RIRDC Completed Projects in 1997-1998 and Research in Progress as at June 1998

TEA TREE OIL

RIRDC Sub-Program 2.8

November 1998

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FOREWORD

This year RIRDC has produced Research in Progress, June '98, which contains short summaries of continuing projects as well as those that were completed during 1997-98 for all of the Corporation’s 21 program areas.

The complete report on all the programs is only available in electronic format on our website at http://www.rirdc.gov.au.

The following report is a hardcopy extract covering Sub-program 2.8. It contains all entries from continuing and completed Tea Tree Oil research projects funded by RIRDC. This program aims to support the continued development of a profitable Australian tea tree oil industry in Australia.

This report is the newest addition to our extensive catalogue of over 250 research reports, videos and CD-Roms of projects supported by RIRDC. Please contact us for the latest publications catalogue or view it on our website.

Peter Core
Managing Director
Rural Industries Research and Development Corporation
## CONTENTS

### COMPLETED PROJECTS

<table>
<thead>
<tr>
<th>PROJECT No</th>
<th>PROJECT TITLE</th>
<th>RESEARCHER</th>
<th>PHONE</th>
<th>ORGANISATION</th>
<th>PAGE No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>UWA-24A</td>
<td>The antimicrobial activity of tea tree oil</td>
<td>Assoc. Professor Tom V Riley</td>
<td>(08) 9346 3690</td>
<td>University of Western Australia</td>
<td>1</td>
</tr>
</tbody>
</table>

### RESEARCH IN PROGRESS

<table>
<thead>
<tr>
<th>PROJECT No</th>
<th>PROJECT TITLE</th>
<th>RESEARCHER</th>
<th>PHONE</th>
<th>ORGANISATION</th>
<th>PAGE No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAN-151A</td>
<td>The improvement of Australian tea tree through selection and breeding (continuation of project DAN-87A)</td>
<td>Dr. Ian Southwell</td>
<td>(02) 6626 1224</td>
<td>Department of Agriculture (NSW)</td>
<td>2</td>
</tr>
<tr>
<td>UNC-7A</td>
<td>Tea tree oil as a topical decolonisation solution for adult inpatients with Methicillin-Resistant <em>Staphylococcus Aureas</em></td>
<td>Professor Richard Heller</td>
<td>(02) 4921 4424</td>
<td>University of Newcastle</td>
<td>2</td>
</tr>
<tr>
<td>UWA-40A</td>
<td>The antiviral activity of tea tree oil in vitro</td>
<td>Assoc. Professor Tom V Riley</td>
<td>(08) 9346 3690</td>
<td>University of Western Australia</td>
<td>3</td>
</tr>
<tr>
<td>UWA-42A</td>
<td>Skin sensitivity testing for tea tree oil</td>
<td>Assoc. Professor Tom V Riley</td>
<td>(08) 9346 3690</td>
<td>University of Western Australia</td>
<td>3</td>
</tr>
</tbody>
</table>
COMPLETED PROJECTS

Project Title
The antimicrobial activity of tea tree oil

RIRDC Project No: UWA-24A
Researcher: Assoc. Professor T. V. Riley
Organisation: Department of Microbiology
The University of Western Australia
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NEDLANDS WA 6009

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Background
Despite the increasing interest in tea tree oil for therapeutic purposes, the vast majority of reports of its efficacy in treating a variety of infections are anecdotal and there is a paucity of information in appropriate peer-reviewed journals. This situation constitutes a significant dilemma for the tea tree oil industry. Early submissions to the Food and Drug Administration in the United States of America for tea tree oil to be registered as an over-the-counter topical antimicrobial have not been successful. One reason for this is that published in vitro efficacy data were lacking.

Research
Adequate data regarding the susceptibility of various pathogens to tea tree oil are required. Therefore, one of the first priorities was to accumulate substantial data on isolates from infections potentially treatable with tea tree oil. In addition, investigations into the antimicrobial activity of the individual components were required. The second area of research was a focus on the mechanism of action of tea tree oil, as no information on this area was available.

