical growth of *Aspergillus fumigatus* by vapour contact. *Mycoses* **43**: 17-23. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Inouye S, Uchida K & Yamaguchi H.** (2001) In vitro and in vivo anti-Trichophyton activity of essential oils by vapour contact. *Mycoses* **44**: 99-107. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Inouye S, Takizawa T & Yamaguchi H.** (2001) Antibacterial activity of essential oils and their major constituents against respiratory tract pathogens by gaseous contact. *Journal of Antimicrobial Chemotherapy* **47**: 565-573. [Research article] [View abstract in Pubmed](#)
- Inouye S, Watanabe M, Nishiyama Y, Takeo K, Akao M & Yamaguchi H.** (1998) Antisporulating and respiration-inhibitory effects of essential oils on filamentous fungi. *Mycoses* **41**: 403-410. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- International Standards Organisation** (1996) Oil of Melaleuca, terpinen-4-ol type (tea tree oil). International Standard ISO 4730:1996(E), International Standards Organisation, Geneva [Standard]
- Jacobs MR & Hornfeldt CS.** (1994) Melaleuca oil poisoning. *Journal of Toxicology Clinical Toxicology* **32**: 461-464. [Case report] [View abstract in Pubmed](#)
- Jancin B.** (2002) Cross-sensitivity common in tea tree oil allergy. *eSkin and Allergy News* **33**: 38. [News]
- Jandera V, Hudson DA, de Wet PM, Innes PM & Rode H.** (2000) Cooling the burn wound: evaluation of different modalities. *Burns* **26**: 265-270. [Research article] [View abstract in Pubmed](#)
- Jandourek A, Vaishampayan JK & Vazquez JA.** (1998) Efficacy of melaleuca oral solution for the treatment of fluconazole refractory oral candidiasis in AIDS patients. *AIDS* **12**: 1033-1037. [Research article] [View abstract in Pubmed](#)
- Johns MR, Johns JE & Rudolph V.** (1992) Steam distillation of tea tree (*Melaleuca alternifolia*) oil. *Journal of the Science of Food & Agriculture* **58**: 49-53. [Research article] [Abstract](#)
- Jones J.** (1999) Tea-tree industry steady as it goes. *Australian Farm Journal* **1999 (September)**: 30-32. [News] [Full text \(PDF\)](#) *Reproduced with permission*
- Kalaf G & Mayo W.** (1993) Dall'Australia sul tea tree oil [Italian] Natural Medicine Conference, 23-24 October 1993. [Conference abstract]
- Kaluziński M.** (2000) Partial paralysis and altered behaviour in dogs treated with melaleuca oil. *Journal of Toxicology – Clinical Toxicology* **38**: 518-519 [Conference abstract]
- Kaplowitz GJ.** (1990) Evaluation of Gutta-percha solvents. *Journal of Endodontics* **16**: 539-40. [Research article] [View abstract in Pubmed](#)
- Kaplowitz GJ.** (1991) The effect of essential oil type on the setting time of Grossman's sealer and Roth root canal cement. *Journal of Endodontics* **17**: 280-281. [Research article] [View abstract in Pubmed](#)
- Kaptchuk TJ.** (1996) Uptake of alternative medicine. *The Lancet* **347**: 1996. [Letter]
- Kawakami M, Sachs RM & Shibamoto T.** (1990) Volatile constituents of essential oils obtained from newly developed tea tree (*Melaleuca alternifolia*) clones. *Journal of Agricultural & Food Chemistry* **38**: 1657-1661. [Research article] [Abstract](#)
- Kedzia B, Alkiewicz J, Han S.** (2000) Tea tree oil and its use in phytotherapy, part I. Composition and biological properties of the oil [Polish]. *Postępy Fitoterapii* **1(2)**: 36-40. [Research article]
- Kedzia B, Alkiewicz J, Han S.** (2000) Tea tree oil and its use in phytotherapy, part II. Therapeutic use [Polish]. *Postępy Fitoterapii* **1(3)**: 33-37. [Research article]
- Kennedy S.** (1990) The dinkum oil. *The Bulletin* **1990 (February 20)**: 96-97. [News]

- Khanna M, Qasem K & Sasseville D.** (2000) Contact sensitization to tea tree oil with erythema multiform-like ID-reaction. Eleventh Annual Meeting of the American Contact Dermatitis Society, March 9, 2000, San Francisco, USA. [Conference abstract]
- Khanna M, Qasem K & Sasseville D.** (2000) Allergic contact dermatitis to tea tree oil with erythema multiforme-like id reaction. *American Journal of Contact Dermatitis* **11**: 238-242. [Case report] [Abstract](#)
- Khanom A & Blackburn J.** (2002) The effect of herbal tinctures on neutrophil activity in vitro. *Immunology* **107(Suppl 1)**: 72 [Conference abstract] | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Kiken DA & Cohen DE.** (2002) Contact dermatitis to botanical extracts. *American Journal of Contact Dermatitis* **13**: 148-152. [Review] [Abstract](#)
- Kim D, Cerven DR, Craig S & DeGeorge GL.** (2002) Tea tree oil administered orally induces specific neurotoxicity in rats. Abstracts of the American Chemical Society National Meeting April 7 2002. **223**: 114-MEDI Part 2. [Conference abstract]
- Kippen C.** (1996) Tea tree oil (Melaleuca oil). *Journal of British Podiatric Medicine* **51**: viii. [News]
- Kippen C.** (2001) The wonders of tea tree oil. *Podiatry Now* **2001 (March)**: 112. [News]
- Kirn TF.** (2003) Tea tree oil offers relief from athlete's foot. *eFamily Practice News* **33**: 22 [News] Same article published in *eSkin and Allergy News* (2002) **33**: 13. [Free full text at journal webpage](#)
- Klimmek J-KW, Nowicki R, Szendzielorz K, Kunicka M, Rosentrit R, Honisz G & Król W.** (2002) Application of tea tree oil and its preparations in combined treatment of dermatomycoses [Polish]. *Mikologia Lekarska* **9**: 93-96. [Research article]
- Kluge H.** (2000) Healthy and beautiful with tea tree oil. Magni Company, McKinney, TX, USA (100 pages) ISBN: 1882330528 [Book]
- Knight TE & Hausen BM.** (1994) Melaleuca oil (tea tree oil) dermatitis. *Journal of the American Academy of Dermatology* **30**: 423-427. [Research article] [View abstract in Pubmed](#)
- Koh KJ, Marshman G & Hart PH.** (2002) Tea tree oil reduces histamine-induced skin inflammation. *British Journal of Dermatology* **147**: 1212-1217. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Köhler P, Borchert S & Petersen RD.** (1998) Improvements in the treatment of impure skin [German]. *Parfümerie und Kosmetik* **11/98**: 28-31. [News]
- Köhler P, Borchert S & Petersen RD.** (1999) Progress in the treatment of problem skin. *Cosmetics and Toiletries Manufacture Worldwide* **1999**: 89-92. No abstract. [News]
- Köhler P, Petersen R-D, Borchert S & Richter K.** (2000) Stabilisation of tea tree oil. *Cosmetics and Toiletries Manufacture Worldwide* **2000**: 36-38. No abstract. [Research article]
- Kranke B.** (1997) Allergy-inducing potency of tea tree oil [German]. *Hautarzt* **48**: 203-204. [Review]
- Kreck M, Scharrer A, Bilke S & Mosandl A.** (2002) Enantioselective analysis of monoterpene compounds in essential oils by stir bar sorptive extraction (SBSE)-enantio-MDGC-MS. *Flavour & Fragrance Journal* **17**: 32-40. [Research article]
- Kristoffersen SS, Atkin PA & Shenfield GM.** (1997) Use of alternative medicines on Sydney's north shore. *The Australian Journal of Hospital Pharmacy* **27**: 367-372. [Research note] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission*
- Kulik E, Lenkeit K & Meyer J.** (2000) Antimicrobial effects of tea tree oil (*Melaleuca alternifolia*) on oral microorganisms [German]. *Acta Medicinæ Dentium Helveticum* **110**: 125-30. [Research article] [View abstract in Pubmed](#)
- Lassak EV & McCarthy T.** (1983) Australian medicinal plants. Methuen Australia, North Ryde, NSW. ASIN: 0454004389 (240 pages) [Book]
- Lawless J.** (2001) Tea tree oil: nature's miracle healer. Thorsons Publishing, London. ISBN: 0007110707 (144 pages) [Book]
- Lawless J.** (1994) Tea tree oil: the new guide to one of nature's most remarkable gifts. Thorsons Publishing, London ISBN 0722530323. (130 pages) [Book]
- Lawrence BM.** (2001) Progress in essential oils: coriander seed and leaf oils, cassia oil, tea tree oil, and balsamite or costmary oil. *Perfumer and Flavorist* **2001(Nov/Dec)**: 44. [Letter]

- Leach DN, Wyllie SG, Hall JG & Kyrtzsis I.** (1993) Enantiomeric composition of the principal components of the oil of *Melaleuca alternifolia*. *Journal of Agricultural and Food Chemistry* **41**: 1627-1632. [Research article] [Abstract](#)
- Lee LS, Brooks LO, Homer LE, Rossetto M, Henry RJ & Baverstock PR.** (2002) Geographic variation in the essential oils and morphology of natural populations of *Melaleuca alternifolia* (Myrtaceae). *Biochemical Systematics & Ecology* **68**: 343-360. [Research article] [View abstract in Pubmed](#)
- Lippert U, Walter A, Hausen B & Fuchs T.** (2000) Increasing incidence of contact dermatitis to tea tree oil. *The Journal of Allergy and Clinical Immunology* **105**: 127. [Conference abstract]
- Lis-Balchin M, Hart SL & Deans SG.** (2000) Pharmacological and antimicrobial studies on different tea-tree oils (*Melaleuca alternifolia*, *Leptospermum scoparium* or Manuka and *Kunzea ericoides* or Kanuka), originating in Australia and New Zealand. *Phytotherapy Research* **14**: 623-629. [Research article] [View abstract in Pubmed](#)
- Lisi P, Meligeni L, Pigatto P, Ayala F, Suppa F, Foti C & Angelini G.** (2000) Prevalence of sensitisation to the essential oil of *Melaleuca* [Italian]. *Annali italiani di Dermatologia allergologica* **54**: 141-144. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission*
- List SE.** (1995) Functional anatomy and clonal multiplication of *Melaleuca alternifolia* cheel. in the Central Queensland region. Central Queensland University [M App Sci Thesis]
- List S, Brown PH & Walsh KB.** (1995) Functional anatomy of the oil glands of *Melaleuca alternifolia* (Myrtaceae). *Australian Journal of Botany* **43**: 629-641. [Research article] [Abstract](#)
- List SE, Brown PH, Low CS & Walsh KB.** (1996) A micropropagation protocol for *Melaleuca alternifolia* (tea tree). *Australian Journal of Experimental Agriculture* **36**: 755-760. [Research article] [Abstract](#)
- Lovell CR.** (1997) Phytodermatitis. *Clinics in Dermatology* **15**: 607-613. [Review] No abstract.
- Low D, Rawal BD & Griffin WJ.** (1974) Antibacterial action of the essential oils of some Australian Myrtaceae with special references to the activity of chromatographic fractions of oil of *Eucalyptus citriodora*. *Planta medica* **26**: 184-189. [Research article] [View abstract in Pubmed](#)
- Lowe R, Murtagh J & Morris S.** (2000) Salt tolerance of tea tree (*Melaleuca alternifolia*). *Australian Forestry* **63**: 252-256. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission*
- MacDonald V.** (1930) The rationale of treatment. *The Australian Journal of Dentistry* **34**: 281-282. [Letter]
- Macready N.** (2001) Tea tree oil applied to abrasion evokes dramatic dermatitis. *eSkin and Allergy News* **32**: 17. [News] [Comment on Khanna *et al.* 2002]
- Maddox CDA.** (1996) Aspects of the biology of *Paropsisisterna tigrina* (Chapius) the major pest species of *Melaleuca alternifolia* (Cheel). University of Queensland [MSc. Thesis]
- Malik R & Quirk CJ.** (2000) Topical applications and perioral dermatitis. *Australasian Journal of Dermatology* **41**: 34-38. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Mann CM, Cox SD & Markham JL.** (2000) The outer membrane of *Pseudomonas aeruginosa* NCTC 6749 contributes to its tolerance to the essential oil of *Melaleuca alternifolia* (tea tree oil). *Letters in Applied Microbiology* **30**: 294-297. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Mann CM & Markham JL.** (1998) A new method for determining the minimum inhibitory concentration of essential oils. *Journal of Applied Microbiology* **84**: 538-544. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Mantle D, Gok MA & Lennard TW.** (2001) Adverse and beneficial effects of plant extracts on skin and skin disorders. *Adverse Drug Reactions & Toxicological Reviews* **20**: 89-103. [Review] [View abstract in Pubmed](#)
- Markham J, Leach DN, Cornwell CP & Griffin SG.** (1995) Antimicrobial activity of monoterpenes in essential oils from Australian flora. Proceedings of the Australian Society for Microbiology Annual Scientific Meeting, Sept 24 - 29 1995, Canberra ACT. [Conference abstract]
- Markham J.** (1999) Antimicrobial effectiveness of tea tree oil. *Cosmetics Aerosols and Toiletries in Australia* **12(5)**: 12-15.

