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The Role of Tea Tree Oil in the Decolonisation of MRSA Positive Wounds

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The Role of Tea Tree Oil in the Decolonisation of MRSA Positive Wounds

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Foreword

Tea tree oil, the essential oil of the native Australian plant *Melaleuca alternifolia*, is widely promoted for a variety of properties including its benefits as a wound care agent. In this context its wound healing and antimicrobial properties, particularly its activity against methicillin-resistant *Staphylococcus aureus*, are frequently touted. While substantial data on the antimicrobial properties of the oil are available detailed information on the effects of tea tree oil on wounds is limited and this study was designed to provide preliminary data on two important outcomes in wound care.

The primary aim of this pilot study was to determine if tea tree oil applied at a low concentration for a brief period of time in the form of a wound irrigant could decolonise wounds colonised with methicillin-resistant *Staphylococcus aureus* (MRSA). The results show that this product when diluted in water to a concentration of 3.3% and used to briefly irrigate and cleanse wounds was unable to decolonise MRSA-positive wounds. The secondary aim of this study was to examine the influence of tea tree oil on wound healing. Tea tree oil applied as part of the wound cleansing procedure had a positive influence on wound healing with many chronic wounds beginning to heal after application of the tea tree oil product. The importance of this report is that it provides preliminary evidence that tea tree oil may promote the healing of chronic wounds. This has not previously been shown before.

As a result of the positive effects seen in this pilot study, tea tree oil producers and product manufacturers should continue to develop and promote tea tree oil products suitable for wound care. More detailed investigations of the effects of tea tree oil on wound healing should be conducted.

This project was funded from industry revenue provided by Novasel Australia Pty. Ltd which was matched by funds provided by the Australian Government through RIRDC's Tea Tree Oil R&D Program.

This report, an addition to RIRDC's diverse range of over 1900 research publications, forms part of our Tea Tree Oil R&D program which aims to support the continued development of an environmentally sustainable and profitable Australian tea tree oil industry that has established international leadership in marketing, in value-adding, and in product reliability and production. In terms of the key long term strategies for this program, this report addresses the goal of demonstrating proof of concept/efficacy for innovative applications of tea tree oil.

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Abbreviations

AMWIS	Advanced Medical Wound Imaging System formerly known as the Alfred/Medseed Wound Imaging System
°C	degrees Celsuis
E. coli	*Escherichia coli*
mm	millimetres
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin-susceptible *Staphylococcus aureus*
P. aeruginosa	*Pseudomonas aeruginosa*
S. aureus	*Staphylococcus aureus*
S. maltophilia	*Stenotrophomonas maltophilia*
sp.	species

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Executive Summary

What the report is about

This report details the results of a pilot study investigating whether tea tree oil is a useful wound treatment product. It is important because tea tree oil is used widely for this purpose despite a lack of comprehensive evidence that it is beneficial. The results of this study begin to address this knowledge void and further support the use of tea tree oil as a wound care agent. This report also helps to fine tune the study designs most likely to succeed in future work examining the use of tea tree oil in wound care products.

Who is the report targeted at?

The report is targeted at product manufacturers who produce and market tea tree oil products, especially those interested in wound care products. It is also targeted at companies that manufacture wound care products and may be interested in developing a range of tea tree oil products. The marked positive effects on wound healing seen in this study are very promising and augur well for the further development of tea tree oil wound care products.

Background

Tea tree oil has been promoted as a wound care product since use of the oil was first popularised in Australia in the 1920s. However, scientific data on the benefits of the oil in wound care have not been forthcoming despite its widespread use for this purpose. Several other properties of tea tree oil including its antibacterial and anti-inflammatory properties have been more-well characterised and evidence for these properties lend support to the oil's use as a wound care product.

Aims/objectives

This pilot study aimed to determine if tea tree oil can eliminate methicillin-resistant *Staphylococcus aureus* (MRSA) from colonised wounds and to determine if tea tree oil is a beneficial treatment for wounds.

