

Tea Tree Oil Usage Guide

**A research-based overview of
the many benefits of tea tree oil.**



Compiled by Dr. Steve Foster for
Essentially KateS



Thanks for your purchase. It is very much appreciated. If this is your first introduction to essential oils, welcome! We're honored you chose Essentialy KateS. In addition to our Tea Tree Oil, we also offer Peppermint and Lavender essential oils, with Rosehip to be available soon, and many more to follow.

It wasn't long ago that I was new to essential oils. I was amazed at all the uses I saw listed on the internet. But being a researcher, I wanted to know what had actually been studied scientifically. The more research I completed, the more impressed I became.

Tea tree oil is a good example. Like many essential oils, it's a great all-purpose cleaner, a natural insect repellent and fungicide, and shown by research to offer *potential* benefit in many areas of human and animal health.

I am limited in what I can say about health. Bloggers can do it, because they are speaking in general. I'm speaking about a specific product. If I made some of the statements you'll find on the internet, it would be considered a claim of treatment and cure for our product, and place it in the category of a drug requiring FDA approval.

I can offer directions for use on topics that are not subject to FDA regulation. On health issues, I can only provide information. For that reason, I have put many hours into assembling the extensive body of research included here.

Though essential oils are "natural" and present little or no toxicity in diluted form, please remember that they can be toxic in concentrated form, especially to small children. Keep out of reach of children at all times. Be cautious in any topical application.

Be careful to wash your hands after use to prevent transfer to the eyes. If that happens, rinse with warm water, but remember that oil is not soluble in water. You may wish to put a drop of carrier oil, such as olive oil in the eye to dilute the irritant effect of the oil until it passes.

Please don't be put off by the length of this guide. Scan through it to see what's here, then look up the topic you need when you need it. If you have questions, e-mail me at support@essentiallykates.com. If you know of a use not included here, please send it along. I have learned more from the kind people like you who buy our products than from all the research I've completed.

Best Regards,
Dr. Steve Foster

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Cleaning

Cleaning is one of the top uses of tea tree oil, which has been shown to be naturally antibacterial, anti-viral, and anti-fungal, and to repel many insects, including flies, in scientific studies. That makes it a great nontoxic cleaner. In addition, it leaves a clean, fresh smelling aroma.

Natural disinfectants are being valued all the time. Studies have shown that adding increasing amounts of chemical disinfectant to disease-causing bacterial culture (*Pseudomonas aeruginosa*) results in the bacteria adapting by genetic mutation, and not only becoming more and more resistant to the disinfectant, but to antibiotics as well. This effect has not been demonstrated with natural oils.

Here are some short quotes from research abstracts that comment on these properties of tea tree oil. The full abstracts are included in the Research Addendum at the end of this guide as well as others not included here. You can also access the full abstract, and in some cases the full article, free at www.pubmed.com. In most cases, there is a fee for the full article. Enter the title reference in the search bar, and follow the links.

Anti-Fungal

J Appl Microbiol. 2003;95(4):853-60.

Antifungal activity of the components of Melaleuca alternifolia (tea tree) oil.

"To investigate the in vitro antifungal activity of the components of Melaleuca alternifolia (tea tree) oil."

"All tea tree oil components, except beta-myrcene, had antifungal activity."

Lett Appl Microbiol. 2003;37(2):185-7.

Antimycotic activity of Melaleuca alternifolia essential oil and its major components.

"The majority of the organisms were sensitive to the essential oil, with TTO and terpinen-4-ol being the most active oils showing antifungal activity at minimum inhibitory concentration values lower than other drugs."

Anti-Bacterial

Can J Microbiol. 2015 Jan;61(1):82-8.

Effect of tea tree (Melaleuca alternifolia) oil as a natural antimicrobial agent in lipophilic formulations.

"There has been increased interest surrounding the use of tea tree oil (TTO) as a natural antimicrobial."

"..low levels of TTO were effective in reducing microbial growth during the use of the product."

Int J Immunopathol Pharmacol. 2006 Jul-Sep;19(3):539-44.

Melaleuca alternifolia essential oil possesses potent anti-staphylococcal activity extended to strains resistant to antibiotics.

"The anti-staphylococcal activity of terpinen-4-ol and TTO were superior to those of antibiotics belonging to the major families.."

Anti-Viral

Molecules. 2013 Aug 9;18(8):9550-66.

Melaleuca alternifolia concentrate inhibits in vitro entry of influenza virus into host cells.

"Our aim was to investigate whether MAC has any in vitro inhibitory effect on influenza virus infection.."

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"..we proved that MAC could prevent influenza virus from entering the host cells by disturbing the normal viral membrane fusion procedure."

Lett Appl Microbiol. 2009 Dec;49(6):806-8.

In vitro antiviral activity of Melaleuca alternifolia essential oil.

"These data show that TTO has an antiviral activity against influenza A/PR/8 virus subtype H1N1 and that antiviral activity has been principally attributed to terpinen-4-ol, the main active component."

"TTO should be a promising drug in the treatment of influenza virus infection."

HNO. 2011 Dec;59(12):1176-84.

[Efficacy of plant products against herpetic infections].

"Balm oil, tea tree oil and peppermint oil demonstrate in vitro a significant antiherpetic activity, mainly related to a direct drug-virus particle interaction, some essential oils also act directly virucidal.

Interestingly, these essential oils are also highly active against acyclovir-resistant herpes simplex virus strains."

Chemical Disinfectants and Antibiotic Resistance

Microbiology. 2010 Jan;156(Pt 1):30-8.

Effect of subinhibitory concentrations of benzalkonium chloride on the competitiveness of Pseudomonas aeruginosa grown in continuous culture.

"This study investigates the link between adaptation to biocides and antibiotics in Pseudomonas aeruginosa. An enrichment continuous culture of P. aeruginosa.. was operated.. with added benzalkonium chloride (BKC). A derivative, PA-29 (696 h), demonstrated a >12-fold decrease in sensitivity to the biocide..."

"The variant demonstrated a 256-fold increase in resistance to ciprofloxacin.."

"These results indicate the importance of environmental conditions on selection and maintenance of biocide adaptation."

A Word About Mixing Oil and Water

Any time you mix oil and water, a small amount of the oil may remain "suspended" in the water, but for the most part, the oil will float on top. It is best to add a small amount of an emulsifier (soap), which helps the oil and water mix.

You can use liquid dish soap for some purposes, but for others, you'll want to buy a liquid nontoxic botanic or castile soap. These are soaps that are made entirely from plants, very much like essential oils. They are generally nontoxic, insecticidal, and very effective cleaners.

There will be cases in which you'll use just a little soap as an emulsifier to help the oil and water mix, and others when you'll want the cleaning benefit of the soap, and so add more. You might choose to convert entirely to nontoxic soaps in the house, as we did many years ago when we started our family.

These soaps should be generally available at any store that carries natural products, such as Sprouts, Vitamin Cottage or a Health Food Store. We plan to offer our own botanic soap product in the not too distant future, so watch for that as well.

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Counters, Tile, and other Hard Surfaces

I suggest making up a spray bottle of 1% tea tree oil and water, which would be six drops of tea tree oil per ounce, or one teaspoon per cup of water, as there are 50 drops in a teaspoon. Always be sure to add a few drops of botanic soap (or dish soap) to help the oil and water mix. If you want something stronger, double the tea tree oil to 2% or more.

I like to add a half cup of vinegar, but that's optional. It's best to use distilled or purified water if you have it available. If you have a water filter that can produce acidic water, use that. Spray and wipe hard surfaces as you would with any cleaner. On stubborn matter, spray and let sit for a few minutes before wiping. Use a brush as needed.

Mold and Mildew

Mold and mildew are both types of fungi, and tea tree oil is anti-fungal. Make up a small amount of a 4 to 5% solution and put it in a spray bottle. To make a 4% solution add 4 teaspoons per cup of water (one teaspoon per cup makes a 1% solution. If you're making less, 6 drops per ounce of water will comprise a 1% solution, as there are 600 drops in an ounce.