- Marking LL, Rach JJ & Schreier TM.** (1994) Evaluation of antifungal agents for fish culture. *The Progressive Fish-Culturist* **56**: 225-231. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission, American Fisheries Society.*
- Martin KW, Ernst E.** (2003) Herbal medicines for treatment of bacterial infections: a review of controlled clinical trials. *Journal of Antimicrobial Chemotherapy* **51**: 241-246. [Review] [View abstract in Pubmed](#)
- Maruzzella JC, Scrandis DA, Scrandis JB & Grabon G.** (1960) Action of odoriferous organic chemicals and essential oils on wood-destroying fungi. *Plant Diseases Reporter* **44**: 789-792. [Research article]
- Maruzzella JC & Sicurella NA.** (1960) Antibacterial activity of essential oil vapors. *Journal of American Pharmaceutical Association* **49**: 692-694. [Research article]
- Maudsley F & Kerr KG.** (1999) Microbiological safety of essential oils used in complementary therapies and the activity of these compounds against bacterial and fungal pathogens. *Supportive Care in Cancer* **7**: 100-102. [Research article] [View abstract in Pubmed](#)
- May J, Chan CH, King A, Williams L & French GL.** (2000) Time-kill studies of tea tree oils on clinical isolates. *Journal of Antimicrobial Chemotherapy* **45**: 639-643. [Research article] [View abstract in Pubmed](#)
- Mayo WL.** (1992) Australian tea tree oil: a summary of medicinal, pharmacological & alternative health research and writings. *International Journal of Alternative & Complementary Medicine* **1992(Dec)**: 13-16. [Review] [Full text \(PDF\)](#) *Reproduced with permission*
- McCage CM, Ward SM, Paling CA, Fisher DA, Flynn PJ, McLaughlin JL.** (2002) Development of a paw paw herbal shampoo for the removal of head lice. *Phytomedicine* **9**: 743-748. [Research article] [Abstract](#)
- McDonald LG & Tovey E.** (1993) The effectiveness of benzyl benzoate and some essential plant oils as laundry additives for killing house dust mites. *Journal of Allergy and Clinical Immunology* **92**: 771-772. [Research article] [View abstract in Pubmed](#)
- McNamara D.** (2003) Popularity of botanical abstracts means more contact dermatitis. *eFamily Practice News* **33**: 33 [News] No abstract. Article also published in *eSkin and Allergy News* **33**: 18 and *Internal Medicine News* **36**: 26. [Free full text at journal webpage](#)
- Mennie A.** (1997) An essential and ancient oil. *Nursing Times* **93**: 31-32. [News] No abstract.
- Mikus J, Harkenthal M, Steverding D & Reichling J.** (2000) In vitro effect of essential oils and isolated mono- and sesquiterpenes on *Leishmania major* and *Trypanosoma brucei*. *Planta Medica* **66**: 366-368. [Research article] [View abstract in Pubmed](#)
- Mondello F, De Bernardis F, Girolamo A, Salvatore G & Cassone A.** (2003) In vitro and in vivo activity of tea tree oil against azole-susceptible and -resistant human pathogenic yeasts. *Journal of Antimicrobial Chemotherapy* **51(5)**: 1223-1229 [Research article] [View abstract in Pubmed](#)
- Mori M, Ikeda N, Kato Y, Minamino M & Watabe K.** (2002) Quality evaluation of essential oils [Japanese]. *Yakugaku Zasshi* **122**: 253-261. [Research article] [Abstract](#)
- Morris MC, Donoghue A, Markowitz JA, Osterhoudt KC.** (2003) Ingestion of tea tree oil (Melaleuca oil) by a 4-year-old boy. *Pediatric Emergency Care* **19(3)**: 169-171 [Case report]
- Moss A.** (1994) Tea tree oil poisoning. *Medical Journal of Australia* **160**: 236. [Letter] [Full text \(PDF\)](#) *Copyright 1994, The Medical Journal of Australia. Reproduced with permission.*
- Mozelsio NB, Harris KE, McGrath KG, Grammer LC.** (2003) Immediate systemic hypersensitivity reaction associated with topical application of Australian tea tree oil. *Allergy & Asthma Proceedings* **24**: 73-75. [Case report] [View abstract in Pubmed](#)
- Murtagh GJ.** (1996) Month of harvest and yield components of tea tree. I. Biomass. *Australian Journal of Agricultural Research* **47**: 801-815. [Research article] [Abstract](#)
- Murtagh GJ & Curtis A.** (1991) Post-harvest retention of oil in tea tree foliage. *Journal of Essential Oil Research* **3**: 179-184. [Research article]
- Murtagh GJ & Etherington RJ.** (1990) Variation in oil concentration and economic return from tea-tree (*Melaleuca alternifolia* Cheel) oil. *Australian Journal of Experimental Agriculture* **30**: 675-679. [Research article] [Abstract](#)

- Murtagh GJ & Smith GR.** (1996) Month of harvest and yield components of tea tree. II. Oil concentration, composition, and yield. *Australian Journal of Agricultural Research* **47**: 817-827. [Research article] [Abstract](#)
- Nelson RR.** (1997) In-vitro activities of five plant essential oils against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecium*. *Journal of Antimicrobial Chemotherapy* **40**: 305-306. [Letter]
- Nelson RR.** (2000) Selection of resistance to the essential oil of *Melaleuca alternifolia* in *Staphylococcus aureus*. *Journal of Antimicrobial Chemotherapy* **45**: 549-550. [Letter]
- 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 Pharmacology* **9**: 388-394. [Research article] [View abstract in Pubmed](#)
- Nicolson D.** (2001) Novel research-driven applications for tea tree oil – part I. *Cosmetics, Aerosols & Toiletries in Australia* **14**: 21-26. [News]
- Nicolson D.** (2001) Novel research-driven applications for tea tree oil – part II. *Cosmetics, Aerosols & Toiletries in Australia* **14**: 27-30. [News]
- Nicholson SS.** (1995) Toxicity of insecticides and skin care products of botanical origin. *Veterinary Dermatology* **6**: 139-143. [Review] [View abstract in Pubmed](#)
- Olsen CB.** (1991) Australian tea tree oil manual. Kali Press, Pagosa Springs, Colo, USA. ASIN: 0962888206 (40 pages) [Book]
- Olsen CB.** (1997) Australian tea tree oil guide: first aid kit in a bottle (3rd edition). Kali Press, Pagosa Springs, Colo, USA. (113 pages) [Book]
- Olsen C.** (1999) Australian tea tree oil handbook - 101 plus ways to use tea tree (2nd edition). Kali Press, Pagosa Springs, Colo, USA. ISBN: 1890941026 (96 pages) [Book]
- Olsen MW, Cassells J & Cross D.** (1988) Control of *Sphaerotheca fuliginea* on cucurbits with an oil extracted from the Australian tea tree. *Phytopathology* **78**: 1595. [Research note]
- Osborne F & Chandler F.** (1998) Australian tea tree oil. *Canadian Pharmaceutical Journal* **131**: 42-46. [Review] No abstract.
- Owen-Turner J.** (1998) Tea tree: a farming lifestyle. Lifestyle Farming, Torbanlea, Qld. ISBN: 0958617902 (89 pages) [Book]
- Palmhart J & Rode H.** (1998) The use of Burnshield in burn wound management. International Society for Burn Injuries World Burn Congress, 1-6 November, 1998, Edmonton, Alberta, Canada. [Conference abstract]
- Peña EF.** (1962) *Melaleuca alternifolia* oil - its use for trichomonal vaginitis and other vaginal infections. *Obstetrics and Gynecology* **19**: 793-795. [Research article] | [Full text \(PDF\)](#) *Reproduced with permission*
- Penfold AR.** (1925) The essential oils of *Melaleuca linariifolia* (Smith), and *M. alternifolia* (Cheel). *Journal and Proceedings of the Royal Society of New South Wales* **59**: 306-324. [Research article] No abstract.
- Penfold AR & Grant R.** (1923) The germicidal values of the principal commercial Eucalyptus oils and their pure constituents, with observations on the value of concentrated disinfectants. *Journal and Proceedings of the Royal Society of New South Wales* **58**: 80-89. [Research article] No abstract.
- Penfold AR & Grant R.** (1924) The germicidal values of the pure constituents of Australian essential oils, together with those for some essential oil isolates and synthetics. Part II. *Journal and Proceedings of the Royal Society of New South Wales* **58**: 117-123. [Research article] No abstract.
- Penfold AR & Grant R.** (1925) The germicidal values of some Australian essential oils and their pure constituents, together with those for some essential oil isolates, and synthetics. Part III. *Journal and Proceedings of the Royal Society of New South Wales* **59**: 346-350. [Research article] No abstract.
- Penfold AR & Grant R.** (1926) The germicidal values of some Australian essential oils and their pure constituents, together with those for some essential oil components, and synthetic substances. Part IV. *Journal and Proceedings of the Royal Society of New South Wales* **60**: 167-170. [Research article] No abstract.