Methods used

An uncontrolled, non-randomised, open pilot study design was used to evaluate the efficacy of tea tree oil as means of decolonising methicillin-resistant *Staphylococcus aureus* from acute and chronic wounds and to gain preliminary data on the effects of tea tree oil on wound healing. Participants with acute or chronic wounds colonised but not infected with methicillin-resistant *Staphylococcus aureus* were recruited. Tea tree oil was applied in the form of a wound irrigant during the wound cleansing steps at each dressing change. A proprietary water-miscible product containing 10% tea tree oil was diluted in sterile water for irrigation to a tea tree oil concentration of 3.3% and used for wound irrigation and cleansing. The treatment product was in contact with the wound for a minimum of 5 minutes. Wound size and MRSA status were determined at enrolment and during weeks 4 and 12.

Results/key findings

Two key findings arose from this study. Firstly, when applied during the wound cleansing step as a wound irrigant, 3.3% tea tree oil was unable to decolonise methicillin-resistant *Staphylococcus aureus* from wounds. Secondly, wounds to which this tea tree oil irrigant was applied began to heal; most wounds (8 of 11) were smaller after the tea tree oil product was used and this included chronic wounds. This is despite most participants being withdrawn from the study before

completing the 12 weeks of treatment due to the commencement of antibiotics or other complications.

An additional finding from this small study was that tea tree oil appeared safe to use and was well-tolerated on open wounds, including some large wounds. Furthermore, there were no irritant or allergic reactions to the tea tree oil product.

Implications for relevant stakeholders for:

Tea tree oil producers and tea tree oil product manufacturers and marketers can pursue further research on the use of tea tree oil products for wound care and promote another application for tea tree oil.

Recommendations

Larger, comparative, randomised, controlled clinical trials evaluating the influence of tea tree oil on the healing of chronic wounds should be conducted, preferably evaluating wound care products formulated with tea tree oil and designed to be left in situ as part of the wound dressing. This will require collaboration between tea tree oil producers, wound care product manufacturers, care agencies and researchers.

Introduction

The essential oil of the Australian native plant *Melaleuca alternifolia*, commonly known as tea tree oil, enjoys remarkable popularity as a complementary and alternative topical antimicrobial agent. Marketed mainly for its antibacterial, antifungal and antiviral properties, the oil also has anti-inflammatory, analgesic, insecticidal and anti-pruritic properties[1].

The spectrum of tea tree oil's antibacterial activity includes *Staphylococcus aureus* (including methicillin-resistant *S. aureus*)[2-5], streptococci[6], coagulase negative staphylococci and coliforms[7]. This spectrum of activity may explain in part the anecdotal evidence supporting the application of tea tree oil to wounds[8]. Furthermore, a cream product containing 10% tea tree oil successfully decolonised MRSA-positive wounds in 16 of 34 (47%) hospital inpatients compared to 8 of 26 (31%) patients that used 1% silver sulfadiazine[9]. Apart from this report, there are only a few publications describing the clinical use of tea tree oil as a wound treatment[8, 10-12] with mixed results. In addition, the specific benefits of its use, particularly its influence on wound healing, are poorly articulated in the literature.

Objectives

The primary aim of this pilot study was to assess whether or not tea tree oil used in a wound cleansing procedure could decolonise MRSA from acute and chronic wounds of mixed aetiology. The secondary aim was to determine if tea tree oil treatment can influence wound healing.

Methodology

Pilot study design

There are no published data on the use of tea tree oil or tea tree oil products to decolonise large MRSA-positive wounds other than those reported in a study by Dryden *et al.*[9] in which the decolonisation of wounds was a co-incident finding. Similarly, while tea tree oil is promoted as having wound healing properties, there are no data on specific wound healing parameters such as reductions in wound size or time to re-epithelialisation. Consequently, in the absence of sufficient preliminary data this pilot study was conducted as an uncontrolled, open, community-based case series.

Sample size

The purpose of this pilot study was to decide whether tea tree oil as a means of decolonising MRSA-positive wounds is worth studying further. There are no preliminary data on incidence of MRSA decolonisation after tea tree oil treatment or on the incidence of spontaneous decolonisation of wounds colonised with MRSA. Despite the lack of data it was still possible to determine a sample size that would effectively test our working hypothesis[13]. Using this method an arbitrary level of activity was set and a small number of participants treated. Depending on the number of treatment successes, the arbitrary level of activity would be supported or refuted, within a reasonable range of error. The arbitrary level of activity of tea tree oil was estimated at 20% and the tolerable limit of error was 5%. This pilot study was designed to provide data that would help us choose between the two following hypotheses regarding MRSA decolonisation:

1. Tea tree oil is unlikely to be effective in 20% of participants or more.

2. Tea tree oil could be effective in 20% of participants or more.

Given that the suggested level of effectiveness was 20% or more, the suggested failure level was 80% or less. If tea tree oil was less effective than this estimate of 20%, it would not be investigated further. Participants were entered into the study and the number of consecutive failures used to estimate whether tea tree oil fell above or below this threshold. The sample size that allows us to accept one of these hypotheses was calculated as follows in Table 1.