If you can, it's best to allow the area to fully dry before spraying. You might accelerate that process by use of a fan, but don't aim it directly at the mold. You don't want to blow mold spores into the air.

Spray the area of mold and mildew thoroughly and allow it to air dry. Brush with a stiff brush and eliminate as much dry matter as possible, then spray again while brushing, and rinse with water.

Considering the potential health risks of mold, be sure to wear a mask and gloves. Once again, you could add a small amount of vinegar in place of some of the water. Acidity seems to promote the anti-fungal effect of tea tree oil. One study that I found, but can't seem to locate now, showed the greatest action at pH 5.5.

After the area is rinsed and dry, wipe it down with the surface spray of tea tree oil described above, and do so whenever you clean. With grout or other porous surfaces, it is unlikely the tea tree oil will remove the discoloration. If you choose to use bleach to remove discoloration, do it after the tea tree cleaning, and then wipe down the area down again w/ the tea tree spray to prevent further growth.

Try to identify the underlying causes of mold/mildew growth, which is most often ongoing or frequent moisture. Do what you can to change the local environment to be less hospitable to mold and mildew.

Hard Floors

Especially with young children, who spend a lot of time close to the floor, it's best to clean floors and carpets with nontoxic cleaners. Add one to two teaspoons of tea tree oil, along with your nontoxic botanic or castile soap, to the mop bucket when cleaning hard surface floors.

Laundry

If you live in a damp or humid climate, add a half teaspoon of tea tree oil to washing machine load of towels and other materials that tend to be prone to moisture, and therefore mold and mildew. Fill the tub at least part way w/ water, add soap, then the tea tree oil, then the material to be washed.

In addition, or as an alternative, spray a washcloth with the tea tree spray nearly to saturation, and throw it in the dryer with towels, sheets, etc. You can use this in place of dryer sheets, or scent dryer balls with tea tree oil.

Dishwasher

Sprinkle a few drops in the soap dispenser of your dishwasher, along with the dishwasher detergent, before running. The detergent will act as the emulsifier to help the oil and water mix when the clean cycle runs. If you wash dishes by hand, add a few drops to the sink.

Dentures and Toothbrushes

Several studies have shown tea tree oil to be effective against oral and denture related bacteria and fungi, including candida albicans, the most common cause of denture stomatitis. Add a few drops of tea tree oil to whatever you're already soaking your dentures in at night. Swirl and let sit.

Toothbrushes are a great place to grow bacteria. Soak your toothbrush in enough water to cover the top of the brush, with a few drops each of tea tree oil and botanic soap. Stir and let sit overnight.

Here are some quotes from scientific abstracts commenting on tea tree oil studied in this capacity. The complete abstracts are included in the Research Addendum at the end of this guide.

Gerodontology. 2014 Dec 19.

Comparative evaluation of antifungal action of tea tree oil, chlorhexidine gluconate and fluconazole on heat polymerized acrylic denture base resin - an in vitro study.

"Candida albicans-associated denture stomatitis is the most common type of denture stomatitis seen in denture wearers. This study evaluates and compares the antifungal action of fluconazole, chlorhexidine gluconate and tea tree oil.."

"Chlorhexidine and tea tree oil inhibited Candida up to the 14th day, whereas antifungal effect of fluconazole was not significant after the 7th day."

Indian J Dent. 2014 Oct;5(4):183-9.

Evaluation of antimicrobial efficacy of garlic, tea tree oil, cetylpyridinium chloride, chlorhexidine, and ultraviolet sanitizing device in the decontamination of toothbrush.

"To assess and compare the efficacy of 3% garlic extract, 0.2% tea tree oil, 0.2% chlorhexidine, 0.05% cetylpyridinium chloride, and ultraviolet (UV) toothbrush sanitizing device as toothbrush disinfectants against Streptococcus mutans."

"Differences of 77.74 colony forming units (CFU) in tea tree oil group.."

"The antimicrobial agents used in this study effectively reduced the S. mutans counts and hence can be considered as toothbrush disinfectants to prevent dental caries."

Hand Washing

Add several drops of tea tree oil (6 drops per ounce would be 1%) to the liquid pump hand soap dispenser in your bathroom or kitchen.

Add 8 drops of tea tree oil per ounce of a non-greasy unscented hand lotion in a small container and shake or stir well for use as a waterless hand sanitizer.

Please be aware that no claims are being made about the bactericidal or virucidal efficiency of either of these methods. The logic is sound, but the results will vary based on ingredients and concentration.

Here are some quotes from a research abstract that comments on tea tree oil studied in this capacity. The full abstract is included in the Research Addendum at the end of this guide.

Rev Lat Am Enfermagem. 2013 Nov-Dec;21(6):1212-9.

Comparison of hand hygiene antimicrobial efficacy: Melaleuca alternifolia essential oil versus triclosan.

"..this study aimed to evaluate the efficacy of hand hygiene performed with two different soap formulations: 0.3% Melaleuca alternifolia essential oil versus 0.5% triclosan.."

"..referring to the soft soap, there was no difference between the performance of soap with 0.3% M. alternifolia and soap containing 0.5% triclosan."

Freshen and Deodorize Stale Carpets

Mix 15 drops of tea tree oil per 1/2 cup of baking soda. Mix well. Sprinkle or sift onto the carpet and brush in lightly. Let sit for several hours and vacuum.

Stale Car Odor

Use the carpet mix to freshen the carpets in your car. Spray and wipe all the hard surfaces with the tea tree oil cleaning spray, spray a little into each of the air vents in the cab, and if you can find the cabin air inlet under the hood, turn the fan on and spray a few sprays into the air inlet. Let the fan run a few minutes.

Changing Tables, Cribs, Baby Carriers, Car seats, Diaper Pail, Toys, etc.

Use a 1 or 2% tea tree oil spray to wipe down exposed surfaces when you clean; especially after use by an ill child or playmate.

Please be aware that no claims are being made about the bactericidal or virucidal efficiency of this application. The logic is sound, but the results will vary based on application.

Sticky Adhesive Residues or Tar

Apply full strength to a disposable rag, wipe on, let sit for a few minutes, then using the rag, scrub with a lot of elbow grease.

Personal care

Deodorant

Underarm odor is due to the bacterial action on perspiration, not the perspiration itself. I have used a very light dilution of botanic soap and essential oil in water as my deodorant for years. It has been effective and nontoxic.. no aluminum chlorhydrate.

Mix up a 2% solution (12 drops per ounce) of concentrated botanic soap with water in a small spritzer spray bottle. Add a few drops of tea tree oil (start w/ a little, you can always add more). Use as you would any spray deodorant. I spray 3 or 4 times each side. If it isn't as effective as needed, increase the concentration of soap and/or tea tree oil.

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Toothpaste

I know I'll incite a few "yucks" for this one, but I have also used a dilute nontoxic mix of botanic soap and essential oil for my toothpaste. Tea tree oil has been shown in scientific study to be active against the most common oral bacteria and fungi.

There are many ways to do this. Simply add a drop to your current toothpaste before brushing, make up your own dry powder by mixing 15 to 20 drops of tea tree oil with a half cup of baking soda, or use a foaming pump, as I do, with about a 2.5% solution of botanic soap to water (15 drops per ounce of water) with 1-2 drops of tea tree oil per ounce of water. It isn't intended to be swallowed, but it's safer than fluoride toothpaste even if you do.

I have also used peppermint oil, and I have to say I like that a little better because it leaves my mouth feeling fresh and tingly. Tea tree oil tastes a bit more "medicinal." I suggest trying both and choosing what you prefer.

Shampoo

Add a few drops of tea tree oil to your shampoo bottle for fresh smelling hair and, a clean and well conditioned scalp.

Here are some quotes from a research abstract that comments on tea tree oil studied in this capacity. The full abstracts are included in the Research Addendum at the end of this guide.

J Am Acad Dermatol. 2002 Dec;47(6):852-5.

Treatment of dandruff with 5% tea tree oil shampoo.

"We conducted a randomized, single-blind, parallel-group study to investigate the efficacy and tolerability of 5% tea tree oil and placebo in patients with mild to moderate dandruff."