- Penfold AR & Grant R.** (1936) Australian tea trees of economic value. Part II. Technological Museum, Sydney, Bulletin No. 14. 1-16. Alfred James Kent, Government Printer, Sydney. [Government publication]
- Penfold AR & Morrison FR.** (1937) Some notes on the essential oil of *Melaleuca alternifolia*. *The Australasian Journal of Pharmacy* **18**: 274-275. [News] No abstract.
- Penfold AR & Morrison FR.** (1946) Australian tea trees of economic value. Part I (3rd edition). Technological Museum, Sydney, Bulletin No. 14. 1-16. Thomas Henry Tennant, Government Printer, Sydney. [Government publication]
- Perrett CM, Evans AV, Russell-Jones R.** (2003) Tea tree oil dermatitis associated with linear IgA disease. *Clinical & Experimental Dermatology* **28(2)**: 167-170. [Case report] [View abstract in Pubmed](#)
- Petry JJ & Hadley SK.** (2001) Medicinal herbs: answers and advice, part 1. *Hospital Practice* **36**: 57-60. [Review] [View abstract in Pubmed](#)
- Pickering GB.** (1956) Perfumery and essential oils - cedarwood oil compounds, silica gel separation, tea-tree oil as nutmeg substitute. *Manufacturing Chemist* **27**: 105-106. [News] [Full text \(PDF\)](#) (*Reproduced with permission*)
- Pippin MA, Pabst KM, Pabst MJ, Haney L & Dabbous MKH.** (1994) Superoxide release by neutrophils is inhibited by tea tree oil. *Journal of Dental Research* **73**: 259. [Conference abstract] *Reprinted with permission from Journal of Dental Research.* [Abstract \(PDF\)](#)
- Polizzi G & Agosteo GE.** (1995) Efficacy of natural fungicides and chemicals in controlling *Graphiola phoenicis*, causal agent of false smut of palms [Italian]. *La Difesa delle Piante* **18**: 122-126. [Research article]
- Poth S.** (1999) Tea tree oil for health & well-being. Sterling Publishing Co. Inc. New York, NY, USA (96 pages) ISBN: 0806948485 [Book]
- Pradhanang PM, Momol MT, Olson SM, Jones JB.** (2003) Effects of plant essential oils on *Ralstonia solanacearum* population density and bacterial wilt incidence in tomato. *Plant Disease* **87**: 423-427. [Research article] [Abstract](#)
- Price J.** (1998) Burnaid. *Burns* **24**: 80-82. [Letter] No abstract.
- Priest D.** (1994) Main camp tea tree oil - green and growing. *Cosmetics, Aerosols & Toiletries in Australia* **8**: 15-16. [News] No abstract.
- Priest D.** (1995) Preserving naturally with tea tree oil. *SOFW-Journal* **7/95**: 486-489. [News] No abstract.
- Priestley CM, Burgess I & Williamson EM.** (1998) Effects of essential oils on house dust mites. *Journal of Pharmacy and Pharmacology* **50 (Suppl)**: 193. [Research note] [Full text \(PDF\)](#) (*Reproduced with permission*)
- Puotnen CJ.** (1999) Nature's antiseptics: tea tree oil and grapefruit seed extract. McGraw-Hill/Contemporary Books, New York. ISBN: 0879837144 (48 pages) [Book]
- Raman A, Weir U & Bloomfield SF.** (1995) Antimicrobial effects of tea-tree oil and its major components on *Staphylococcus aureus*, *Staph. epidermidis* and *Propionibacterium acnes*. *Letters in Applied Microbiology* **21**: 242-245. [Research article] [Abstract](#) | [Full text \(PDF\)](#) (*Reproduced with permission from Blackwell Publishers*)
- Ramacciato JC, Simões RP, Flório FM, Cecanho R, Groppo FC & Mattos-Filho TRM.** (2000) Antimicrobial activity of *Melaleuca alternifolia* against streptococci and *S. aureus*. *Journal of Dental Research* **79(5)**: 1071 (abstract, A-018). [Conference abstract] *Reprinted with permission from Journal of Dental Research.* [Abstract \(PDF\)](#)
- Reichling J & Saller R.** (1996) Australian tea tree oil [German] *Zeitschrift für Phytotherapie* **17**: 111-112. [Review] German abstract.
- Reichling J, Weseler A, Landvatter U & Saller R.** (2002) Bioactive essential oils used in phytomedicine as anti-infective agents: Australian tea tree oil and manuka oil. *Acta Phytotherapeutica* **1**: 26-32. [Research article] [Abstract](#) | [Full text \(PDF\)](#) (*Reproduced with permission*)
- Reichling J, Harkenthal M, Geiss HK & Saller R.** (1997) Quality, adulterations, effects and toxicity of Australian tea tree oil [German]. *Österreichischen Apotheker-Zeitung* **51**: 652-660. [Review] German abstract.

- Reichling J, Harkenthal M, Landvatter U, Geiss HK, Schnitzler P, Hoppe-Tichy T & Saller R.** (2001) Australian tea tree oil (*Melaleuca aetheroleum*): pharmaceutical quality, efficacy and toxicity [German]. *Pz Prisma* **8(4)**: 228-238. [Review]
- Riedl RW.** (1997) Practical methods for using tea tree oil. *Agro-Food-Industry Hi - Tech* **8**: 34-36. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission*
- Reindl H, Gall H, Hausen BM, Peter RU.** (2000) Acute allergic contact dermatitis of the scalp due to tea tree oil [German]. *Allergo Journal* **9**: 100-103 [Research article] [View abstract in Pubmed](#)
- RM Barry Publications** (1995) The ultimate melaleuca guide. RM Barry Publications; Englewood, CO, USA. ISBN: 0966592433 (192 pages) [Book]
- RM Barry Publications** (2002) The Melaleuca quick reference. RM Barry Publications, Englewood, CO, USA. ISBN: 0966592476 (64 pages) [Book]
- Rodger E.** (1997) Chronic mucocutaneous candidiasis - a case study. *Journal of British Podiatric Medicine* **52**: 9-10. [Case report] No abstract.
- Rossetto M, Harriss FCL, McLauchlan A, Henry RJ, Baverstock PR & Lee LS.** (2000) Interspecific amplification of tea tree (*Melaleuca alternifolia* - Myrtaceae) microsatellite loci - potential implications for conservation studies. *Australian Journal of Botany* **48**: 367-373. [Research article] [Abstract](#)
- Rossetto M, McLauchlan A, Harriss FCL, Henry RJ, Baverstock PR, Lee LS, Maguire TL & Edwards KJ.** (1999) Abundance and polymorphism of microsatellite markers in the tea tree (*Melaleuca alternifolia*, Myrtaceae). *Theoretical & Applied Genetics* **98**: 1091-1098. [Research article] [View abstract in Pubmed](#)
- Rossetto M, Slade RW, Baverstock PR, Henry RJ & Lee LS.** (1999) Microsatellite variation and assessment of genetic structure in tea tree (*Melaleuca alternifolia*-Myrtaceae). *Molecular Ecology* **8**: 633-643. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Rubel DM, Freeman S & Southwell IA.** (1998) Tea tree oil allergy: what is the offending agent? Report of three cases of tea tree oil allergy and review of the literature. *Australasian Journal of Dermatology* **39**: 244-247. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Rushton RT, Davis NW, Page JC & Durkin CA.** (1997) The effect of tea tree oil extract on the growth of fungi. *The Lower Extremity* **4**: 113-116. [Research article]
- Russell M & Southwell I.** (2002) Monoterpenoid accumulation in *Melaleuca alternifolia* seedlings. *Phytochemistry* **59**: 709-716. [Research article] [View abstract in Pubmed](#)
- Russell M & Southwell I.** (2003) Monoterpenoid accumulation in 1,8-cineole, terpinolene and terpinen-4-ol chemotypes of *Melaleuca alternifolia* seedlings. *Phytochemistry* **62**: 683-689. [Research article] [View abstract in Pubmed](#)
- Sachs RM, Lee CI, Cartwright SA, Reid MS.** (1990) *Melaleuca alternifolia*: new crop for California? *California Agriculture* **44**: 27-29. [Research article] [Abstract](#)
- Saller R & Reichling J.** (1995) Tea tree oil - a natural universal remedy [German] *Deutsche Apotheker Zeitung* **135**: 40-48. [Review]
- Saller R, Berger T, Reichling J & Harkenthal M.** (1998) Pharmaceutical and medicinal aspects of Australian tea tree oil. *Phytomedicine* **5**: 489-495. [Review] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission*
- Sammataro D, Degrandihoffman G, Needham G & Wardell G.** (1998) Some volatile plant oils as potential control agents for varroa mites (Acari, Varroidae) in honey bee colonies (Hymenoptera, Apidae). *American Bee Journal* **138**: 681-685. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission*
- Santos FA & Rao VSN.** (1997) Mast cell involvement in the rat paw oedema response to 1,8-cineole, the main constituent of *Eucalyptus* and Rosemary oils. *European Journal of Pharmacology* **331**: 253-258. [Research article] [View abstract in Pubmed](#)
- Satchell AC, Saurajen A, Bell C & Barnetson RStC.** (2002) Treatment of dandruff with 5% tea tree oil shampoo. *Journal of the American Academy of Dermatology* **47**: 852-855. [Research article] [View abstract in Pubmed](#)