There was a less than 5% chance that treatment failure would happen 14 times in a row if tea tree oil was truly effective 20% of the time. Conversely, there was a greater than 95% chance that one or more treatment successes (MRSA elimination) would have occurred in 14 consecutive participants if tea tree oil was truly effective 20% of the time. However, if there were 14 consecutive failures, the first hypothesis would be accepted. The chance that tea tree oil may be rejected when it does have ≥20% effectiveness was less than 5%. If you wanted to reduce the risk of incorrectly rejecting tea tree oil for further investigation to less than 2.5%, then 17 participants should have been be treated.

Table 1. Estimation of the sample size required to determine if tea tree oil is likely to be at least 20% effective at decolonising MRSA from wounds.

Consecutive participants	Equation	Chance of Rx failure in given number of consecutive participants
1	0.8^{1}	0.800
2	0.8^{2}	0.640
3	0.8^{3}	0.512
4	0.8^{4}	0.410
5	0.8^{5}	0.328
6	0.8^{6}	0.262
7	0.8^{7}	0.210
8	0.8^{8}	0.168
9	0.8^{9}	0.134
10	0.8^{10}	0.107
11	0.8^{11}	0.086
12	0.8^{12}	0.069
13	0.8^{13}	0.055
14	0.8^{14}	$0.044^{\dagger}$
15	0.8^{15}	0.035
16	0.8^{16}	0.028
17	0.8^{17}	$0.023^{\ddagger}$

† and ‡ indicate the points at which the chance of incorrectly rejecting tea tree oil for further investigation fall below 5% and 2.5%, respectively.

Recruitment

Participants

Participants were recruited from metropolitan clients receiving care from the Silver Chain Nursing Association domiciliary nursing service for all acute or chronic wound types.

To enhance recruitment, approximately nine months into the clinical phase of the study, an oral presentation describing tea tree oil, its properties and the purpose of the pilot study was given at each of the five major metropolitan Silver Chain Nursing Association sites. The aim was to heighten awareness of the ongoing pilot study and boost the referral of suitable participants to the study nurse by other Silver Chain staff.

Inclusion and exclusion criteria

Participants had to be 18 years or older, able to give informed consent, receiving care for any non-infected wound type, available for the 12 weeks following enrolment and with previously known or suspected MRSA colonisation that was confirmed upon enrolment. Exclusion criteria were a known allergy to tea tree oil, wound infection, pregnancy, lactation or non-use of effective contraception in women of child bearing age, the presence of fistulas or cavities in the wound, current use of antibiotics or topical antimicrobial pharmaceutical or wound care products or prescribed use of occlusive dressings.

Informed consent

Clients willing to participate in the study gave their informed, signed consent as required by the institutional review boards of the Silver Chain Nursing Association and The University of Western Australia. All participants were given an information sheet to keep describing the study and their role in it. They were also given an opportunity to ask and have answered any questions and were aware if they declined to participate at any time during the trial any information about them would be destroyed.

Tea tree oil product

The tea tree oil product used in this pilot study was formulated and kindly provided by Novasel Australia Pty. Ltd. Bottles of 25 ml of a water-soluble solution containing 10% tea tree oil were provided. The tea tree oil complied with the international standard for ‘Oil of *Melaleuca* – terpinen-4-ol type’.[14]

Wound swabs

After enrolment, participants had their wound swabbed to confirm the presence of MRSA. Wound swabs were taken by removing the dressing and irrigating with sterile water to remove dressing debris, exudates and loose devitalised tissue. The study wound was then swabbed by passing the swab stick over the wound in a zigzag pattern while gently rotating the tip of the swab for at least one full rotation. If the wound was relatively dry, the swab tip was pre-moistened with sterile water prior to swabbing. If available, only granulation tissue was swabbed. If not, the wound bed or freshly expressed pus was swabbed. Necrotic tissue or slough was avoided if possible as were the perimeters of the wound.