The 5% tea tree oil shampoo group showed a 41% improvement in the quadrant-area-severity score compared with 11% in the placebo group.."

Braz J Microbiol. 2012 Oct;43(4):1347-54.

Inhibitory effect of essential oils against Trichosporon ovoides causing Piedra Hair Infection.

"Piedra, is an asymptomatic fungal infection of the hair shaft, resulting in the formation of nodules of different hardness on the infected hair."

"The essential oils of Cymbopogon winterians, Mentha piperita, Cinnamomum zeylanicum, Melaleuca alternifolia and Eucalyptus globulus were proved to be most effective against the fungus Trichosporon ovoides."

J Environ Biol. 2013 Jan;34(1):17-22.

Screening of some essential oils against Trichosporon species.

In this study 25 essential oils were extracted and screened against two Trichosporon species i.e. Trichosporon asahii and Trichosporon cutaneum.

The results showed that the maximum anti-yeast activity against T. asahii and T. cutaneum was demonstrated by oil of Mentha piperita showing full inhibition of both the fungi, Melaleuca alternifolia with an inhibition zone of 45 and 40 mm..

These results support that the essential oils can be used to cure superficial mycoses and these oils may have significant role as pharmaceuticals and preservatives.

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Foot Soak

Soak your feet in a solution of 2% tea tree oil and warm water. Add a few drops of botanic or castile soap to help the oil and water mix, and some epsom salts if available. Let soak for five or ten minutes, then brush around the cuticles and nails with a small soft brush.

Facial Cleanse

Make a strong cup of your favorite herb tea, chamomile works great. Mix 1/4 cup of liquid castile soap, 1/2 teaspoon of olive, rosehip, or other light carrier oil, add 10 drops of tea tree oil, and enough tea to make up a total of 4 ounces. You could also add several drops of vitamin E oil if you have it on hand. Mix well, and place in a small pump or dispenser bottle. Work into a wet washcloth, wash face and rinse.

Freshen Breath

Mix up a spray of six drops of tea tree oil per ounce of distilled water. Shake well and spray into the mouth and throat, add a little water, gargle for 30 seconds and rinse.

Skin

There has been a great deal of study in this area, much of which is included in the research addendum. Here is the reference for a complete short article available free at www.pubmed.com. Just search the title in the search bar and follow the links. At the time of this writing, this was a direct link to the article.. <http://www.nature.com/jid/journal/v123/n4/full/5602496a.html>

**J Invest Dermatol. 2004 Oct;123(4):xviii-xix.
The Wizard of Oz, or the intriguing tale of the tea tree.**

Free full text

Garden

Tea Tree oil has been shown by scientific study not only to prevent fungal growth on plants, but even to kill many species of fungi.

To address current garden or plant fungal infections, mix 3 to 4 teaspoons of tea tree oil per cup of water in a spray bottle (a 3 to 4% solution). Add a little soap as an emulsifier. Apply directly to infected plants once or twice a week. It's probably best to spray in the evenings, or at least when it isn't too hot or in direct sun. Always test spray a few leaves and observe for tolerance at the concentration used.

To prevent future fungal growth on plants and leaves, cut the concentration in half, and spray every 4 to 7 days.

If plants have some blight on leaves but not the stems or fruit, carefully clip off the bad leaves (be sure to bag and discard), spray the clipped ends and the rest of the plant.

Tea tree oil is also an excellent natural insect repellent, and you'll reap additional benefits in this respect.

Tree Trimming

Especially with fruit trees, but really with all trees and ornamentals, dip in or spray the cutting tool with a 2% tea tree oil solution between cuts to prevent the spread of any known or unknown disease. It's also a

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good idea to spray the fresh cut limbs of fruit trees, and others too, for the same reason. This is especially true if you have known infection present.

Repelling Insects

Very many essential oils have been shown by scientific research to be effective natural insect repellents. Tea tree oil is no exception.

Tea tree oil can be diffused into the air and sprayed onto surfaces (1 to 2% solution of tea tree oil in water with a little soap as an emulsifier) to discourage both flying and crawling insects.

Here are some short quotes from research abstracts that comment on tea tree oil studied in this capacity. The full abstracts are included in the Research Addendum at the end of this guide.

Trop Biomed. 2015 Mar;32(1):160-6.

In vitro repellent effect of tea tree (Melaleuca alternifolia) and andiroba (Carapa guianensis) oils on Haemotobia irritans and Chrysomya megacephala flies.

"This study aimed to evaluate the repellent effect of tea tree (Melaleuca alternifolia) and andiroba (Carapa guianensis) essential oils on two species of flies.."

"The study demonstrated that all three oils used showed in vitro repellent effect against both species of flies."

Vet Parasitol. 2012 Mar 23;184(2-4):271-8.

Insecticidal and repellent effects of tea tree (Melaleuca alternifolia) oil against Lucilia cuprina.

"Laboratory studies were conducted to assess the effect of tea tree oil (TTO) from Melaleuca alternifolia (terpinen-4-ol chemotype) against different stages of the Australian sheep blowfly Lucilia cuprina."

"Formulations containing 1% TTO caused 100% mortality of L. cuprina eggs and 1st instar larvae and 2.5% TTO caused mortality of most second and third instar larvae in agar feeding assays."

Med Vet Entomol. 2014 Aug;28 Suppl 1:33-9.

Insecticidal and repellent effects of tea tree and andiroba oils on flies associated with livestock.

"This study aimed to evaluate the insecticidal and repellent effects of tea tree, Melaleuca alternifolia.."

"Tea tree oil at a concentration of 5.0% was able to kill M.domestica with 100.0% efficacy after 12h of exposure."

"It is possible to conclude that these essential oils have insecticidal and repellent effects against the species of fly used in this study."

Aromatherapy Options

There are several options for getting tea tree oil aroma into the air.

1. Place several open shallow containers of tea tree oil.
2. Add a few drops of oil to an old style steam humidifier.
2. Use a diffuser.
3. Use a simmering pot, which is a small ceramic pot with an electric heating element.

Diffusers do not heat the oil, which is considered an advantage by some. However, I have been unable to find evidence that moderate heating in a water bath alters the characteristics of the oil. Diffusers require

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more attention. Depending on their size, they must be refilled as often as every few hours. They also go through more oil.

I have seen studies in which aromatherapy was performed by leaving an open container near the subject, by wearing a small peppermint oil sachet on the lapel, by use of oxygen mask infusion, by diffuser, and even by heating it in a "simmering pot."

I have had responses from people that spray their furnace, a/c, or humidifier filters. I learned with peppermint oil that, if my intention was to get the aroma into my sinuses and/or lungs, the best method was to put a few drops of oil on a "surgeon's mask, and wear the mask. It was extremely effective, and I had only applied a few drops of oil to the mask.

As far as getting the aroma into room air, I maintain a small heated ceramic pot in my office which I purchased at WalMart for \$10. It is easily maintained. I add a few drops of oil each morning (from a large selection), and about a half cup of distilled water every 3 to 4 days. I do empty it and clean it occasionally, but it isn't really necessary, as the oils keep it clean. It is set on a timer that comes on an hour before we arrive, and shuts off an hour before we leave. Rarely a day goes by that someone doesn't say "It always smells so good in here!"

When in doubt, dilute. You can always add more.