- Satchell AC, Saurajen A, Bell C & Barnetson RStC.** (2002) Treatment of interdigital tinea pedis with 25% and 50% tea tree oil solution: a randomized, placebo-controlled, blinded study. *Australasian Journal of Dermatology* **43**: 175-178. [Research article] [Abstract](#) | [Full text \(PDF\)](#)  
*Reproduced with permission from Blackwell Publishers*
- Schaller M & Korting KC.** (1995) Allergic airborne contact dermatitis from essential oils used in aromatherapy. *Clinical and Experimental Dermatology* **20**: 143-145. [Case report] [View abstract in Pubmed](#)
- Schempp CM, Schopf E & Simon JC.** (2002) Plant-induced toxic and allergic dermatitis (phytodermatitis) [German]. *der Hautarzt* **53**: 93-97. [Review] [View abstract in Pubmed](#)
- Schmolz E, Doebner R, Auste R, Daum R, Welge G & Lamprecht I.** (1999) Bioenergetic investigations on tea-tree and related essential oils. *Thermochimica Acta.* **337**: 71-81. [Research article]
- Schnitzler P, Schoen K & Reichling J.** (1999) Antiviral activity of tea tree oil against herpes simplex virus. International Congress on Antimicrobial Agents and Chemotherapy, Sept 26-29 1999, San Francisco, USA. [Conference abstract]
- Schnitzler P, Schoen K & Reichling J.** (2001) Antiviral activity of Australian tea tree oil and eucalyptus oil against herpes simplex virus in cell culture. *Pharmazie* **56**: 343-347. [Research article] [Abstract](#)
- Schulze I-S.** (2001) Eczema of the oral mucosa and the lips in multiple allergic contact dermatitis including tea tree oil contact allergy. *Zeitschrift fur Hautkrankheiten* **76**: 559-560. [Conference abstract]
- Seawright A.** (1993) Tea tree oil poisoning. *Medical Journal of Australia* **159**: 831. [Letter] [Full text \(PDF\)](#) *Copyright 1993, The Medical Journal of Australia. Reproduced with permission.*
- Selvaag E, Eriksen B & Thune P.** (1994) Contact allergy due to tea tree oil and cross-sensitization to colophony. *Contact Dermatitis* **31**: 124-125. [Case report] | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Selvaag, E, Holm J-O & Thune P.** (1995) Allergic contact dermatitis in an aromatherapist with multiple sensitizations to essential oils. *Contact Dermatitis* **33**: 354-355. [Case report] | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Shapiro S, Meier A & Guggenheim B.** (1994) The antimicrobial activity of essential oils and essential oil components towards oral bacteria. *Oral Microbiology & Immunology* **9**: 202-208. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Shellie R, Marriott P & Cornwell C.** (2000) Characterization and comparison of tea tree and lavender oils by using comprehensive gas chromatography. *HRC Journal of High Resolution Chromatography* **23**: 554-560. [Research article] [View abstract in Pubmed](#)
- Shellie R, Marriott P & Cornwell C.** (2001) Application of comprehensive two-dimensional gas chromatography (GCXGC) to the enantioselective analysis of essential oils. *Journal of Separation Science* **24**: 823-830. [Research article] [View abstract in Pubmed](#)
- Shelton D, Aitken K, Doimo L, Leach D, Baverstock P & Henry R.** (2002) Genetic control of monoterpene composition in the essential oil of *Melaleuca alternifolia* (Cheel). *Theoretical & Applied Genetics* **105**: 377-383. [Research article] [View abstract in Pubmed](#)
- Shelton D, Leach D, Baverstock P & Henry R.** (2002) Isolation of genes involved in secondary metabolism from *Melaleuca alternifolia* (Cheel) using expressed sequence tags (ESTs). *Plant Science* **162**: 9-15. [Research article] [View abstract in Pubmed](#)
- Shemesh A & Mayo WL.** (1991) Australian tea tree oil: a natural antiseptic and fungicidal agent. *The Australian Journal of Pharmacy* **72**: 802-803. [Research article] [Full text \(PDF\)](#) *Reproduced with permission*
- Sherry E, Boeck H & Warnke PH.** (2001) Topical application of a new formulation of eucalyptus oil phytochemical clears methicillin-resistant *Staphylococcus aureus* infection. *American Journal of Infection Control* **29**: 346. [Letter]
- Sherry E, Boeck H & Warnke PH.** (2001) Percutaneous treatment of chronic MRSA osteomyelitis with a novel plant-derived antiseptic. *BioMed Central Surgery* **1**: 1. [Case report] | [View full text at journal website](#)

- Shin S.** (2003) Anti-Aspergillus activities of plant essential oils and their combination effects with ketoconazole or amphotericin B. *Archives of Pharmacal Research* **26(5)**: 389-393. [Research article] [View abstract in Pubmed](#)
- Slawson D.** (2003) Tea tree oil shampoo in the treatment of dandruff. *American Family Physician* **67(9)**: 1985. [News]
- Small BEJ.** (1981) Effects of plant spacing and season on growth of *Melaleuca alternifolia* and yield of tea tree oil. *Australian Journal of Experimental Agriculture & Animal Husbandry* **21**: 439-442. [Research article] [Abstract](#)
- Smith KE.** (1995) Stopping the burn. *Occupational Health & Safety* **64**: 159-160. [Research article] No abstract.
- Smith MD & Navilliat PL.** (1996) A new protocol for antimicrobial testing of oils. *Journal of Microbiological Methods* **28**: 21-24. [Research article] [View abstract in Pubmed](#)
- Smith DW, Carson CF, Ashton L, Dry L & Riley TV.** (2000) A randomised, placebo-controlled, single-blind pilot study to evaluate the efficacy of tea tree oil gel (6%) in the treatment of herpes labialis. *Journal of Clinical Virology* **18**: 265-266 (Abstract #P-348) [Conference abstract]
- Soderberg TA, Johansson A & Gref R.** (1996) Toxic effects of some conifer resin acids and tea tree oil on human epithelial and fibroblast cells. *Toxicology* **107**: 99-109. [Research article] [View abstract in Pubmed](#)
- Sommer C & Juhl H.** (2001) Determination of the content of tea tree oil in cosmetics by capillary gas chromatographic quantification of the key component terpinen-4-ol. [German] *Deutsche Lebensmittel-Rundschau* **97**: 8-11. [Research article]
- Southwell IA.** (1988) Australian tea tree: oil of melaleuca, terpinen-4-ol type. *Chemistry in Australia* **55**: 400-402. [Research article] [Full text \(PDF\)](#) *Reproduced with permission*
- Southwell IA, Freeman S & Rubel D.** (1997) Skin irritancy of tea tree oil. *Journal of Essential Oil Research* **9**: 47-52. [Research article]
- Southwell IA, Hayes AJ, Markham J & Leach DN.** (1993) The search for optimally bioactive Australian tea tree oil. *Acta Horticulturae* **344**: 256-265. [Research article] [Abstract](#)
- Southwell IA & Lowe R. [Eds]** (1999) Tea tree: the genus melaleuca. Harwood Academic, Amsterdam. ISBN 9057024179 (296 pages) [Book]
- Southwell IA, Maddox CDA & Zalucki MP.** (1995) Metabolism of 1,8-cineole in tea tree (*Melaleuca alternifolia* and *M. linariifolia*) by pyrigo beetle (*Paropsisterna tigrina*). *Journal of Chemical Ecology* **21**: 439-453. [Research article] [Abstract](#)
- Southwell IA, Markham J & Mann C.** (1996) Is cineole detrimental to tea tree oil? *Perfumer and Flavorist* **21**: 7-10. [Research article] No abstract.
- Southwell IA, Markham J & Mann C.** (1997) Significance of cineole for bioactivity and irritancy in tea tree oil. RIRDC project 104A, RIRDC publication R97/054, 128 pp. ISBN: 0731098080 [Government publication]
- Southwell IA & Russell MF.** (2002) Volatile oil comparison of cotyledon leaves of chemotypes of *Melaleuca alternifolia*. *Phytochemistry* **59**: 391-393. [Research article] [View abstract in Pubmed](#)
- Southwell IA & Russell MF.** (2003) The sequential onset of terpenoid biogenesis in seedlings: implications for *Melaleuca alternifolia* chemotype identification prior to plantation establishment. *Acta Horticulturae* **597**: 31-47. [View abstract at journal website](#)
- Southwell IA & Stiff IA.** (1989) Ontogenetical changes in monoterpenoids of *Melaleuca alternifolia* leaf. *Phytochemistry* **28**: 1041-1051. [Research article] [View abstract in Pubmed](#)
- Southwell IA & Stiff IA.** (1990) Differentiation between *Melaleuca alternifolia* and *M. linariifolia* by monoterpenoid comparison. *Phytochemistry* **29**: 3529-3533. [Research article] [View abstract in Pubmed](#)
- Southwell IA, Stiff IA & Brophy JJ.** (1992) Terpinolene varieties of *Melaleuca*. *Journal of Essential Oil Research* **4**: 363-367. [Research article]
- Southwell IA & Wilson RW.** (1993) The potential for tea tree oil production in northern Australia. *Acta Horticulturae* **331**: 223-227. [Research article] [Abstract](#)
- Standards Association of Australia** (1967) Oil of *Melaleuca alternifolia* AS K175 [Standard]
- Standards Association of Australia** (1985) Essential oils - oil of Melaleuca, terpinen-4-ol type, AS 2782-1985: Standards Association of Australia, Sydney [Standard]

- Standards Association of Australia** (1997) Oil of *Melaleuca*, terpinen-4-ol type (Tea Tree oil) AS 2782-1997: Standards Association of Australia, Sydney [Standard]
- Stevensen CJ.** (1998) Aromatherapy in dermatology. *Clinics in Dermatology* **16**: 689-694. [Research article] No abstract.
- Stiff IA.** (1995) Australian "tea tree" oil: composition, extraction, analysis, ontogeny, rectification. Macquarie University, Sydney [PhD Thesis]
- Stockley JK, Chan C-H & Williams LR.** (1999) The antimicrobial activity of cloned tea tree oils. *Cosmetics Aerosols and Toiletries in Australia* **12(4)**: 14-18 [Research article] No abstract.
- Subramanian R, Saelih H, Lea KE, Ismail R.** (2002) Antispasmodic action of tea tree oil compared to atropine on isolated rabbit ileum. *Federation of American Societies for Experimental Biology (FASEB) JOURNAL* **16**: A388. [Conference abstract]
- Sutton BG, Virtue J & Murtagh J.** (1997) Towards non-chemical control of weeds in tea trees. RIRDC project US-20A, RIRDC publication R97/063, 98pp. [Government publication]
- Swords G & Hunter GLK.** (1978) Composition of Australian tea tree oil (*Melaleuca alternifolia*). *Journal of Agricultural and Food Chemistry* **26**: 734-737. [Research article] [Abstract](#)
- Syed TA, Qureshi ZA, Ali SM, Ahmad S & Ahmad SA.** (1999) Treatment of toenail onychomycosis with 2% butenafine and 5% *Melaleuca alternifolia* (tea tree) oil in cream. *Tropical Medicine & International Health* **4**: 284-287. [Research article] [Abstract](#) | [Full text \(PDF\)](#)  
*Reproduced with permission from Blackwell Publishers*
- Takahashi N, Kida A, Ishizuka Y, Hiraishi M.** (2002) Aromatic oil inhalation the reduction of pain after tonsillectomy [Japanese]. *Oto-Rhino-Laryngology Tokyo* **45 (suppl 1)**: 5-7 [Research article]
- Taylor R.** (1996). Tea tree - boosting oil production. *Rural Research* **172**: 17-18. [News]
- Thomson KF & Wilkinson SM.** (2000) Allergic contact dermatitis to plant extracts in patients with cosmetic dermatitis. *British Journal of Dermatology* **142**: 84-88. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Tisserand R.** (1988) Australian tea tree oil. *International Journal of Aromatherapy* **1**: 6-7. [Review] No abstract.
- Tong MM, Altman PM & Barnetson RStC.** (1992) Tea tree oil in the treatment of tinea pedis. *Australasian Journal of Dermatology* **33**: 145-9. [Research article] [Abstract](#) | [Full text \(PDF\)](#)  
*Reproduced with permission from Blackwell Publishers*
- Trueby ME.** (2001) Teatree water in small animal veterinary practice - experiences and case reports. [German] *Ganzheitliche Tiermedizin* **15**: 76-79. [Research article]
- Treudler R, Richter G, Geier J, Schnuch A, Orfanos CE & Tebbe B.** (2000) Increase in sensitization to oil of turpentine: recent data from a multicenter study on 45,005 patients from the German-Austrian Information Network of Departments of Dermatology (IVDK). *Contact Dermatitis* **42**: 68-73. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Tyrrell R & Robinson C.** (2000) Are we losing the fight against infection? *The Foot* **10**: 90-96. [Review]
- van der Valk PG, de Groot AC, Bruynzeel DP, Coenraads PJ & Weijland JW.** (1994) Allergic contact eczema due to 'tea tree' oil [Dutch]. *Nederlands Tijdschrift voor Geneeskunde* **138**: 823-825. [Case report]
- Varma S, Blackford S, Statham BN & Blackwell A.** (1999) Tea tree oil and lavender oil allergy masquerading as chronic vulvovaginitis. *Journal of the European Academy of Dermatology and Venereology* **12 (Suppl 2)**: S192-S193. [Conference abstract] | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Varma S, Blackford S, Statham BN & Blackwell A.** (2000) Combined contact allergy to tea tree oil and lavender oil complicating chronic vulvovaginitis. *Contact Dermatitis* **42**: 309-310. [Case report] | [Full text \(PDF\)](#) *Reproduced with permission from Blackwell Publishers*
- Vass A.** (2001) Website of the week: headlice. *British Medical Journal* **323**: 1136. [News]
- Vazquez JA, Arganoza MT, Boikov D, Vaishampayan JK & Akins RA.** (2000) In vitro susceptibilities of *Candida* and *Aspergillus* species to *Melaleuca alternifolia* (tea tree) oil. *Revista*