Wound swabs were forwarded to PathWest Laboratory Medicine WA, Nedlands campus for microscopy, culture and susceptibility testing. The presence and abundance or absence of MRSA was reported. Abundance was reported qualitatively as not seen, scanty, moderate or abundant. For analysis, these were scaled as 0, 1, 2 and 3, respectively. The growth and abundance of other major wound pathogens was also noted. Microorganisms other than MRSA detected by culture were reported at species, genus or other level. The Gram stain type, morphology and abundance of microorganisms seen by microscopy was reported as was abundance of leucocytes (inflammatory cells).

Initial wound data

After enrolment, the initial evaluation of the wound was made using the Silver Chain wound assessment or lower leg assessment forms and grid. This included linear circumferential and depth measures. In addition, a digital photograph was taken and the Advanced Medical Wound Imaging System (AMWIS), a validated digital planimetry tool[15], was used to calibrate healing progress. An initial data collection form was also completed which included the Charlson co-morbidity index so that the co-existence of other morbidities in the participants could be recorded and evaluated.

Where participants had multiple wounds, one was nominated as the primary wound for inclusion in the study but all were irrigated with the tea tree oil product.

Participants with infected wounds were excluded from the study. Participants whose wounds became infected during the course of the study were withdrawn. Wound infection was determined on the basis of wound swab results and clinical signs and symptoms. The signs and symptoms of wound infection included pain, erythema, edema, heat, purulence, friable granulation tissue, wound breakdown and foul odour.

Subsequent wound data

Wound assessments performed as described previously were made fortnightly from weeks 2-12 and if infection occurred using the Ongoing Data Collection Form.

Microbiological assessments were performed 3 weeks after the enrolment week (week 4) with 2 swabs at least 24 hours apart and then again during week 12. Two swabs at least 24 hours apart were taken for both the week 4 and week 12 assessments. All swabs were taken at least 3 days after the last tea tree oil usage.

The final assessment for both the primary and secondary measures of efficacy was done when the wound was completely healed or no later than 12 weeks. Table 2 summarises the schedule for swab collection and wound assessment. Participants in whom wounds had not healed continued to receive appropriate care until healing was complete.

The test of cure evaluations were planned for week 4 and 12, the first day of treatment constituting the beginning of week 1.

Week 4 evaluation

The wound site was examined again and further specimens collected to determine whether or not MRSA had been eliminated. Two swabs were taken at least 24 hours apart and at least 3 days after the last tea tree oil irrigation. As at the enrolment visit, on the first day of swabbing in week 4 an evaluation of the wound was made using the Ongoing Data Collection Form.

Week 12 evaluation

The wound site was examined again and further specimens collected to determine whether or not MRSA had been eliminated. Two swabs were taken at least 24 hours apart and at least 3 days after the last tea tree oil irrigation. As at the enrolment visit, on the first day of swabbing in week 12 an evaluation of the wound was made using the Ongoing Data Collection Form.

Table 2. Schedule for swab collection and wound assessment

Week	Swab (number to be taken)	Wound assessment
1	yes (1)	yes
2	no	yes
3	no	yes
4	yes (2 swabs, 24 h apart, at least 3 days after last irrigation)	yes
5-11	no	yes
12	yes (2 swabs, 24 h apart, at least 3 days after last irrigation)	yes
anytime[‡]	yes (1)	yes

[‡] at any stage during the study if infection occurs, a swab will be taken to determine MRSA status

Application of tea tree oil product

For application, two 25 ml bottles of tea tree oil product were added to 100 ml of sterile water for irrigation (Baxter Healthcare Pty. Ltd.), re-capped and mixed manually by shaking before being decanted to irrigate and cleanse the wounds. Where larger volumes of treatment product were required, additional bottles of tea tree oil product and sterile water were mixed, always with a two to one ratio, respectively. The concentration of tea tree oil applied to the wound was therefore 3.3% vol/vol. Wounds were liberally irrigated with the treatment wash, the excess allowed to drain and then the dressing applied. The wound treatment product was allowed to stay in contact with the wound for a minimum of 5 minutes prior to dressing application.