Topical application of full strength essential oil in small amounts is not a problem for most, but can be too much for some individuals, and for children. You can dilute essential oils with any of several carrier oils, including rosehip, jojoba, fractionated coconut oil, olive oil, or even vegetable oil, if that is all you have available. Start at a lower concentration than you think. It's easier to add a few drops more of essential oil than many more of carrier oil

Dilution Ratio Chart

<u>Desired Dilution Ratio</u>	<u>1%</u>	<u>2%</u>	<u>3%</u>	<u>5%</u>	<u>10%</u>	<u>25%</u>
Drops of oil per 1 teaspoon (5 ml, 1/6 oz.)	1	2	3	5	10	25
Drops of oil per 2 teaspoons (10 ml, 1/3 oz.)	2	4	6	10	20	50
Drops of oil per 3 teaspoons (15 ml, 1/2 oz.)	3	6	9	15	30	75
Drops of oil per 4 teaspoons (20 ml, 2/3 oz.)	4	8	12	20	40	100
Drops of oil per 5 teaspoons (25 ml, 5/6 oz.)	5	10	15	25	50	125
Drops of oil per 6 teaspoons (30 ml, 1 oz.)	6	12	18	30	60	150

Research Addendum

There is a substantial body of research showing *potential* health benefits of tea tree oil. However, the only way these kinds of studies ever advance to large clinical trials and submission to the FDA for approval as a "drug" is if there is a great deal of money to be made. As tea tree oil is a natural substance and cannot be patented, that is highly unlikely.

Though the research is often clear in showing benefit, and any risk of use is generally minimal to none, it is not possible for me to offer specific recommendations or to advocate the use of our tea tree oil in any human or animal health related capacity. To do so would place our product in the category of a drug, subject to FDA approval and regulation.

Therefore, in no instance is the information provided in this guide intended to diagnose, treat, mitigate, or cure any human or animal health complaint or disease that is under the regulation of the FDA. The research abstracts included here are provided for informational purposes only.

This research were discovered by exhaustive word search at www.pubmed.com, a great resource that few people know about. If there is a particular topic of interest to you, you may find more information by searching in the same manner at pubmed. If it says "Free Full Text," or "Free PMC Article" below the abstract, the full article is available free at pubmed.

I have included only the scientific abstracts here. The full article is sometimes available free, and virtually always available for purchase. The links will show when you view the abstract at pubmed.

Feel free to e-mail me (support@essentiallykates.com) with questions, or requests for information on specific topics. If I know of related research, I'll be glad to send it to you.

I have loosely organized these abstracts into categories, but you'll find that there is a lot of overlap. Please don't let the technical terminology discourage you. This is the best information available on these topics.

Dr. Steve Foster

Skin Infection & Inflammation

Evid Based Complement Alternat Med. 2014;2014:726341.

Essential oils for complementary treatment of surgical patients: state of the art.

Aromatherapy is the controlled use of plant essences for therapeutic purposes. Its applications are numerous (i.e., wellbeing, labour, infections, dementia, and anxiety treatment) but often they have not been scientifically validated. The aim of the present study is to review the available literature to determine if there is evidence for effectiveness of aromatherapy in surgical patients to treat anxiety and insomnia, to control pain and nausea, and to dress wound. Efficacy studies of lavender or orange and peppermint essential oils, to treat anxiety and nausea, respectively, have shown positive results. For other aspects, such as pain control, essential oils therapy has shown uncertain results. Finally, there are encouraging data for the treatment of infections, especially for tea tree oil, although current results are still inconclusive. It should also be considered that although they are, allergic reactions and toxicity can occur after oral ingestion. Therefore, while rigorous studies are being carried out, it is important that the therapeutic use of essential oils be performed in compliance with clinical safety standards.

Free PMC Article

Int J Dermatol. 2013 Jul;52(7):784-90.

A review of applications of tea tree oil in dermatology.

Tea tree oil (TTO) is an essential oil, steam-distilled from the Australian native plant, *Melaleuca alternifolia*. It has a minimum content of terpinen-4-ol and a maximum content of 1, 8-cineole. Terpinen-4-ol is a major TTO component which exhibits strong antimicrobial and anti-inflammatory properties. Tea tree oil exerts antioxidant activity and has been reported to have broad-spectrum antimicrobial activity against bacterial, viral, fungal, and protozoal infections affecting skin and mucosa. Several studies have suggested the uses of TTO for the treatment of acne vulgaris, seborrheic dermatitis, and chronic gingivitis. It also accelerates the wound healing process and exhibits anti-skin cancer activity. This review opens up new horizons for dermatologists in the use of this herbal agent.

J Drugs Dermatol. 2012 Mar;11(3):349-54.

Combination of essential oil of *Melaleuca alternifolia* and iodine in the treatment of molluscum contagiosum in children.

Molluscum contagiosum is a common childhood viral skin condition and is increasingly found as a sexually transmitted disease in adults. Current treatment options are invasive, requiring tissue destruction and attendant discomfort. Fifty-three children (mean age 6.3+5.1 years) with the diagnosis of molluscum contagiosum were treated with twice daily topical application of either essential oil of *Melaleuca alternifolia* (TTO), a combination of TTO and organically bound iodine (TTO-I), or iodine alone. At the end of 30 days, 48 children were available for follow up. A greater than 90% reduction in the number of lesions was observed in 16 of 19 children treated with TTO-I, while 1 of 16 and 3 of 18 children met the same criteria for improvement in the iodine and TTO groups ($P < 0.01$, ANOVA) respectively by intention-to-treat analysis. No child discontinued treatment due to adverse events. The combination of essential oil of *M. alternifolia* with organically bound iodine offers a safe therapeutic alternative in the treatment of childhood molluscum.

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Br J Dermatol. 2002 Dec;147(6):1212-7.

Tea tree oil reduces histamine-induced skin inflammation.

BACKGROUND: Tea tree oil is the essential oil steam-distilled from *Melaleuca alternifolia*, an Australian native plant. In recent years it has become increasingly popular as an antimicrobial for the treatment of conditions such as tinea pedis and acne.

OBJECTIVES: To investigate the anti-inflammatory properties of tea tree oil on histamine-induced weal and flare.

METHODS: Twenty-seven volunteers were injected intradermally in each forearm (study and control assigned on an alternating basis) with histamine diphosphate (5 microg in 50 microL). Flare and weal diameters and double skin thickness were measured every 10 min for 1 h to calculate flare area and weal volume. At 20 min, 25 microL of 100% tea tree oil was applied topically to the study forearm of 21 volunteers. For six volunteers, 25 microL paraffin oil was applied instead of tea tree oil.

RESULTS: Application of liquid paraffin had no significant effect on histamine-induced weal and flare. There was also no difference in mean flare area between control arms and those on which tea tree oil was applied. However, mean weal volume significantly decreased after tea tree oil application (10 min after tea tree oil application, $P = 0.0004$, Mann-Whitney U-test).

CONCLUSIONS: This is the first study to show experimentally that tea tree oil can reduce histamine-induced skin inflammation.

Acne

J Dermatol Sci. 2012 Aug;67(2):120-9.

Topically applied *Melaleuca alternifolia* (tea tree) oil causes direct anti-cancer cytotoxicity in subcutaneous tumour bearing mice.

BACKGROUND: *Melaleuca alternifolia* (tea tree) oil (TTO) applied topically in a dilute (10%) dimethyl sulphoxide (DMSO) formulation exerts a rapid anti-cancer effect after a short treatment protocol. Tumour clearance is associated with skin irritation mediated by neutrophils which quickly and completely resolves upon treatment cessation.

OBJECTIVE: To examine the mechanism of action underlying the anti-cancer activity of TTO.

METHODS: Immune cell changes in subcutaneous tumour bearing mice in response to topically applied TTO treatments were assessed by flow cytometry and immunohistochemistry. Direct cytotoxicity of TTO on tumour cells in vivo was assessed by transmission electron microscopy.

RESULTS: Neutrophils accumulate in the skin following topical 10% TTO/DMSO treatment but are not required for tumour clearance as neutrophil depletion did not abrogate the anti-cancer effect. Topically applied 10% TTO/DMSO, but not neat TTO, induces an accumulation and activation of dendritic cells and an accumulation of T cells. Although topical application of 10% TTO/DMSO appears to activate an immune response, anti-tumour efficacy is mediated by a direct effect on tumour cells in vivo. The direct cytotoxicity of TTO in vivo appears to be associated with TTO penetration.

CONCLUSION: Future studies should focus on enhancing the direct cytotoxicity of TTO by increasing penetration through skin to achieve a higher in situ terpene concentration. This coupled with boosting a more specific anti-tumour immune response will likely result in long term clearance of tumours.

Med J Aust. 1990 Oct 15;153(8):455-8.