Outcomes:
As a first step methods were developed and validated and finally, a broth micro-dilution method was used to examine the susceptibility of various bacteria. All bacteria tested were susceptible to tea tree oil with only one, Pseudomonas being slightly less susceptible. For example, methicillin-resistant strains of S. aureus (MRSA), an important cause of hospital-acquired infections was inhibited by 0.25% tea tree oil suggesting tea tree oil may be useful in the treatment of MRSA. Other studies indicated that tea tree oil, when formulated into appropriate products, may be useful in the treatment of bacterial vaginal infections. The antimicrobial activity of eight components of tea tree oil was evaluated using disc diffusion and broth microdilution methods. Terpinen-4-ol was active against all the test organisms while p-cymene demonstrated no antimicrobial activity. Linalool and α-terpineol were active against all organisms with the exception of Pseudomonas.

The Food and Drug Administration requires that the in vitro antimicrobial spectrum of compounds intended for use as a health-care antiseptic be determined. We therefore tested a range of normal and commensal isolates of the type found on skin. The result suggested that tea tree oil may be useful in removing transient skin flora while suppressing but maintaining resident flora.

Treatment of E. coli suspensions with tea tree oil or components resulted in significant reductions in optical density. These results suggested that the membrane was a site of action in E. coli. Other experiments showed that genetic material was being lost from bacterial cells through damage to the membrane. C. albicans cells were not lysed with terpinen-4-ol treatment and by electron microscopy, appeared unaltered. In contrast, E. coli cells appeared as empty “ghost” cells by electron microscopy. The appearance of terpinen-4-ol S. aureus also suggested damage to the cell membrane or wall. The original premise, that tea tree oil and/or its components act on the cell membrane or wall, was confirmed. While further evidence is required to corroborate these observations, the possibility that other sites of action may exist, must be considered.

Implications
This project has firmly established that tea tree oil has significant antimicrobial activity. The results have been published in mainstream medical and scientific journals and generated considerable interest in Australia and, in particular, Europe and the United States. The industry now has a firm basis for the next step in the promotion of tea tree oil as a bona fide topical antibiotic. This is to establish that tea tree oil products work in the clinical setting. To do this randomised clinical trials will need to be conducted at appropriate testing centres. This is an expensive exercise, however, the potential benefits to the industry should justify the outlay.
**RESEARCH IN PROGRESS**

**Project Title**
The improvement of Australian tea tree through selection and breeding (continuation of project DAN-87A)

**RIRDC Project No:** DAN-151A  
**Start Date:** 1 July, 1996  
**Finish Date:** 30 June, 2001  
**Researcher:** Dr. Ian Southwell  
**Organisation:** Department of Agriculture (NSW) Wollongbar Agricultural Institute Bruxner Highway WOLLONGBAR NSW 2477  
**Contacts:** Phone: (02) 6626 1224  
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**Objectives**
To systematically improve the yield and quality of oil from tea tree (*Melaleuca spp*) by:
- Continuing current, and establishing new selection trials.
- Production of improved seed lines with yields up to 17% higher than current industry selections by 1997, 30% higher by 1999, and 60% higher by 2003.

**Current Progress**
The tea tree breeding project released its first seed to the industry in 1997. There was great interest in the seed, with the sale being oversubscribed. Most recipients have now planted this seed and will expect their first harvest in 98/99. Our yield trial results for this seed will not be available until 99/00, but we conservatively estimate that this material will give an 18% improvement in yield over what most growers would get from their regular seed sources.

The success of the first sale augurs well for the second release expected later this month (June). For this release, 2.7 kg of seed is available. A fully subscribed sale of this seed would bring the program closer to self-funding.

The annual sale of selected bush seed will continue until we can supply highly improved seed from the Seedling Seed Orchard (SSO).