If required, wound swabs and wound data were always collected prior to application of the tea tree oil product.

The frequency of tea tree oil treatments was governed by the frequency of dressing changes deemed necessary by the nurse following assessment of the wound. Cleansing and dressing was done in the following manner at the enrolment visit and at least weekly:

1. The wound was washed with sterile water and, if required, debrided. If a swab was scheduled to be taken, it was collected at this stage.

2. The wound and the surrounding skin were then irrigated and cleansed with the tea tree oil product. The contents of two 25 ml bottles of water miscible 10% tea tree oil product (Novabac supplied by Novasel Australia Pty. Ltd., Mudgeeraba, Qld) were added to a 100 ml bottle of sterile water for irrigation (Baxter Healthcare Pty. Ltd.), shaken and used for the irrigation and cleansing.

3. A primary dressing was applied. No antimicrobial dressings, antimicrobial agents or occlusive dressings were used.

4. A secondary dressing was applied and fixed. Again, occlusive dressings were not used.

Results

A total of 21 participants was enrolled into the study over the period from April to December 2007 and commenced treatment of their wound(s) with the tea tree oil product. After microbiological analysis of the swabs, 14 (63.6%) were confirmed to be MRSA-positive at enrolment. Summary data for these 14 participants are shown in Table 3. Seven participants had wounds that were colonised with methicillin-sensitive *Staphylococcus aureus* rather then the required MRSA and were withdrawn from the study.

Of the 14 participants confirmed to have MRSA, eight were withdrawn due to the commencement of antibiotics and one each due to an adverse side effect (see below), death (unrelated to treatment), admission to hospital and because they were outside the geographical catchment area for the study.

The one participant withdrawn due to an adverse event (#5) experienced pain during the cleansing procedure that may or may not have been due to the irrigation with the tea tree oil mixture. Two further adverse events of pain occurred. One (in participant #16) was due to a compression bandage that was incorrectly applied. The clinical consensus was that the pain was unrelated to the use of tea tree oil product in the wound irrigation and cleansing procedure. The participant continued in the study and completed the 12 weeks of treatment. The other (in participant #21) may or may not have been due to the irrigation with the diluted tea tree oil product. There were no other adverse events reported.

All participants were still MRSA-positive at their final swab.

Notable changes in the organisms cultured from the wound swabs included the disappearance of coliforms in the week 4 cultures from one participant (#2) in which they were present at enrolment. A second participant (#8) whose enrolment swab grew coliforms (*Escherichia coli)* died during week 3 of her participation. No swabs were available to determine whether the coliforms remained. Her death was unrelated to her wounds and her participation in the study. Swabs from two participants (#5 and #20) in whom coliforms were not noted from the enrolment swab subsequently grew coliforms; in participant #5 *Citrobacter* sp. grew from one of the two swabs taken during week 4 and in participant #20 mixed coliforms were noted from the swabs taken during week 4. Finally, the abundant Gram positive bacilli seen on microscopy in the final swab specimen from participant #22 were characterised as coryneform. *Corynebacteria* are commensal skin flora and their appearance in the wound is likely indicative of the healing status of this venous leg ulcer which had reduced in size by more than 40% during the 12 weeks of treatment with the tea tree oil irrigant.

Wound size data for the 14 MRSA positive participants are shown in Table 4. Using area data from AMWIS eight of the 14 participants (57.1%) had smaller wounds, three (21.4%) had larger wounds and the change in three (21.4%) was unknown because they were withdrawn almost immediately upon being enrolled since two were prescribed antibiotics and one was discovered to be outside the geographical catchment area for the study. In comparison, using wound measurements of area taken manually, four wounds were smaller and seven larger at their last measurement and three unknown at their withdrawal almost immediately after enrolment. Each of the wound measurement methods has drawbacks and these are addressed in the Discussion.

Using area AMWIS data, of the eight wounds that were reduced in size after treatment with the tea tree oil irrigant, five were leg ulcers made up of four venous ulcers and one unclassified leg ulcer. The patient-reported duration of these wounds ranged from seven weeks to 22 months so it is significant that these wounds became smaller during treatment. The three wounds that were not leg ulcers and were reduced in size after treatment were shingles, a dehiscence and a pressure ulcer of three weeks, eight months and two months duration, respectively.