- Iberoamericana de Micologia* **17**: 60-63. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission*
- Vazquez JA.** (1999) Options for the management of mucosal candidiasis in patients with AIDS and HIV infection. *Pharmacotherapy* **19**: 76-87. [Review] [View abstract in Pubmed](#)
- Vazquez JA & Zawawi AA.** (2002) Efficacy of alcohol-based and alcohol-free melaleuca oral solution for the treatment of fluconazole-refractory oral candidiasis in patients with AIDS. *AIDS* **12**: 1033-1037. [Research article] [View abstract in Pubmed](#)
- Veal L.** (1996) The potential effectiveness of essential oils as a treatment for headlice, *Pediculus humanus capitis*. *Complementary Therapies in Nursing & Midwifery* **2**: 97-101. [Research article] [View abstract in Pubmed](#)
- Verghese J, Jacob CV, Kartha CVK, McCarron M, Mills Allan J & Whittaker D.** (1996) Indian tea tree (*Melaleuca alternifolia* Cheel) essential oil. *Flavour & Fragrance Journal* **11**: 219-221. [Research article]
- Villar D, Knight MJ, Hansen SR & Buck WB.** (1994) Toxicity of melaleuca oil and related essential oils applied topically on dogs and cats. *Veterinary & Human Toxicology* **36**: 139-142. [Review] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission*
- Viollon C, Leger D & Chaumont JP.** (1993) In vitro antagonistic activities of some natural volatile compounds towards microorganisms of the vaginal flora [French]. *Plantes médicinales et phytothérapie* **26**: 17-22.
- Viollon C, Mandin D & Chaumont JP.** (1996) Antagonistic activity, in vitro, of several essential oils and constituent volatile compounds against the growth of *Trichomonas vaginalis* [French]. *Fitoterapia* **63**: 279-281.
- Virtue JG.** (1997) Weed interference in the annual regrowth cycle of plantation tea tree (*Melaleuca alternifolia*). The University of Sydney. [PhD Thesis]
- Virtue JG, Sutton BG, Murtagh GJ & Cousens RD.** (2000) Weed interference reduces yield of coppiced tea tree (*Melaleuca alternifolia*). *Australian Journal of Experimental Agriculture* **40**: 1157-1164. [Research article] [Abstract](#)
- Wabner D.** (2002) The peroxide value – a new tool for the quality control of essential oils. *The International Journal of Aromatherapy* **12**: 142-144. [Research article] No abstract.
- Walker M.** (1972) Clinical investigation of Australian *Melaleuca alternifolia* oil for a variety of common foot problems. *Current Podiatry* **1972**: 7-15 [Research article] No abstract.
- Walsh LJ & Longstaff J.** (1987) The antimicrobial effects of an essential oil on selected oral pathogens. *Periodontology* **8**: 11-15. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission.*
- Walsh N.** (2002) Tea tree oil for infections. *Internal Medicine News* **35**: 16. [Letter] No abstract. *Same article also published in eFamily Practice News* **32**: 13. [Free full text at journal webpage](#)
- Walton SF, Myerscough MR & Currie BJ.** (2000) Studies in vitro on the relative efficacy of current acaricides for *Sarcoptes scabiei* var. *hominis*. *Transactions of the Royal Society of Tropical Medicine & Hygiene* **94**: 92-96. [Research article] [View abstract in Pubmed](#)
- Washington WS, Engleitner S & MacFarlane J.** (1989) Effect of fungicides and biological treatments on the control of two-spotted mite of strawberry. *Fungicide and Nematicide Tests* **46**: 106. [Research note]
- Washington WS, Engleitner S, Boontjes G & Shanmuganathan N.** (1999) Effect of fungicides, seaweed extracts, tea tree oil, and fungal agents on fruit rot and yield in strawberry. *Australian Journal of Experimental Agriculture* **39**: 487-494. [Research article] [Abstract](#)
- Weseler A, Geiss HK, Saller R & Reichling J.** (2002) Antifungal effect of Australian tea tree oil on *Malassezia pachydermatis* isolated from canines suffering from cutaneous skin disease. *Schweizer Archiv Fuer Tierheilkunde* **144**: 215-221. [Research article] [View abstract in Pubmed](#)
- West C.** (1998) Australian tea tree oil: first aid for animals. Kali Press, Pagosa Springs, Colorado USA. ASIN: 0962888273 (160 pages) [Book]
- Whish, JPM.** (1996) Improving tea tree oil production: technology, plant selection and propagation. University of New England [Masters Rur. Sci. Thesis]

- Whish JPM & Williams RR.** (1996) Effects of post harvest drying on the yield of tea tree oil (*Melaleuca alternifolia*). *Journal of Essential Oil Research* **9**: 47-51. [Research article]
- Wilkinson JM, Hipwell M, Ryan T, Cavanagh HM.** (2003) Bioactivity of *Backhousia citriodora*: antibacterial and antifungal activity. *Journal of Agriculture and Food Chemistry* **51**: 76-81. [Research article] [Abstract](#)
- Williams LR.** (1995) Selection and breeding of superior plants of *Melaleuca* to increase the production and antimicrobial activity of tea tree oil. Proceedings of 13th international congress of flavours, fragrances and essential oils, Istanbul, Turkey, 15-19 October, pp. 408-417. [Conference paper]
- Williams LR.** (1998) Clonal production of tea tree oil high in terpinen-4-ol for use in formulations for the treatment of thrush. *Complementary Therapies in Nursing & Midwifery* **4**: 133-136. [Review] [View abstract in Pubmed](#)
- Williams LR, Asre S & Home V.** (1994) Topical applications containing tea tree oil for vaginal conditions. *Cosmetics, Aerosols and Toiletries in Australia*. **8**: 23-26. [Research article]
- Williams LR & Home VN.** (1988) Plantation production of oil of melaleuca (tea tree oil) - a revitalised Australian essential oil industry. *Search* **19**: 294-297. [Research article] [Full text \(PDF\)](#) *This article is reproduced from Search, which is now published as Australasian Science [www.control.com.au](http://www.control.com.au)*
- Williams LR & Home VN.** (1989) Plantations of *Melaleuca alternifolia* - a revitalized Australian tea tree oil industry. Proceedings of the 11th International Congress of Essential Oils, Fragrances and Flavours. New Delhi, India, 12-16 November. pp. 49-53, Aspect Publishing, London, UK: 1990. 49-53. [Conference paper]
- Williams LR & Home VN.** (1995). A comparative study of some essential oils for potential use in topical applications for the treatment of the yeast *Candida albicans*. *Australian Journal of Medical Herbalism* **7**: 57-62. [Research article] [Full text \(PDF\)](#) *Reproduced with permission from the Australian Journal of Medical Herbalism and the Herbalists Association of Australia.*
- Williams LR & Home VN.** (1995) Factors determining the quality of tea tree oil in formulations for clinical use. *Cosmetics, Aerosols and Toiletries in Australia* **9**: 14-18, 24. [Research article] No abstract.
- Williams LR, Home V & Asre S.** (1990) Antimicrobial activity of oil of Melaleuca (tea tree oil): It's potential use in cosmetics and toiletries. *Cosmetics, Aerosols and Toiletries in Australia*. **4**: 12-13, 16-18,22. [Research article] No abstract.
- Williams LR, Home V & Asre S.** (1990) Oils of *Melaleuca alternifolia*, their antifungal activity against *Candida albicans* in perspective. *International Journal of Aromatherapy* **2**: 12-13 [Research article] No abstract.
- Williams LR, Home VN & Lusunzi I.** (1993) An evaluation of the contribution of cineole and terpinen-4-ol to the overall antimicrobial activity of tea tree oil. *Cosmetics, Aerosols and Toiletries in Australia* **7**: 25-28, 34. [Research article] No abstract.
- Williams LR, Home VN, Zhang X & Stevensen I.** (1988) The composition and bactericidal activity of oil of *Melaleuca alternifolia* (tea tree oil). *International Journal of Aromatherapy* **1**: 15-17. [Research article] No abstract.
- Williams LR & Lusunzi I.** (1992) Essential oil from *Melaleuca dissitiflora*: a potential source of high quality tea tree oil. *Industrial Crops & Products* **2** : 211-217. [Research article]
- Williams LR, Stockley JK, Home VN & Wang Y.** (1997) Therapeutic use for tea tree oil. *Australian Journal of Pharmacy* **78**: 285-287. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission.*
- Wilson CL, Solar JM, El Ghaouth A & Wisniewski ME.** (1997) Rapid evaluation of plant extracts and essential oils for antifungal activity against *Botrytis cinerea*. *Plant Disease* **81**: 204-210. [Research article] [Abstract](#)
- Winters J.** (1986) Breakthrough: Tea tree oil, in search of an Australian legend. Vinton Publishing, Las Vegas NV, USA. ISBN 1885026-01-3 (65 pages) [Book]
- Wolf J.** (1996) Tea tree oil [German]. *Pharmazie* **45**: 61. [Letter]