A comparative study of tea-tree oil versus benzoylperoxide in the treatment of acne.

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Tea-tree oil (an essential oil of the Australian native tree *Melaleuca alternifolia*) has long been regarded as a useful topical antiseptic agent in Australia and has been shown to have a variety of antimicrobial activities; however, only anecdotal evidence exists for its efficacy in the treatment of various skin conditions. We have performed a single-blind, randomised clinical trial on 124 patients to evaluate the efficacy and skin tolerance of 5% tea-tree oil gel in the treatment of mild to moderate acne when compared with 5% benzoyl peroxide lotion. The results of this study showed that both 5% tea-tree oil and 5% benzoyl peroxide had a significant effect in ameliorating the patients' acne by reducing the number of inflamed and non-inflamed lesions (open and closed comedones), although the onset of action in the case of tea-tree oil was slower. Encouragingly, fewer side effects were experienced by patients treated with tea-tree oil.

Indian J Dermatol Venereol Leprol. 2007 Jan-Feb;73(1):22-5.

The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: a randomized, double-blind placebo-controlled study.

BACKGROUND: Finding an effective treatment for acne that is well tolerated by the patients is a challenge. One study has suggested the efficacy of tea tree oil in treatment of the acne vulgaris.

AIM: To determine the efficacy of tea tree oil in mild to moderate acne vulgaris.

METHODS: This was a randomized double-blind clinical trial performed in 60 patients with mild to moderate acne vulgaris. They were randomly divided into two groups and were treated with tea tree oil gel (n=30) or placebo (n=30). They were followed every 15 days for a period of 45 days. Response to treatment was evaluated by the total acne lesions counting (TLC) and acne severity index (ASI). The data was analyzed statistically using t-test and by SPSS program.

RESULTS: There were no significant differences regarding demographic characteristics between the two groups. There was a significant difference between tea tree oil gel and placebo in the improvement of the TLC and also regarding improvement of the ASI. In terms of TLC and ASI, tea tree oil gel was 3.55 times and 5.75 times more effective than placebo respectively. Side-effects with both groups were relatively similar and tolerable.

CONCLUSION: Topical 5% tea tree oil is an effective treatment for mild to moderate acne vulgaris.

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Psoriasis

Skin Pharmacol Physiol. 2012;25(3):162-3.

Tea tree oil as a novel antipsoriasis weapon.

Psoriasis is a clinical skin disease that is characterized by erythematous scaling plaques and involves the extensor site of the extremities, the scalp and other surfaces of the skin. Tea tree oil (TTO) is considered an essential oil, obtained by steam distillation of the leaves and terminal branchlets of *Melaleuca alternifolia*. Notably, terpinen-4-ol, the major TTO constituent, has been found to have potent anti-inflammatory properties. It is suggested that terpinen-4-ol may be a novel potential agent against psoriasis. This article draws attention to the antipsoriatic effect of TTO and provides a theoretical molecular approach.

Adverse Drug React Toxicol Rev. 2001 Jun;20(2):89-103.

Adverse and beneficial effects of plant extracts on skin and skin disorders.

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Plants are of relevance to dermatology for both their adverse and beneficial effects on skin and skin disorders respectively. Virtually all cultures worldwide have relied historically, or continue to rely on medicinal plants for primary health care. Approximately one-third of all traditional medicines are for treatment of wounds or skin disorders, compared to only 1-3% of modern drugs. The use of such medicinal plant extracts for the treatment of skin disorders arguably has been based largely on historical/anecdotal evidence, since there has been relatively little data available in the scientific literature, particularly with regard to the efficacy of plant extracts in controlled clinical trials. In this article therefore, adverse and beneficial aspects of medicinal plants relating to skin and skin disorders have been reviewed, based on recently available information from the peer-reviewed scientific literature. **Beneficial aspects of medicinal plants on skin include: healing of wounds and burn injuries (especially Aloe vera); antifungal, antiviral, antibacterial and acaricidal activity against skin infections such as acne, herpes and scabies (especially tea tree (*Melaleuca alternifolia*) oil); activity against inflammatory/immune disorders affecting skin (e.g. psoriasis); and anti-tumour promoting activity against skin cancer (identified using chemically-induced two-stage carcinogenesis in mice).** Adverse effects of plants on skin reviewed include: irritant contact dermatitis caused mechanically (spines, irritant hairs) or by irritant chemicals in plant sap (especially members of the Ranunculaceae, Euphorbiaceae and Compositae plant families); phytophotodermatitis resulting from skin contamination by plants containing furocoumarins, and subsequent exposure to UV light (notably members of the Umbelliferae and Rutaceae plant families); and immediate (type I) or delayed hypersensitivity contact reactions mediated by the immune system in individuals sensitized to plants or plant products (e.g. peanut allergy, poison ivy (*Toxicodendron*) poisoning).

Eczema

Arch Dermatol Res. 2011 Jul;303(5):333-8. doi

Tea tree oil attenuates experimental contact dermatitis.

Herbs and minerals have been used in clinical dermatology for hundreds of years and herbal ingredients are becoming increasingly popular with the public in treatment of various dermatological conditions characterised by inflammation and pruritus. The aim of this study was to compare the efficacy of traditional topical therapeutic agents with a moderate potency topical glucocorticoid on experimental contact dermatitis and contact urticaria. The effects of ichthammol 10% pet, zinc oxide 20% pet, camphor 20% pet, levomenthol 10% pet, tea tree oil 20 or 50% and clobetasol butyrate 0.05% ointment were studied in the following experimental models: elicitation of allergic contact dermatitis to nickel, irritant contact dermatitis to benzalkonium chloride, and in immediate reactions to histamine and benzoic acid (non-immunological contact urticaria) respectively. Delayed reactions were evaluated using a clinical scoring system and immediate reactions were estimated by planimetry. Histamine-induced pruritus was evaluated using VAS. **Tea tree oil reduced allergic contact dermatitis by 40.5%** ($p = 0.003$), zinc oxide by 17.4% ($p = 0.04$) and clobetasol butyrate by 23.5% ($p = 0.01$). Zinc oxide reduced histamine induced flare by 18.5% ($p = 0.01$), ichthammol by 19.2% ($p = 0.02$) and clobetasol butyrate by 44.1% ($p = 0.02$). Irritant contact dermatitis and non-immunological contact urticaria were not influenced by the pre-treatments. Pruritus induced by histamine also remained unchanged. In conclusion, **tea tree oil seems to be a more effective anti-eczematic agent than zinc oxide and clobetasone butyrate,** while clobetasone butyrate is superior to both ichthammol and zinc oxide in topical treatment of urticarial reactions.

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Skin Cancer

Cancer Chemother Pharmacol. 2010 Nov;66(6):1095-102.

Inhibition of established subcutaneous murine tumour growth with topical *Melaleuca alternifolia* (tea tree) oil.

PURPOSE: Systemic toxicity coupled with long treatment regimes of approved topical chemotherapeutic agents such as imiquimod and 5-fluorouracil (5-FU) are limiting. There is now more focus on the potential use of topical terpene agents as skin cancer treatments. Here, we show for the first time that topical *Melaleuca alternifolia* (tea tree) oil (TTO), abundant in terpenes, has *in vivo* antitumour activity.

METHOD: Topical TTO formulations applied to immunocompetent tumour-bearing mice were assessed for antitumour efficacy by monitoring tumour growth and by histological analysis following treatment.

RESULTS: Four, daily, topical treatments of 10% TTO/DMSO regressed subcutaneous AE17 mesotheliomas in mice for a period of 10 days and significantly retarded the growth of subcutaneous B16-F10 melanomas. The antitumour effect of topical 10% TTO/DMSO was accompanied by skin irritation similar to other topical chemotherapeutic agents, but unlike other approved topical agents, quickly and completely resolved. Furthermore, we show that topical 10% TTO/DMSO caused an influx of neutrophils and other immune effector cells in the treated area, with no evidence of systemic toxicity.

CONCLUSION: TTO combined with an effective carrier significantly inhibited the growth of aggressive, subcutaneous, chemo-resistant tumours in immunocompetent mice. Taken together, these findings highlight the potential of topical TTO as an alternative topical antitumour treatment.