Apart from the three wounds that received no treatment, the three wounds that did not diminish in size during treatment were an arterial, an unclassified and a mixed leg ulcer of three, six and 19 months in duration, respectively.

The degree of pain reported by participants was reduced by two degrees or more in five participants and by one degree in an additional participant (see Table 5). It remained absent in one further participant. Pain was reportedly increased in four participants and in each case was increased by greater than two degrees on the scale of 1 to 10.

Table 3. Demographic and treatment summary data for recruited participants (n=14) with wounds subsequently confirmed to be MRSA positive

Participant	Wound type (Wound duration)	Age (yrs)	Withdrawal			No. of treatments (Treatment frequency)	Microorganisms (other than MRSA)[†] detected at:			Wound size (mm^2)[‡] measurement at:		Adverse events
			Yes/ No	Week	Reason		Enrolment (1 swab)	Week 4 (2 swabs)	Week 12 (2 swabs)	Enrolment	Last measure (taken in week no.)	
2	leg ulcer mixed (19 months)	85	yes	2	antibiotics	8 (daily)	MSSA coliforms	none	nd	1043	1427 (1)	no
5	leg ulcer venous (12 months)	66	yes	6	adverse event	15 (3/week)	none	*Citrobacter*	nd	512	68 (6)	pain
6	pressure ulcer	34	yes	1	antibiotics	0	none	nd	nd	nd	nd	no
7	leg ulcer unclassified	91	yes	1	antibiotics	0	none	nd	nd	nd	nd	no
8	leg ulcer unclassified (18 months)	83	yes	3	death	7 (3/week)	*E. coli* *Candida* sp.	nd	nd	184	160 (1)	no
9	leg ulcer venous	68	yes	1	outside catchment area	0	none	nd	nd	nd	nd	no
10	leg ulcer unclassified (6 months)	91	yes	2	hospitalised	13 (daily)	*P. aeruginosa*	nd	nd	2579	6383 (1)	no
12	leg ulcer arterial	77	yes	11	antibiotics	30 (3/week)	none	none	nd	54	62 (11)	no

Participant	Wound type (Wound duration)	Age (yrs)	Withdrawal			No. of treatments (Treatment frequency)	Microorganisms (other than MRSA)[†] detected at:			Wound size (mm^2)[‡] measurement at:		Adverse events
			Yes/ No	Week	Reason		Enrolment (1 swab)	Week 4 (2 swabs)	Week 12 (2 swabs)	Enrolment	Last measure (taken in week no.)	
	(3 months)											
14	shingles (3 weeks)	57	yes	2	antibiotics	3 (3/week)	none	nd	nd	55	17 (2)	no
15	leg ulcer venous (22 months)	68	yes	8	antibiotics	22 (3/week)	none	none	nd	60	44 (8)	no
16	leg ulcer venous (5 months)	95	no	-	-	35 (3/week)	none	none	*S. maltophilia* anaerobes	594	485 (10)	no
20	pressure ulcer (2 months)	36	yes	6	antibiotics	35 (daily)	*S. maltophilia*	*P. aeruginosa* coliforms	nd	1932	1073 (4)	no
21	dehiscence (8 months)	72	yes	8	antibiotics	8 (3/week)	none	none	nd	3922	3447 (8)	pain
22	leg ulcer venous (7 weeks)	80	no	-	-	33 (3/week)	none	none	Gram positive bacilli	17152	9947 (12)	no

[†] MRSA was detected on all initial and subsequent swabs [‡] AMWIS area data nd not done shaded rows indicate wounds that reduced in size

Table 4. Wound measurement data using manual and AMWIS measurements

Overall change in size	Manual data (by volume [mm^3])	Manual data (by area [mm^2])	AMWIS data (area [mm^2])
Decreased	5	4	8
Increased	6	7	3
Unknown	3	3	3
Total	14	14	14

Table 5. Degree and frequency or occurrence of pain as indicated by the evaluable (n=11) MRSA-positive participants¤.