- Wolner-Hanssen P & Sjoberg I.** (1998) Warning against a fashionable cure for vulvovaginitis - tea tree oil may substitute *Candida* itching with allergy itching [Swedish]. *Lakartidningen* **95**: 3309-3310. [Case report]
- Wong V, Wyllie SG, Cornwell CP & Tronson D.** (2001) Supercritical fluid extraction (SFE) of monoterpenes from the leaves of *Melaleuca alternifolia* (tea tree). *Molecules* **6**: 92-103. [Research article] [Abstract](#) | [Full text \(PDF\)](#) *Reproduced with permission.*
- Woolf A.** (1999) Essential oil poisoning. *Journal of Toxicology Clinical Toxicology* **37**: 721-727. [Review] No abstract.
- Wooltorton E.** (2003) Concerns over lindane treatment for scabies and lice. *CMAJ Canadian Medical Association Journal* **168(11)**: 1447-1448. [News]
- Wu W-J & Wang P.** (2002) The chemical components of three *Melaleuca* oils [Chinese]. *Acta Botanica Yunnanica* **24**: 133-136. [Research article]
- Xiaoqi Z, Xiong L, Yian L.** (2002) Preliminary studies on quality standards of main ingredients of tea tree oil products of *Melaleuca alternifolia* in Guangdong. *Guangdong Chemical Industry* **29(6)**: 12-16. [Research article] No abstract.
- Xu Yingbao Ling S & Gan W.** (1997) A preliminary report on introduction adaptability and cultivation trials of *Melaleuca alternifolia*. *Forest Research* **10**: 383-388. [Research article]
- Zabaras D, Spooner-Hart RN & Wyllie SG.** (2002) Effects of mechanical wounding on concentration and composition of essential oil from *Melaleuca alternifolia* leaves. *Biochemical Systematics & Ecology* **30**: 399-412. [Research article] [View abstract in Pubmed](#)
- Zabaras D & Wyllie SG.** (2001) Quantitative analysis of terpenoids in the gas phase using headspace solid-phase microextraction (HS-SPME). *Flavour & Fragrance Journal* **16**: 411-416. [Research article]
- Zhang SY & Robertson D.** (2000) A study of tea tree oil ototoxicity. *Audiology & Neuro Otology* **5**: 64-68. [Research article] [View abstract in Pubmed](#)
- Zhang X, Liang G-L, Yan Y, Yu Y, Yang G-W, Yang T-X.** (2000) Rapid propagation and polyploidy induction in *Melaleuca alternifolia* [Chinese]. *Journal of Southwest Agricultural University* **22**: 507-509. [Research article] [View abstract in Pubmed](#)

## **Appendix 2 – Responses of publishers to permission requests**

| Full Journal Title  | Publisher   | Response of publisher to permission request                   |
|---|---|---|
| Yakugaku Zasshi   | Pharmaceutical Society of Japan                                   | Abstract and figures granted                                  |
| New forests   | Kluwer Academic Publishers  | Abstract only granted   |
| Annales de Dermatologie et Venerologie                            | SPPIF – Masson Service  | Abstract only granted   |
| Journal of the American Podiatric Medical Association             | American Podiatric Medical Association                            | Abstract only granted   |
| Journal of Chemical Ecology                                       | Kluwer Academic Publishers  | Abstract only granted   |
| Journal of Dental Research  | International Association of Dental Research                      | Abstract only granted   |
| Acta Horticulturae  | International Society for Horticultural Sciences                  | Abstract only granted   |
| Australian Journal of Experimental Agriculture & Animal Husbandry | CSIRO Publishing  | Abstract only granted   |
| Australian Journal of Agricultural Research                       | CSIRO Publishing  | Abstract only granted   |
| Australian journal of botany                                      | CSIRO Publishing  | Abstract only granted   |
| Australian journal of Experimental Agriculture                    | CSIRO Publishing  | Abstract only granted   |
| Archiv fur Hydrobiologie  | E. Schweizerbart'sche Verlagsbuchhandlung                         | Abstract only granted   |
| Fungicide and Nematicide tests                                    | American Phytopathological Society Press                          | Abstract only granted   |
| Phytopathology  | American Phytopathological Society Press                          | Abstract only granted   |
| Plant Disease   | American Phytopathological Society Press                          | Abstract only granted   |
| Antimicrobial Agents and Chemotherapy                             | American Society for Microbiology                                 | Abstract only granted   |
| Perfusion   | Arnold Publishers   | Abstract only granted   |
| American Journal of Contact Dermatitis                            | BC Decker   | Abstracts only granted  |
| Journal of Family Practice  | Dowden Health Media   | Abstracts only granted  |
| Perfumer and Flavourist   | Allured Publishing Corp.  | Abstracts only granted  |
| Journal of Essential Oil Research                                 | Allured Publishing Corp.  | Abstracts only granted  |
| Journal of Medical & Veterinary Mycology                          | Taylor and Francis  | Abstracts only granted  |
| Journal of Agricultural and Food Chemistry                        | American Chemical Society   | Abstracts, figures, tables, bibliographic information granted |
| Langmuir  | American Chemical Society   | Abstracts, figures, tables, bibliography granted              |
| EFamily Practice News   | <b>Contact:</b> J. Sheffer  | Denied  |
| Business Review Weekly  | Fairfax   | Denied  |
| Plant Systematics and Evolution                                   | Springer  | Denied  |
| Journal of Nihon School of Dentistry                              | Contact: M. Nomura  | Denied  |
| Journal of Antimicrobial Chemotherapy                             | Oxford University Press   | Fee payable   |
| New Zealand Pharmacy  | Methode Media   | Fee payable (\$200 NZ article)                                |
| Acta Dermato Venereologica  | Taylor & Francis Health Sciences                                  | Fee payable (\$250 USD/article)                               |
| Hautarzt  | Springer  | Fee payable (~\$1561 AUD/ article)                            |
| Support Care Cancer   | Springer  | Fee payable (~\$1561 AUD/article)                             |
| Theoretical and Applied Genetics                                  | Springer  | Fee payable (~\$1561 AUD/article)                             |
| Oecologia   | Springer Verlag AG  | Fee payable (~\$1561 AUD/article)                             |
| British Medical Journal   | BMJ Group   | Fee payable (~\$180 AUD/ article)                             |
| Skin Pharmacology   | Karger  | Fee payable (~\$266 AUD/ article)                             |
| Audiology & Neuro Otology   | Karger  | Fee payable (~\$266 AUD/article)                              |
| Journal of Chemotherapy   | <a href="http://www.jchemother.it/">http://www.jchemother.it/</a> | Fee payable (\$200 US/ article)                               |

| Full Journal Title  | Publisher                                    | Response of publisher to permission request                      |
|---|--|--|
| American Journal of Clinical Dermatology AND Adverse Drug Reactions & Toxicological Reviews | ADIS   | Fee payable (US\$1000/ article or \$500/ abstract (1 year only)) |
| Am J Alzheimers Dis Other Dement  | Prime National Publishing Corporation        | Fee payable for full text, abstract granted                      |
| Phytotherapy  | Urban and Fischer                            | Full text (Saller); abstract only (McCage) granted               |
| Archives of Dermatology   | Contact: R. Bailey                           | Full text denied, abstracts \$150 USD each                       |
| The Bulletin  | Contact: M. Cameron                          | Full text granted  |
| Search  | Control Publications                         | Full text granted  |
| Chemistry In Australia  | Contact: H Hugel                             | Full text granted  |
| Aroma Research  | Contact: R. Kimura                           | Full text granted  |
| Veterinary and Human Toxicology   | Contact: Prof Fred Oehme                     | Full text granted  |
| Molecules   | Contact: Dr Shu-Kun Lin                      | Full text granted  |
| Medical Journal of Australia  | Australasian Medical Publishing Company      | Full text granted  |
| Journal of Tropical Agriculture & Food Science  | Malaysian Agriculture R&D Institute          | Full text granted  |
| Alternative and Complementary Therapies   | Mary Ann Liebert Inc Publications            | Full text granted  |
| Int. Journal of Alternative & Complementary Medicine.                                       | Mary Ann Liebert Inc Publications            | Full text granted  |
| American Bee Journal  | Dadant & Sons Inc.                           | Full text granted  |
| International Dental Journal  | FDI World Dental Press, Ltd                  | Full text granted  |
| The Progressive Fish-Culturist  | Allen Press                                  | Full text granted  |
| Austrian Journal of Pharmacy  | Austrian Pharmaceutical Publishing Co. Ltd   | Full text granted  |
| Journal of Veterinary Diagnostic Investigation  | Contact: J Kreeger                           | Full text granted  |
| The Australian Journal of Hospital Pharmacy   | Revista Iberoamericana de Micologia          | Full text granted  |
| Revista Iberoamericana de Micologia   | Contact: B. Taylor                           | Full text granted  |
| Periodontology  | Institute of Foresters of Australia          | Full text granted  |
| Austrian Forestry   | Pharmaceutical Soc. of Australia             | Full text granted  |
| Austrian Pharmacist   | Sevak Publications                           | Full text granted  |
| Chemical Weekly   | Wilmington Publications                      | Full text granted  |
| Manufacturing Chemist   | Tekno Scienze sr, Italy                      | Full text granted  |
| Agro-Food-Industry Hi – Tech  | Contact: P. Francis                          | Full text granted  |
| Austrian Farm Journal   | National Herbalists Association of Australia | Full text granted  |
| Austrian Journal of Medical Herbalism   | Luciano de Fiore                             | Full text granted  |
| Aromatherapy today  | California Agriculture                       | Full text granted  |
| Acta Phytotherapeutica  | Govi Verlag                                  | Full text granted  |
| Annali italiani di Dermatologia allergologica   | Govi Verlag                                  | Full text granted  |
| Austrobaileya   | Blackwell                                    | Full text granted  |
| California Agriculture  | Pharmaceutical Press, London,                | Full text granted  |
| Pz Prisma   |  |  |
| Pharmazie (die Pharmazie)   |  |  |
| Australasian Journal of Experimental Biology and Medicine                                   |  |  |
| Journal of the National Medical Association   |  |  |
| Journal of Pharmacy and Pharmacology  |  |  |

| Full Journal Title   | Publisher  | Response of publisher to permission request |
|--|--|---|
| Journal of the Science of Food and Agriculture                 | Blackwell  | Full text granted                           |
| Veterinary Dermatology   | Blackwell  | Full text granted                           |
| Clinical and Experimental Dermatology                          | Blackwell  | Full text granted                           |
| Australasian Journal of Dermatology                            | Blackwell  | Full text granted                           |
| Contact Dermatitis   | Blackwell  | Full text granted                           |
| Dermatologic Therapy   | Blackwell  | Full text granted                           |
| Immunology   | Blackwell  | Full text granted                           |
| Journal of Applied Microbiology                                | Blackwell  | Full text granted                           |
| Journal of the European Academy of Dermatology and Venereology | Blackwell  | Full text granted                           |
| Letters in Applied Microbiology                                | Blackwell  | Full text granted                           |
| Mycoses  | Blackwell  | Full text granted                           |
| Oral Microbiology & Immunology                                 | Blackwell  | Full text granted                           |
| Tropical Medicine & International Health                       | Blackwell  | Full text granted                           |
| Molecular Ecology  | Blackwell  | Full text granted                           |
| British Journal of Dermatology                                 | Blackwell  | Full text granted                           |
| Aquaculture Research   | Blackwell  | Full text granted                           |
| Australian Journal of Biotechnology                            | Australian Biotechnology Association   | Full text granted (from author)             |
| The Foot   | Harcourt   | No response                                 |
| Allergo Journal  | Urban and Vogel  | No response                                 |
| Medycyna sportowa  | <a href="http://www.medsport.pl/">http://www.medsport.pl/</a> (publishers website) | No response                                 |
| Nursing times  |  | No response                                 |
| Ganzheitliche Tiermedizin                                      |  | No response                                 |
| Inflammation research  |  | No response                                 |
| Mikologia lekarska   |  | No response                                 |
| Perfumery and Essential oil records                            |  | No response                                 |
| Acta Botanica Sinica   |  | No response                                 |
| Grand Rounds   |  | No response                                 |
| HRC Journal of High Resolution Chromatography                  |  | No response                                 |
| Canadian Pharmaceutical Journal                                | Wiley  | No response                                 |
| British Journal of Phytotherapy                                | Canadian Pharmacists Association   | No response                                 |
| Soap Perfumery and cosmetics                                   | School of Phytotherapy, East Sussex  | No response                                 |
| Schweizer Archiv für Tierheilkunde                             | Wilmington Publications  | No response                                 |
| Microbiology and Immunology                                    | VERLAG HANS HUBER AG   | No response                                 |
| Journal of British Podiatric Medicine                          | Centre for Academic Publishing, Japan  | No response                                 |
| Advances in Food Science                                       | Soc. of Chiropractists & Podiatrists, UK   | No response                                 |
| Journal of the American Holistic Veterinary Association        | AFS  | No response                                 |
| Cosmetics and Toiletries Manufacture Worldwide                 | American Holistic Veterinary Medical Assoc.  | No response                                 |
| Phytochemistry   | Aston Publishing   | No response                                 |
| Antiviral Research   | Elsevier   | No response                                 |
| BioMed Central Surgery   | Elsevier   | No response                                 |
|  | Birkhäuser Publishing Ltd.   |   |
|  | Science publications   |   |