Planta Med. 2011 Jan;77(1):54-6.

Tea tree oil might combat melanoma.

In this study we present new data from experiments focused on the antitumor activity of tea tree oil (TTO), an essential oil distilled from *Melaleuca alternifolia*. TTO proved to be capable of inhibiting the growth of melanoma cells and of overcoming multidrug resistance (MDR), as we reported in our previous study.

Moreover, the survival role of the MDR-marker P-glycoprotein appears to be involved in the mechanism of invasion of melanoma cells. The results reported herein indicate that TTO and its main active component, terpinen-4-ol, can also interfere with the migration and invasion processes of drug-sensitive and drug-resistant melanoma cells.

J Invest Dermatol. 2004 Feb;122(2):349-60.

Terpinen-4-ol, the main component of *Melaleuca alternifolia* (tea tree) oil inhibits the *in vitro* growth of human melanoma cells.

The search for innovative therapeutic approaches based on the use of new substances is gaining more interest in clinical oncology. In this *in vitro* study the potential anti-tumoral activity of tea tree oil, distilled from *Melaleuca alternifolia*, was analyzed against human melanoma M14 WT cells and their drug-resistant counterparts, M14 adriamycin-resistant cells. Both sensitive and resistant cells were grown in the presence of tea tree oil at concentrations ranging from 0.005 to 0.03%. Both the complex oil (tea tree oil) and its main active component terpinen-4-ol were able to induce caspase-dependent apoptosis of melanoma cells and this effect was more evident in the resistant variant cell population. Freeze-fracturing and scanning electron microscopy analyses suggested that the effect of the crude oil and of the terpinen-4-ol was mediated by their interaction with plasma membrane and subsequent reorganization of membrane lipids. In conclusion, tea tree oil and terpinen-4-ol are able to impair the growth of human M14 melanoma cells and

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appear to be more effective on their resistant variants, which express high levels of P-glycoprotein in the plasma membrane, overcoming resistance to caspase-dependent apoptosis exerted by P-glycoprotein-positive tumor cells.

Chiggers

Exp Appl Acarol. 2009 Mar;47(3):257-62.

Laboratory evaluation of aromatic essential oils from thirteen plant species as candidate repellents against *Leptotrombidium chiggers* (Acari: Trombiculidae), the vector of scrub typhus.

Scrub typhus, a rickettsial disease transmitted by several species of *Leptotrombidium chiggers* (larvae), is endemic in many areas of Asia. The disease is best prevented by the use of personal protective measures, including repellents. In this study commercially produced aromatic, essential oils of 13 plant species and ethanol (control) were tested in the laboratory for repellency against host-seeking chiggers of *Leptotrombidium imphalum* Vercammen-Grandjean and Langston (Acari: Trombiculidae). A rapid, simple and economic in vitro test method was used by exposing the chigger for up to 5 min. Repellency was based on relative percentages of chiggers attracted to test and control substances. **Four of the 13 essential oils showed promise as effective repellent against *L. imphalum* chiggers. *Syzygium aromaticum* (clove) oil exhibited 100% repellency at 5% concentration (dilution with absolute ethanol), whereas *Melaleuca alternifolia* (tea tree) oil exhibited 100% repellency at 40% concentration.** Undiluted oils of *Zingiber cassamunar* (plai) and *Eucalyptus globules* (blue gum) exhibited 100% repellency. Of the remaining nine essential oils, only 100% *Pelargonium graveolens* (geranium) exhibited >50% repellency (viz. 57%). *Styrax torkinensis* (benzoin) oil did not exhibit any repellency. These findings show that several aromatic, essential oils of plants may be useful as chigger repellent for the prevention of scrub typhus. *Syzygium aromaticum* oil may be safer and more economical to prevent chigger attacks than commercially available synthetic chemicals, such as DEET that may have harmful side effects.

Scabies

Lancet. 2006 May 27;367(9524):1767-74.

Scabies.

Scabies is a neglected parasitic disease that is a major public health problem in many resource-poor regions. It causes substantial morbidity from secondary infections and post-infective complications such as acute post-streptococcal glomerulonephritis. Disease control requires treatment of the affected individual and all people they have been in contact with, but is often hampered by inappropriate or delayed diagnosis, poor treatment compliance, and improper use of topical compounds such as permethrin, lindane, or benzyl benzoate. In addition to concerns over toxicity with such compounds, parasite resistance seems to be increasing. Oral ivermectin is an alternative that has been used successfully in community control programmes. **Plant derivatives such as turmeric, neem, and tea tree oil are also promising future treatments.** The disease is strongly associated with poverty and overcrowding, and the associated stigma can ostracise affected individuals. Treatment of scabies in poor countries needs to integrate drug treatment programmes with efforts to improve the socioeconomic conditions and education programmes to reduce stigma. We expect the future to bring more sensitive and specific clinical and laboratory-based diagnostic methods, as well as new therapeutic strategies.

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Warts

Complement Ther Clin Pract. 2008 Nov;14(4):225-7.

Successful topical treatment of hand warts in a paediatric patient with tea tree oil (*Melaleuca alternifolia*).

Tea tree oil (TTO) (*Melaleuca alternifolia*) has been used recently as an effective topical application for the treatment of skin infections due to a variety of aetiological microbial agents, including mainly bacterial infections. We detail the first report in the peer-reviewed literature of the successful treatment with TTO of a paediatric patient with warts on her right middle finger. TTO was applied topically once daily to the lesions for 12 days, with a successful outcome, including complete re-epithelization of the infected areas. The case highlights the potential use of TTO in the treatment of common warts due to human papilloma virus.

Dandruff

J Am Acad Dermatol. 2002 Dec;47(6):852-5.

Treatment of dandruff with 5% tea tree oil shampoo.

BACKGROUND: Dandruff appears to be related to the yeast *Pityrosporum ovale*. Tea tree oil has antifungal properties with activity against *P ovale* and may be useful in the treatment of dandruff.

OBJECTIVE: We conducted a randomized, single-blind, parallel-group study to investigate the efficacy and tolerability of 5% tea tree oil and placebo in patients with mild to moderate dandruff.

METHODS: One hundred twenty-six male and female patients, aged 14 years and older, were randomly assigned to receive either 5% tea tree oil shampoo or placebo, which was used daily for 4 weeks. The dandruff was scored on a quadrant-area-severity scale and by patient self-assessment scores of scaliness, itchiness, and greasiness.

RESULTS: The 5% tea tree oil shampoo group showed a 41% improvement in the quadrant-area-severity score compared with 11% in the placebo group ($P < .001$). Statistically significant improvements were also observed in the total area of involvement score, the total severity score, and the itchiness and greasiness components of the patients' self-assessments. The scaliness component of patient self-assessment improved but was not statistically significant. There were no adverse effects.

CONCLUSION: Five percent tea tree oil appears to be effective and well tolerated in the treatment of dandruff.

Athlete's Foot

Australas J Dermatol. 2002 Aug;43(3):175-8.

Treatment of interdigital tinea pedis with 25% and 50% tea tree oil solution: a randomized, placebo-controlled, blinded study.

Tea tree oil has been shown to have activity against dermatophytes in vitro. We have conducted a randomized, controlled, double-blinded study to determine the efficacy and safety of 25% and 50% tea tree oil in the treatment of interdigital tinea pedis. One hundred and fifty-eight patients with tinea pedis clinically and microscopy suggestive of a dermatophyte infection were randomized to receive either placebo, 25% or 50% tea tree oil solution. Patients applied the solution twice daily to affected areas for 4 weeks and were reviewed after 2 and 4 weeks of treatment. There was a marked clinical response seen in

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68% of the 50% tea tree oil group and 72% of the 25% tea tree oil group, compared to 39% in the placebo group. Mycological cure was assessed by culture of skin scrapings taken at baseline and after 4 weeks of treatment. The mycological cure rate was 64% in the 50% tea tree oil group, compared to 31% in the placebo group. Four (3.8%) patients applying tea tree oil developed moderate to severe dermatitis that improved quickly on stopping the study medication.