Participant	Degree† and frequency/occurrence‡ of pain	
	First measurement	Final measurement
2	**9, int**	**6, int**
5	6, int	10, const
8	0, none	10, cleans
10	10, int	9, const
12	**0, none**	**0, none**
14	**5, noct**	**0, none**
15	0, none	8, const
16	**5, cleans**	**2, int**
20	0, none	3, int
21	**6, int**	**2, int**
22	**8, int**	**6, int**

† degree of pain on a scale of 0-10 where 0 is no pain and 10 is extreme

‡ frequency or occurrence of pain. Options were none, intermittent (int), constant (const), nocturnal (noct), only at time of wound cleansing (cleans) or unknown.

¤ both measures are as indicated by participant.

Bold values indicate pain reduced by ≥ 2 degrees or remained absent.

Shaded rows indicate wounds that reduced in size.

Discussion

The primary outcome, decolonisation of MRSA positive wounds, was not achieved in any participant. This is somewhat surprising since topical application of tea tree oil products has previously been reported to successfully decolonise MRSA positive wounds.[9] However, the product used in the previous report was a 10% tea tree oil cream applied to wounds once a day for five days. It resulted in the clearance of MRSA from 16 of the 34 (46%) wounds treated compared to 8 of the 24 wounds (31%) that were treated with silver sulfadiazine. It seems likely that the higher tea tree oil concentration and the leave-on nature of the product used in the previous report[9] contributed to the greater success in decolonising MRSA compared to the results obtained in this pilot study with a lower concentration (3.3%) and a rinse-off product. In addition, this pilot study was designed to determine if this particular tea tree oil product had at least a 20% efficacy at decolonising MRSA-positive wounds. To achieve this aim required data from 14 consecutive participants. Since full outcome data were not obtained for the required sample size, no conclusion as to whether tea tree oil meets this aim can be made from this data. The possibility that this product may be at least 20% effective remains. However, lessons from this and previous work suggest that changes to the concentration of tea tree oil in the applied product, the manner in which tea tree oil is applied and the contact time with the wound would be wise and enhance the chances of successfully decolonising wounds. Recruitment and retention would need to be improved for any subsequent study. One way of enhancing recruitment would be to recruit participants with wounds colonised with *S. aureus*, either MRSA or methicillin-sensitive. Retention may be improved by allowing participants who commence antibiotics to continue on the trial as a sub-set of the trial population.

In contrast, the secondary outcome (influence on wound healing) yielded some positive results when analysed on an intention-to-treat basis with eight of 14 participants having smaller wounds after brief use of the tea tree oil product as part of the wound irrigation and cleansing procedure. Bearing in mind that three participants (#6, #7 and #9) were withdrawn immediately upon enrolment and received no tea tree oil irrigations, this means that eight of the 11 participants that received the study treatment had wounds that reduced in size. Previous work[16] evaluating the use of a tea tree oil product as a wound treatment reported several negative outcomes including maceration of the wound and colonisation of wounds with multiple Gram negative organisms after the commencement of treatment. The product used was a 20% tea tree oil blemish gel and it was left in place under the dressing at least weekly. Another report of wound maceration after the use of a leave-on tea tree oil product has also appeared in the literature.[17] No maceration of the wound edges was observed in this pilot study and the widespread acquisition of Gram negative bacteria such as *Pseudomonas aeruginosa* and coliforms reported previously[16] also did not occur. Coliforms may be defined as rod-shaped Gram negative non-spore forming bacteria that ferment lactose with the production of acid and gas when incubated at 35-37°C. They are abundant in the faeces of warm-blooded animals but can also be found in the aquatic environment, in soil and on vegetation. They include genera such as *Citrobacter*, *Escherichia*, *Klebsiella* and *Serratia*. They are not commensal skin organisms but frequently colonise wounds, particularly chronic ones. Coliforms not previously noted in the enrolment swab were detected later in only two of the 14 participants. The absence of wound edge maceration and the low-level of coliform acquisition seen in this study suggests they may be product specific effects and that presentation of the tea tree oil in an appropriate format may confer the benefits of tea tree oil without some of the previously observed problems.

Previous work evaluating the cytotoxicity of tea tree oil on in vitro cell cultures[18-20] prompted the suggestion that tea tree oil may be toxic to regenerating skin.[21] The fact that most wounds began to heal and that the incidence of adverse effects was low provides evidence that tea tree oil is not toxic to healing wounds under the conditions tested here. A larger comparative trial would be required to provide definitive evidence that tea tree oil enhances rather than hinders wound healing.