To promote heavy flowering in the SSO this year, irrigation and a chemical hormone are being trialed. From the 1998 flowering, mature seed will be available in early 2000. Plantations established from this improved seed would give returns by 2001/2002. Based on work with other species, a 30% increase in yield from using this seed should be achievable. This level of improvement will be maintained for two years (2002 and 2003) to early 2004 when the first harvests giving a 60% improvement should be made.

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**Objectives**
- Develop efficacy and safety data packages to support the registration of Tea Tree Oil for use as a medical product by providing sound epidemiological data to support its acceptance as an effective and safe antimicrobial agent by national and international registration authorities.

**Current Progress**
The pilot study commenced in December 1997 and was intended to be completed within three months. However, due to an internal patient management issue regarding adult inpatients with MRSA in the aged care setting, this has reduced the number of available subjects by 30%. Therefore it is estimated the pilot study will not be completed until July 1998.

To date a total of 20 participants have been successfully recruited onto the study program. Randomisation in blocks of ten has ensured 10 participants in each arm of the study. It is intended that a total of 30 participants will be required to be recruited before the pilot study is completed.

To date no participants have been withdrawn from the study program due to adverse reactions/events. Daily visits by the research assistant ensures the participants are able to access the study team to discuss any concerns or changes in their nasal mucosa or skin integrity.

MRSA isolates from the participants have been stored (frozen) for analysis at the completion of the pilot study.

It is anticipated that the results of the pilot study will be available for release later in 1998.
**Project Title**  
The antiviral activity of tea tree oil in vitro

**RIRDC Project No:** UWA-40A  
**Start Date:** 1 October, 1997  
**Finish Date:** 30 July, 2000  
**Researcher:** Assoc. Professor Tom V Riley  
**Organisation:** University of Western Australia  
**Queen Elizabeth II Medical Centre**  
**NEDLANDS WA 6009**  
**Contacts:**  
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**Objectives**  
- The aim of this project is to develop and validate methods suitable for testing the antiviral activity of tea tree oil in vitro and to use these methods to assess its potential as a topical antiviral therapeutic agent.  
- The outcomes will be the development of methods, the validation of these methods and an assessment of the suitability of tea tree as a topical antiviral agent.

**Current Progress**  
Work so far has been concentrated in the following areas:  
- the production of suitable stocks of Herpes virus for assays (once virus titres reach high enough levels these stocks are frozen at minus 70 degrees for future work)  
- the production of various tissue culture cell line for investigation (likewise these stocks are frozen for various assays)  
- various solubilising agents for tea tree oil have been assessed  
- a plaque reduction assay system has been developed and tested.

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**Project Title**  
Skin sensitivity testing for tea tree oil

**RIRDC Project No:** UWA-42A  
**Start Date:** 10 January, 1998  
**Finish Date:** 30 September, 1998  
**Researcher:** Assoc. Professor Tom V Riley  
**Organisation:** University of Western Australia  
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**Objectives**  
- The aim of this project is to evaluate the skin sensitivity of tea tree oil and its major components. Sensitivity reactions to tea tree oil will be assessed and the components or fractions responsible for the reactions determined.

**Current Progress**  
Work on the project commenced in late February with the employment of Ms. Jane Greig to coordinate the research. Progress is therefore approximately 2 months behind the original time scale. Regular meetings are held with all investigators to ensure steady progress. The first two milestones have been reached, that is  
1) Establish a protocol after determining regulatory authority requirements;  
2) Seek Human Rights Committee approval.  
Appropriate testing procedures have been determined, and the necessary paperwork has been prepared. Standard allergen series have been purchased to allow determination of the relative reactivity of subjects.  
The main components of tea tree oil have been acquired and arrangements have been made to prepare them in a suitable form for testing. Samples of each tea tree oil have been submitted for thorough component analysis. Volunteer recruitment has yielded about 50 suitable individuals thus far.  
Other means for soliciting volunteers are planned, and will be instigated once testing has been completed for some of the initial subjects. The recent arrival of the last of the tea tree oil samples has allowed testing to commence on the first five subjects.
TEA TREE OIL
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