Wound Healing

J Altern Complement Med. 2013 Dec;19(12):942-5.

The effect of tea tree oil (*Melaleuca alternifolia*) on wound healing using a dressing model.

Numerous studies have shown the promising antibacterial effects of *Melaleuca alternifolia*, or tea tree essential oil. The study detailed here replicates in humans a 2004 in vitro study that used a dressing model over Petri dishes to determine the antimicrobial effects of the fumes of tea tree essential oil. The current study used the same dressing model with patients who had wounds infected with *Staphylococcus aureus*. Ten participants volunteered for the quasi-experimental study, and four of the 10 were used as matched participants to compare wound healing times between conventional treatment alone and conventional treatment plus fumes of tea tree essential oil. The results demonstrated decreased healing time in all but one of the participants treated with tea tree oil. The differences between the matched participants were striking. The results of this small investigational study indicate that additional study is warranted.

Am J Infect Control. 2004 Nov;32(7):402-8.

Staphylococcus aureus and wounds: a review of tea tree oil as a promising antimicrobial.

Antibiotic-resistant bacteria continue to be a major health concern worldwide. In particular, *Staphylococcus aureus*, both methicillin-resistant and -sensitive, are of concern in their ability to cause difficult skin and underlying tissue infections. *Melaleuca alternifolia* (tea tree oil), an essential oil, has demonstrated promising efficacy in treating these infections. Tea tree oil has been used for centuries as a botanical medicine, and has only in recent decades surfaced in the scientific literature as a promising adjunctive wound treatment. Tea tree oil is antimicrobial, anti-inflammatory, and has demonstrated ability to activate monocytes. There are few apparent side effects to using tea tree oil topically in low concentrations, with contact dermatitis being the most common. Tea tree oil has been effective as an adjunctive therapy in treating osteomyelitis and infected chronic wounds in case studies and small clinical trials. There is a need for larger clinical trials to further examine efficacy of tea tree oil as an adjunctive wound therapy, as well as improved guidelines for developing plant-based medicines.

Acta Cir Bras. 2015 Jun;30(6):401-6.

Antimicrobial activity of *Melaleuca* sp. oil against clinical isolates of antibiotics resistant *Staphylococcus aureus*.

PURPOSE: To extract the *Melaleuca* sp. oil and to assess its in vitro inhibitory effect against *Staphylococcus aureus* isolates obtained from lower limb wounds and resistant to several antibiotics.

METHODS: A total of 14 test-tubes containing Mueller-Hinton broth were used to determine the Minimum Inhibitory Concentration (MIC). The following concentrations of the *Melaleuca* sp. oil were added to the first 11 tubes: 8; 4; 2; 1; 0.5; 0.2; 0.1; 0.05; 0.025; 0,0125 and 0.00625%. The 12th and 13th tubes, with and without oil, were used as the positive and negative controls, respectively. The experimental study was carried out in triplicate at 37°C for 18 hours. The Minimum Bactericidal Concentration (MBC),

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able of killing all the microorganisms, was also determined. Two *S. aureus* isolates were obtained from lower limb wounds of female patients and the identification of the microorganisms (*Staphylococcus aureus*) and the test for susceptibility to the antimicrobial agents were carried out by automation using the apparatus MicroScan(r). After identification, the isolates were preserved in liquid Trypticase Soy medium, and inoculated for determination of the MIC and MBC.

RESULTS: The MIC was 0.2% and the MBC was 0.4%.

CONCLUSION: The *Melaleuca* sp. oil showed antimicrobial properties in vitro against strains isolated from lower limb wounds which were resistant to multiple antibiotics.

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Lice

Med Parazitol (Mosk). 2014 Apr-Jun;(2):37-42.

[Pediculicidal activity of plant essential oils and their based preparations].

The pediculicidal activity of eight plant essential oils in 75% isopropyl alcohol was in vitro investigated. Of them, the substances that were most active against lice were tea tree (*Melaleuca*), eucalyptus, neem, citronella (*Cymbopogon nardus*), and clove (*Syzygium aromaticum*) oils; KT50 was not more than 3 minutes on average; KT95 was 4 minutes. After evaporating the solvent, only five (tea tree, cassia, clove, anise (*Anisum vulgare*), and Japanese star anise (*Illicium anisatum*) oils) of the eight test botanical substances were active against lice. At the same time, KT50 and KT95 showed 1.5-5-fold increases. Citronella and anise oils had incomplete ovicidal activity. Since the lice were permethrin-resistant, the efficacy of preparations based on essential oils was much higher than permethrin.

Parasitol Res. 2012 Nov;111(5):1985-92.

Activity of tea tree oil and nerolidol alone or in combination against *Pediculus capitis* (head lice) and its eggs.

Head lice infestation is an emerging social problem in undeveloped and developed countries. Because of louse resistance increasing, several long-used insecticidal compounds have lost their efficacy, and alternatives, such as essential oils, have been proposed to treat this parasitic infestation. The present study investigated the efficacy of two natural substances: tea tree (*Melaleuca alternifolia*) oil and nerolidol (3,7,11-trimethyl-1,6,10-dodecatrien-3-ol) against lice and its eggs. Products were used alone and in combination (ratio 1:1 and 1:2) from 8 % dilution. The in vitro effect of natural substances at different concentrations were evaluated against 69 head lice (adults and nymphs) and 187 louse eggs collected from school children in Chieti-Pescara (Central Italy) over a 6-month period. The lice mortality was evaluated for 24 h by a stereo light microscope. The ovicidal activity was monitored by microscopic inspections for 15 days. Tea tree oil was more effective than nerolidol against head lice with 100 % mortality at 30 min and 1 % concentration. On the contrary, nerolidol expressed a more pronounced ovicidal activity inducing the failure of 50 % of the eggs to hatch at 1 % concentration after 4 days; the same effect was achieved by using a twice concentration of tea tree oil. The association of the two substances both in ratios 1:1 and 1:2 combined efficaciously their insecticidal and ovicidal effect; in particular, the ratio 1:2 (tea tree oil 0.5 % plus nerolidol 1 %) acted producing both the death of all head lice at 30 min and the abortive effect of louse eggs after 5 days. These results offer new potential application of natural compounds and display a promising scenario in the treatment of pediculosis resistant cases. The development of novel pediculicides containing essential oils could be, in fact, an important tool to control the parasitic infestation.

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BMC Dermatol. 2011 Aug 24;11:14.

An ex vivo, assessor blind, randomised, parallel group, comparative efficacy trial of the ovicidal activity of three pediculicides after a single application--melaleuca oil and lavender oil, eucalyptus oil and lemon tea tree oil, and a "suffocation" pediculicide.

BACKGROUND: There are two components to the clinical efficacy of pediculicides: (i) efficacy against the crawling-stages (lousicidal efficacy); and (ii) efficacy against the eggs (ovicidal efficacy). Lousicidal efficacy and ovicidal efficacy are confounded in clinical trials. Here we report on a trial that was specially designed to rank the clinical ovicidal efficacy of pediculicides. Eggs were collected, pre-treatment and post-treatment, from subjects with different types of hair, different coloured hair and hair of different length.

METHOD: Subjects with at least 20 live eggs of *Pediculus capitis* (head lice) were randomised to one of three treatment-groups: a melaleuca oil (commonly called tea tree oil) and lavender oil pediculicide (TTO/LO); a eucalyptus oil and lemon tea tree oil pediculicide (EO/LTTO); or a "suffocation" pediculicide. Pre-treatment: 10 to 22 live eggs were taken from the head by cutting the single hair with the live egg attached, before the treatment (total of 1,062 eggs).

TREATMENT: The subjects then received a single treatment of one of the three pediculicides, according to the manufacturers' instructions. Post-treatment: 10 to 41 treated live eggs were taken from the head by cutting the single hair with the egg attached (total of 1,183 eggs). Eggs were incubated for 14 days. The proportion of eggs that had hatched after 14 days in the pre-treatment group was compared with the proportion of eggs that hatched in the post-treatment group. The primary outcome measure was % ovicidal efficacy for each of the three pediculicides.