Different proportions of the 14 evaluable wounds were reported to have become smaller using the manual (4/14) and AMWIS (8/14) data. Wound size was determined manually by measuring the length and width of the wound and multiplying those two measurements to estimate area. Irregularities in wound shape profoundly affect the accuracy of this method. The AMWIS, a validated digital planimetry tool,[15] overcomes this problem; a photograph of the wound is calibrated against a standard measure of length allowing the area of the wound to be more accurately estimated by electronically tracing the perimeter. Depth measurements allowing for the calculation of wound volume were also taken manually and estimated photographically but introduce a greater degree of uncertainty and have not been used in this analysis.

The degree and frequency of pain reported by participants suggest that some pain relief may be offered by irrigation with the tea tree oil product. Pain was reduced in 6 of the 11 participants and remained absent in one more. The wounds got smaller in 4 of these 7 participants. Although the numbers are small, they suggest that irrigation with the tea tree oil product may provide some pain relief in some cases. Given that irrigation with sterile water would offer no pain relief, this may be another advantage for a tea tree oil-based product.

Implications

When used as a wound irrigant in contact with wounds for a minimum of 5 minutes during wound cleansing and before dressing application, tea tree oil at a concentration of 3.3% did not decolonise MRSA positive wounds. However, when included in the wound irrigation and cleansing procedure, even this brief exposure does seem to promote the healing of several previously chronic, non-healing wounds. This effect alone warrants further scrutiny. The low incidence of adverse effects attributable to tea tree oil also provides further support for the safety of topical application of tea tree oil products to open wounds. Although much further work is required, tea tree oil should continue to be considered and evaluated as a wound treatment product. It is possible that a higher concentration of tea tree oil formulated in a product designed to stay in contact with a wound may decolonise MRSA from wounds and this possibility should be investigated further. Certainly the concentration (3.3%) and contact time (5 minutes) used here did not appear to compromise wound healing and may have even promoted it. Bearing in mind that excessively high tea tree oil concentrations and/or prolonged occluded contact time may increase the risk of adverse effects, dosing studies may be necessary to optimise these variables and identify the concentration that would offer the greatest healing and/or decolonisation benefit without causing adverse effects.

Recommendations

This study was always intended to be a pilot study conducted as a prelude to a much larger study and, as such, it has provided much useful data, some of which contradicts previously published work. Recruitment for the study was difficult and many participants were lost due to the commencement of antibiotics, and other complications. Any subsequent clinical work should recruit participants with one type of wound that is colonised or critically colonised but not infected with *Staphylococcus aureus*, either methicillin-sensitive or methicillin-resistant strains. A dosing study may be necessary to guide selection of the tea tree oil concentration required to not only promote healing but also to decolonise *S. aureus*.

Since a significant proportion of the chronic wounds to which a tea tree oil solution was briefly applied was reduced in size, many after only short-term use, tea tree oil as a means of initiating wound healing in chronic wounds should be investigated further. This would best be done in a clinical trial setting in which participants all have wounds of a similar type such as venous leg ulcers. A control group of participants matched for wound type that receives no tea tree oil intervention would be ideal although recruiting sufficient numbers to have matched controls may not be possible.

Additionally, the possibility remains that higher concentrations of tea tree oil left in contact with wounds for extended periods of time may decolonise MRSA. Discussions with wound product manufacturers regarding suitable product formats would be helpful and may lead to a wound dressing product that incorporates tea tree oil for its wound-healing and antimicrobial properties. The links forged with staff of the Silver Chain Nursing Association, who are keen to pursue research with tea tree oil in this area, should be maintained and built upon in future projects.

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The Role of Tea Tree Oil in the Decolonisation of MRSA Positive Wounds

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by CF Carson, M Edmondson, K Carville, N Newall, J Smith and TV Riley

This report details the results of a pilot study investigating whether tea tree oil is a useful wound treatment product. It is important because tea tree oil is used widely for this purpose despite a lack of comprehensive evidence that it is beneficial.

The results of this study begin to address this knowledge void and further support the use of tea tree oil as a wound care agent. This report also helps to fine tune the study designs most likely to succeed in future work examining the use of tea tree oil in wound care products.

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