| Full Journal Title   | Publisher                                    | Response of publisher to permission request |
|--|--|---|
| ESkin and Allergy News   | Elsevier                                     | No response                                 |
| European Journal of Pharmacology                                 | Elsevier                                     | No response                                 |
| Lancet   | Elsevier                                     | No response                                 |
| Obstetrics and Gynecology  | Elsevier                                     | No response                                 |
| Thrombocytosis Acta  | Elsevier                                     | No response                                 |
| Industrial Crops & Products                                      | Elsevier                                     | No response                                 |
| Biochemical Systematics and Ecology                              | Elsevier                                     | No response                                 |
| Plant Science  | Elsevier                                     | No response                                 |
| Fitoterapia  | Elsevier                                     | No response                                 |
| Journal of Microbiological Methods                               | Elsevier                                     | No response                                 |
| Journal of Chromatography A                                      | Elsevier                                     | No response                                 |
| Journal of Hospital Infection                                    | Elsevier                                     | No response                                 |
| Burns  | Elsevier                                     | No response                                 |
| Clinics in Dermatology   | Elsevier                                     | No response                                 |
| American Journal of Infection Control                            | Elsevier                                     | No response                                 |
| Toxicology   | Elsevier                                     | No response                                 |
| Clinics in Podiatric Medicine and Surgery                        | Elsevier                                     | No response                                 |
| Complementary Therapies in Nursing & Midwifery                   | Elsevier                                     | No response                                 |
| The Foot   | Elsevier                                     | No response                                 |
| Journal of Allergy and Clinical Immunology                       | Elsevier                                     | No response                                 |
| Journal of the American Academy of Dermatology                   | Elsevier                                     | No response                                 |
| Food and Chemical Toxicology                                     | Elsevier                                     | No response                                 |
| Seminars in Cutaneous Medicine and Surgery                       | Elsevier                                     | No response                                 |
| Journal of Manipulative and Physiological Therapies              | Elsevier                                     | No response                                 |
| Complementary Therapies in Medicine                              | Elsevier                                     | No response                                 |
| International Journal of Aromatherapy                            | Elsevier                                     | No response                                 |
| FASEB Journal  | Elsevier                                     | No response                                 |
| Aktuelle Dermatologie  | Fed. American Soc. of Experimental Biology   | No response                                 |
| Planta Medica  | Georg Thieme Verlag                          | No response                                 |
| Water Science and Technology                                     | Georg Thieme Verlag                          | No response                                 |
| Forschende Komplementärmedizin und Klassische Naturheilkunde     | IWA publishing                               | No response                                 |
| AIDS   | Karger                                       | No response                                 |
| Journal of Endodontics   | Lippincott Williams & Wilkins                | No response                                 |
| Cosmetics Aerosols and Toilettries in Australia                  | Lippincott Williams & Wilkins                | No response                                 |
| Journal of Toxicology – Clinical Toxicology                      | Manor Enterprises P/L                        | No response                                 |
| Asthma and Allergy Proceedings                                   | Marcel Dekker, Inc.                          | No response                                 |
| Revista Iberoamericana de Micología                              | OceanSide Publications, Inc                  | No response                                 |
| Transactions of the Royal Society of Tropical Medicine & Hygiene | Revista Iberoamericana de Micología          | No response                                 |
| Podiatry Now   | Royal Society of Tropical Medicine & Hygiene | No response                                 |
| British Journal of Biomedical Science                            | Soc. Chiropractists & Podiatrists, UK        | No response                                 |
|  | Step Publishing Ltd, UK                      | No response                                 |

| <b>Full Journal Title</b>                                    | <b>Publisher</b>                              | <b>Response of publisher to permission request</b> |
|--|---|--|
| Occupational Health and Safety                               | Stevens Publishing Corp., USA                 | No response  |
| Pathology  | Taylor & Francis Health Sciences              | No response  |
| Phytotherapy Research  | Wiley   | No response  |
| Flavour and Fragrance Journal                                | Wiley   | No response  |
| Journal of Separation Science                                | Wiley   | No response  |
| Acta Botanica Yunnanica                                      | (Not found)                                   | Not contacted                                      |
| Bulletin from SADRAC   | Swedish Medical Products Agency, Sweden       | Not contacted                                      |
| Current Podiatry   | (Not found)                                   | Not contacted                                      |
| Dermatosen   | (Not found)                                   | Not contacted                                      |
| Deutsche Lebensmittelrundschau                               | Wissenschaftliche Verlagsgesellschaft MBH     | Not contacted                                      |
| Eurocosmetics  | Inter-Euro Medien GmbH                        | Not contacted                                      |
| Forest Research  | (Not found)                                   | Not contacted                                      |
| Journal of Southwest Agricultural University                 | (Not found)                                   | Not contacted                                      |
| La Difesa delle Piante                                       | (Not found)                                   | Not contacted                                      |
| Microbios  | Faculty Press                                 | Not contacted                                      |
| Nederlands Tijdschrift voor Geneeskunde                      | Kluwer Academic Publishers                    | Not contacted                                      |
| Oto-Rhino-Laryngology Tokyo                                  | (Not found)                                   | Not contacted                                      |
| Phytotherapy   | (Not found)                                   | Not contacted                                      |
| Plantes médicinales et phytothérapie                         | (Not found)                                   | Not contacted                                      |
| Postepy Fitoterapii  | (Not found)                                   | Not contacted                                      |
| Progress in Essential oil research                           | (Not found)                                   | Not contacted                                      |
| Schweizer Monatsschrift für Zahnmedizin                      | Offizielles organ der Schweizerischen         | Not contacted                                      |
| SOFW journal   | Jahresbezugspreis Inland DM                   | Not contacted                                      |
| Swedish Journal of Biological Medicine                       | (Not found)                                   | Not contacted                                      |
| The Lower Extremity  | (Not found)                                   | Not contacted                                      |
| Deutsche Apotheker Zeitung,                                  | (Not found)                                   | Not contacted                                      |
| Fortschritte der Medizin,                                    | (Not found)                                   | Not contacted                                      |
| Guangdong Chemical Industry,                                 | (Not found)                                   | Not contacted                                      |
| Lakartidningen,  | (Not found)                                   | Not contacted                                      |
| Parfümerie und Kosmetik,                                     | (Not found)                                   | Not contacted                                      |
| Tw Dermatologie,   | (Not found)                                   | Not contacted                                      |
| Ugeskrift for Laeger   | (Not found)                                   | Not contacted                                      |
| Zeitschrift für Hautkrankheiten,                             | (Not found)                                   | Not contacted                                      |
| Zeitschrift für Phytotherapie,                               | (Not found)                                   | Not contacted                                      |
| Österreichischen Apotheker-Zeitung                           | (Not found)                                   | Not contacted                                      |
| Hospital and Healthcare                                      | Yaffa publishing                              | Not contacted (Copyright belongs to each author)   |
| Nature and Health  | Yaffa Publishing                              | Not contacted (Copyright belongs to each author)   |
| Journal of Food Protection                                   | International Association for Food Protection | Undecided  |
| Journal and Proceedings of the Royal Soc. of New South Wales | Royal Society of New South Wales              | Undecided  |

# Appendix 3 – Material Safety Data Sheet

**NOTE:**

- 1) Do not photocopy this MSDS.
- 2) The document in its original format can be obtained from ATTIA.

# MATERIAL SAFETY DATA SHEET

Classified as hazardous according to the criteria of NOHSC Australia

## 1. IDENTIFICATION

**Name:** Tea tree oil  
**Other names:** melaleuca oil, *Melaleuca alternifolia* oil, T36-C7, teebaumol  
**Recommended use:** Topical antibacterial agent, antiseptic, anti-inflammatory agent  
**SUSDP name:** Melaleuca oil (tea-tree oil)  
**Supplier name:** (Manufacturer to complete)  
**Street address:** (Manufacturer to complete)  
**Telephone:** (Manufacturer to complete)  
**Emergency contact:** (Manufacturer to complete)

## 2. HAZARDS IDENTIFICATION

**Hazard classification:** Classified as Hazardous according to the criteria of NOHSC Australia.  
Classified as Dangerous Goods for the purpose of transport by road or rail.

**Risk phrases:** R10 Flammable  
R22 Harmful if swallowed  
R36/37/38 Irritating to eyes, respiratory system and skin

**Safety phrases:** S26 In case of contact with eyes, rinse immediately with plenty of water and contact a doctor or Poisons Information Centre (13 11 26, Australia wide).  
S36 Wear suitable protective clothing

**HAG phrases:** (9) Form: liquid (62) Avoid personal/skin contact  
(15) Flammable (83) Fire fighting: foam  
(18) Combustible (85) Fire fighting: dry agent  
(51) Does not mix with water

**RTECS number** RJ3697600

## 3. COMPOSITION

**Chemical identity:** Melaleuca oil (tea-tree oil)  
**Common names:** melaleuca oil, *Melaleuca alternifolia* oil, T36-C7, teebaumol, Tea tree (melaleuca alternifolia) oil  
**CAS#:** 68647-73-4, 85085-48-9, 8022-72-8

## 4. FIRST AID MEASURES

Poison Information Centres can provide additional assistance on 13 11 26 (Australia wide).

**Eye:** Irrigate with copious amounts of water. Seek immediate medical attention.

**Inhalation:** If over-exposure occurs leave exposure area immediately. If other than minor symptoms are displayed seek immediate medical attention.

**Skin:** Gently flush affected areas with water. Remove contaminated clothing and wash thoroughly before re-use. Seek medical attention if irritation develops.

**Ingestion:** If swallowed do NOT induce vomiting. Give a glass of water. Seek immediate medical attention.

**Facilities:** Eye wash facilities and safety shower are recommended.

## 5. FIRE FIGHTING MEASURES

**Suitable extinguishing media:** Dry agent, carbon dioxide, foam or water fog. Do not use full water jet.

**Hazards from combustion products:** May evolve toxic gases (hydrocarbons, carbon oxides) if burning.

**Precautions and special protective equipment:** Evacuate area and contact emergency services. Remain upwind and notify those downwind of hazard. Wear full protective equipment including Self Contained Breathing Apparatus when combating fire. Use waterfog to cool intact containers and nearby storage areas.

**Hazchem code:** 3[Y]

# MATERIAL SAFETY DATA SHEET

## 6. ACCIDENTAL RELEASE MEASURES

**Spillage:** In case of spillage (bulk), wear splash-proof goggles, PVC/rubber gloves, coveralls and rubber boots (see section 8). Keep people away, evacuate area.

**Containment and clean up:** Absorb spill with sand or similar, collect and place in sealable containers using non-sparking tools and transport outdoors for disposal. Ventilate area and wash spill site after material pick-up is complete. Prevent spill from entering drains or waterways. Caution: slippery when spilt.

## 7. HANDLING AND STORAGE

**Handling:** Measures should be taken to prevent materials from being splashed into the eyes or on the skin. Wear eye-shields and protective clothing. Smoking should not be permitted in work areas. Provide adequate ventilation.

**Storage:** Store in a cool, dry, well-ventilated area, away from oxidising agents (eg hypochlorites), acids (eg sulfuric acid), heat and light sources, and foodstuffs. Ensure containers are adequately labelled, protected from physical damage and sealed when not in use. Keep only in original container. Check regularly for leaks or spills. Large storage areas should have appropriate ventilation systems. This material is a Scheduled Poison (S6) and must be stored, maintained and used in accordance with the relevant regulations.

## 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

**National exposure standards:** No exposure standard allocated

**Biological limits:** No biological limit allocated

**Engineering controls:** Ensure adequate ventilation. In poorly ventilated areas, mechanical explosion-proof extraction ventilation is recommended. Keep containers closed when not in use.

**PPE:** Wear coveralls, splash-proof goggles and PVC or rubber gloves. Where an inhalation risk exists, wear a Type A (organic vapour) Respirator. In a laboratory situation, wear a laboratory coat.

## 9. PHYSICAL AND CHEMICAL PROPERTIES

**Appearance:** Colourless to pale yellow liquid

**Odour:** Characteristic, myristic

**Solubility:** Insoluble in water, 1 part miscible with 2 parts ethanol (85% v/v) at 20°C.

|                                      |                                   |
|--------------------------------------|-----------------------------------|
| <b>pH:</b>                           | Not applicable                    |
| <b>Vapour pressure:</b>              | Not available                     |
| <b>Vapour density:</b>               | Not available                     |
| <b>Boiling point/range:</b>          | 116° – 265°C                      |
| <b>Freezing point:</b>               | Not available                     |
| <b>Specific density:</b>             | 0.885 - 0.906 at 20°C.            |
| <b>Flash point:</b>                  | 57° - 60°C (closed cup)           |
| <b>Fire point:</b>                   | 72°C (Cleveland open cup (IP 36)) |
| <b>Upper flammable limit in air:</b> | Not available                     |
| <b>Lower flammable limit in air:</b> | Not available                     |
| <b>Ignition temperature:</b>         | Not available                     |
| <b>Specific heat value:</b>          | Not available                     |
| <b>Percent volatile:</b>             | 100%                              |
| <b>Refractive index:</b>             | 1,475 0 – 1,482 0 at 20°C.        |
| <b>Optical rotation:</b>             | Between +5° and +15° at 20°C.     |

## 10. STABILITY AND REACTIVITY

**Chemical stability:** Stable

**Conditions to avoid:** Heat, light, open flames and other sources of ignition

**Incompatible materials:** Strong oxidising or reducing agents. Protect from air.

**Hazardous decomposition products:** Carbon monoxide and carbon dioxide (from combustion).

**Hazardous reactions:** Hazardous polymerisation will not occur.

# MATERIAL SAFETY DATA SHEET

## 11. TOXICOLOGICAL INFORMATION

### ACUTE EFFECTS

**Eye contact:** Severe irritant

**Skin contact:** Irritant. May cause erythema, irritation or oedema. Repeated or prolonged skin contact may lead to allergic contact dermatitis.

**Inhalation:** Potential irritant. Over-exposure at high levels may result in mucous membrane irritation of the nose and throat with coughing.

**Ingestion:** May be harmful if swallowed. Swallowing can result in allergic dermatitis, hallucinations, ataxia, diarrhoea, central nervous system depression, sleep or coma.

### Acute toxicity\*:

Ear TD (guinea pig): 100% (instilled for 30 min)

Toxic effects: D40 (change in acuity)<sup>11</sup>

Dermal LD<sub>50</sub> (rabbit): >5 g/kg<sup>1</sup>

Dermal LDLo (rabbit): 5 g/kg<sup>1</sup>

Dermal TD (cat): 5-7 mL/kg<sup>2</sup>

Toxic effects: F19 (ataxia); P72 (changes in leucocyte count)

Dermal TD (dog): 0.143 – 0.164 g/kg<sup>3</sup>

Toxic effects: F07 (somnolence), F19 (ataxia), partial paralysis

Dermal TD (human adult): > 25% (in white soft paraffin, applied for 21 d)<sup>4</sup>

Oral LD<sub>50</sub> (rat): 1.9 g/kg (1.4 – 2.7 g/kg)<sup>1</sup>

Oral LD<sub>50</sub> (rat): 1.9 – 2.6 g/kg<sup>13</sup>

Oral TD (rat): 1.5 g/kg<sup>5</sup>

Toxic effects: F07 (somnolence) F18 (muscle weakness), F19 (ataxia), partial paralysis

Oral TD (human adult): 21 µL/kg (after repeated low dose exposure)<sup>6</sup>

Toxic effects: P20 (changes in cell count (unspecified)); R01 (dermatitis, allergic); R03 (dermatitis, other)<sup>4</sup>

Oral TD (human adult): 0.5-1.0 mL/kg<sup>7</sup>

Toxic effects: F08 (hallucinations, distorted perceptions); F24 (coma); K12 (hypermotility, diarrhoea)

Oral TD (human child): 0.5 mL/kg<sup>8</sup>

Toxic effects: F04 (sleep); F19 (ataxia)

Oral TD (human child): 0.5 mL/kg<sup>9</sup>

Toxic effects: F08 (hallucinations, distorted perceptions); F19 (ataxia)<sup>5</sup>

Oral TD (human child): 0.6 mL/kg (approx.)<sup>10</sup>

Toxic effects: F07 (somnolence), F19 (ataxia), F24 (coma)

**Chronic toxicity:** No information available

**Sensitisation potential:** Low (modified FCA method, guinea pig model)<sup>12</sup>

**Other:** Not mutagenic as determined by the AMES test

\* see Toxic Effects Code from the Registry of Toxic Effects of Chemical Substances (RTECS)

## 12. ECOLOGICAL INFORMATION

**Ecotoxicity:** Not acutely toxic to fish (LC<sub>50</sub> > 100 mg/l OECD 206)

**Persistence/Degradability:** Readily biodegradable (OECD301F)

**Mobility:** No information available

# MATERIAL SAFETY DATA SHEET

## 13. DISPOSAL CONSIDERATIONS

**Disposal methods:** Dispose of small amounts at an approved landfill site. For larger amounts contact a licensed professional waste disposal service.

**Precautions:** Prevent contamination of drains or waterways.

## 14. TRANSPORT INFORMATION

**UN number:** 2319

**UN proper shipping name:** TERPENE HYDROCARBONS, N.O.S.

**Un Packing group:** III

**ADG proper shipping name:** Not listed in ADG code

**Class and subsidiary risk(s):** Class 3. No subsidiary risks listed.

**Hazchem:** 3 [Y]

**EPG:** 3A1

**Special precautions for user:** Classified as dangerous goods for the purpose of transport by road or rail. Class 3 Flammable Liquid. Do not transport with chemicals of class ; 1 (Explosives), 2.1/2.3 (Flammable/Toxic gases), 4.2 (Spontaneously combustibles), 5.1 (Oxidising agents), 5.2 (Organic peroxides), 6 (Toxics), 7 (Radioactives) and foodstuffs.

## 15. REGULATORY INFORMATION

**Poison Schedule:** 6

**AICS:** This material is listed on the Australian Inventory of Chemical substances

**EINECS:** This material is listed on the European Inventory of Existing Commercial Substances

## 16. OTHER INFORMATION

**This document was last modified on: 18th July 2003**

### ABBREVIATIONS

**ADG** (Australian Dangerous Goods); **AICS** (Australian Inventory of Chemical Substances); **CAS** (Chemical Abstract Service); **EINECS** (European Inventory of Existing Commercial Substances); **EPG** (Emergency Procedure Guide); **FCA** (Freund's Complete Adjuvant); **HAG** (Hazmat Action Guide); **LD<sub>50</sub>** (Dose lethal for 50% of the test population); **LDLo** (Lowest Published Lethal Dose); **N.O.S.** (Not Otherwise Specified); **NOHSC** (National Occupational Health and Safety Commission); **PPE** (Personal Protective Equipment); **RTECS** (Registry of Toxic Effects of Chemical Substances); **SUSDP** (Standard for the Uniform Scheduling of Drugs and Poisons); **TD** (Toxic Dose); **TDLo** (Lowest Published Toxic Dose); **UN** (United Nations)

### REFERENCES

(1) Ford RA. *Food Chem Toxicol* 1988; **26**: 407; (2) Bischoff K & Guale F. *J Vet Diagn Invest* 1998; **10**: 208-210; (3) Kaluzienski M. *J Toxicol Clin Toxicol* 2000; **38**: 518-519; (4) Southwell IA *et al. J Essent Oil Res* 1997; **9**: 47-52; (5) Kim D. *et al. American Chemical Society National Meeting* 2002. **223**: 114-MEDI Part 2; (6) Elliot C. *Med J Aust* 1993; **159**: 830-831; (7) Seawright A. *Med J Aust* 1993; **159**: 831; (8) Del Beccaro MA. *Vet Human Toxicol* 1995; **37**: 557-558; (9) Jacobs MR & Hornfeldt CS. *J Toxicol – Clin Toxicol* 1994; **32**: 461-464; (10) Morris MC *et al. Pediatric Emergency Care* 2003; **19**: 169-171; (11) Zhang SY & Robertson D. *Audiol Neuro-Otol* 1999; **5**: 64-68; (12) Hausen BM *et al. Am J Contact Dermatitis* 1999; **10**: 68-77; (13) Bolt AG. Report for the Australian Tea Tree Oil Industries Association, 1989

### DATA SOURCES

International Standards Organisation (1996) Oil of Melaleuca, terpinen-4-ol type (tea tree oil). International Standard ISO 4730:1996(E), International Standards Organisation, Geneva.

Sweet DV. (Editor) (1997) Registry of toxic effects of chemical substances (RTECS), comprehensive guide. U.S. Department of Health and Human Services, Cincinnati, Ohio.

**Disclaimer:** This Material Safety Data Sheet was prepared according to the National Code of Practice for the Preparation of Material Safety Data Sheets [NOHSC:2011(2003)]. The above information is believed to be correct but does not claim to be all inclusive and shall be used only as a guide.

- END OF REPORT -