RESULTS: 722 subjects were examined for the presence of eggs of head lice. 92 of these subjects were recruited and randomly assigned to: the "suffocation" pediculicide (n = 31); the melaleuca oil and lavender oil pediculicide (n = 31); and the eucalyptus oil and lemon tea tree oil pediculicide (n = 30 subjects). The group treated with eucalyptus oil and lemon tea tree oil had an ovicidal efficacy of 3.3% (SD 16%) whereas the group treated with melaleuca oil and lavender oil had an ovicidal efficacy of 44.4% (SD 23%) and the group treated with the "suffocation" pediculicide had an ovicidal efficacy of 68.3% (SD 38%).

CONCLUSION: Ovicidal efficacy varied substantially among treatments, from 3.3% to 68.3%. The "suffocation" pediculicide and the melaleuca oil and lavender oil pediculicide (TTO/LO) were significantly more ovicidal than eucalyptus oil and lemon tea tree oil pediculicide (EO/LTTO) ($P < 0.0001$). Ranking: 1. "Suffocation" pediculicide (68.3% efficacy against eggs); 2. Melaleuca oil and lavender oil (44.4%) pediculicide; 3. Eucalyptus oil and lemon tea tree oil (3.3%) pediculicide. The "suffocation" pediculicide and TTO/LO are also highly efficacious against the crawling-stages. Thus, the "suffocation" pediculicide and TTO/LO should be recommended as first line treatments.

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BMC Dermatol. 2010 Aug 20;10:6.

A randomised, assessor blind, parallel group comparative efficacy trial of three products for the treatment of head lice in children--melaleuca oil and lavender oil, pyrethrins and piperonyl butoxide, and a "suffocation" product.

BACKGROUND: There are many different types of pediculicides available OTC in Australia. In this study we compare the efficacy and safety of three topical pediculicides: a pediculicide containing melaleuca oil

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(tea tree oil) and lavender oil (TTO/LO); a head lice "suffocation" product; and a product containing pyrethrins and piperonyl butoxide (P/PB).

METHOD: This study was a randomised, assessor-blind, comparative, parallel study of 123 subjects with live head lice. The head lice products were applied according to the manufacturer's instructions (the TTO/LO product and the "suffocation" product were applied three times at weekly intervals according to manufacturers instructions (on Day 0, Day 7 and Day 14) and the P/PB product was applied twice according to manufacturers instructions (on Day 0 and Day 7)). The presence or absence of live lice one day following the last treatment was determined.

RESULTS: The percentage of subjects who were louse-free one day after the last treatment with the product containing tea tree oil and lavender oil (41/42; 97.6%) and the head lice "suffocation" product (40/41, 97.6%) was significantly higher compared to the percentage of subjects who were louse-free one day after the last treatment with the product containing pyrethrins and piperonyl butoxide (10/40, 25.0%; adj. $p < 0.0001$).

CONCLUSION: The high efficacy of the TTO/LO product and the head lice "suffocation" product offers an alternative to the pyrethrins-based product.

Free PMC Article

Fitoterapia. 2007 Dec;78(7-8):521-5. Epub 2007 Jul 3.

An investigation and comparison of the bioactivity of selected essential oils on human lice and house dust mites.

The insecticidal potency of some essential oils suggests that they may find an application in the control of house dust mites, but current in vitro assays for mites do not appear to give consistent results. A simple, novel, mite chamber assay was therefore developed to carry out testing. Different species of insects are susceptible to different essential oil components, so we compared the relative acaricidal and pediculicidal activity of three essential oils: tea tree, lavender and lemon, because the activity of their constituents on lice ranges from highly active to virtually inactive. The most effective essential oil against both lice and mites was tea tree oil; lavender was the second most effective, and lemon oil the least, although it did show activity against mites, unlike lice. The assay proved simple and effective and gave reproducible results.

Periodontal & Oral Health

J Indian Soc Periodontol. 2013 Jul;17(4):444-8.

Effect of local application of tea tree (*Melaleuca alternifolia*) oil gel on long pentraxin level used as an adjunctive treatment of chronic periodontitis: A randomized controlled clinical study.

BACKGROUND: Conventional non-surgical periodontal therapy has been proven to be an effective treatment for patients with chronic periodontitis. Tea tree oil (TTO) can be used as adjunct to conventional periodontal therapy in patient with chronic periodontitis. The aim of this study was to evaluate the effectiveness of adjunctive treatment of TTO on the clinical parameters and the level of pentraxin-3 (PTX3) in chronic periodontitis.

MATERIALS AND METHODS: A total of 40 patients with moderate to severe chronic periodontitis were divided into two groups, Group I received scaling and root planing (SRP) only, Group II received SRP and TTO gel. Clinical parameters were recorded and gingival crevicular fluid (GCF) samples were collected from each subject for measuring PTX3 levels at baseline, 1, 3 and 6 months after treatment.

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RESULTS: In all evaluation periods, there was statistically significant reduction in each of the studied clinical parameters and PTX3 level in Group II as compared with Group I.

CONCLUSIONS: The local delivery of TTO gel in case of chronic periodontitis may have some beneficial effects to augment the results of the conventional periodontal therapy. Moreover, it places a focus on the value of monitoring GCF levels of PTX3 as a marker of periodontal tissue healing.

Free PMC Article

Indian J Dent. 2014 Oct;5(4):183-9.

Evaluation of antimicrobial efficacy of garlic, tea tree oil, cetylpyridinium chloride, chlorhexidine, and ultraviolet sanitizing device in the decontamination of toothbrush.

OBJECTIVE: To assess and compare the efficacy of 3% garlic extract, 0.2% tea tree oil, 0.2% chlorhexidine, 0.05% cetylpyridinium chloride, and ultraviolet (UV) toothbrush sanitizing device as toothbrush disinfectants against *Streptococcus mutans*.

MATERIALS AND METHODS: A double blind randomized controlled parallel study was done on 210 dental students. The subjects were divided into one control group using distilled water and five study groups representing 0.2% tea tree oil, 3% garlic extract, 0.2% chlorhexidine gluconate, 0.05% cetylpyridinium chloride and UV toothbrush sanitizing device. Participants were provided with new toothbrushes and toothpastes for both baseline and intervention phases. The toothbrushes were collected after two weeks for microbial analysis in both phases. The data were analysed and compared using appropriate statistical analysis.

RESULTS: On comparing pre- and post-intervention, *S. mutans* colony counts, a highly significant ($P < 0.001$) difference was observed in all the groups. Differences of 77.74 colony forming units (CFU) in tea tree oil group, 102.87 CFU in garlic group, 68.13 CFU in chlorhexidine group, 82.47 CFU in cetylpyridinium group and 42.67 CFU in UV toothbrush sanitizer group were observed. Garlic group showed the highest reduction (100%) whereas UV toothbrush sanitizer group showed the least reduction (47.4%) in *S. mutans* colonies.

CONCLUSIONS: The antimicrobial agents used in this study effectively reduced the *S. mutans* counts and hence can be considered as toothbrush disinfectants to prevent dental caries. The 3% garlic was the most effective among the antimicrobial agents.

Phytother Res. 2007 Jul;21(7):641-3.

Reduction of mouth malodour and volatile sulphur compounds in intensive care patients using an essential oil mouthwash.

The aim of this study was to explore the effect of an essential oil solution on levels of malodour and production of volatile sulphur compounds (VSC) in patients nursed in intensive care unit (ICU). Thirty two patients received 3 min of oral cleaning using an essential oil solution (mixture of tea tree, *Melaleuca alternifolia*, peppermint, *Mentha piperita* and lemon, *Citrus limon*) on the first day, and Tantum (benzylamine hydrochloride) on the second day. Two trained nurses measured the level of malodour with a 10 cm visual analogue scale (VAS) and VSC with a Halimeter before (Pre), 5 min after (Post I) and 1 h following treatment (Post II). The level of oral malodour was significantly different following the essential oil session, and differed significantly between two sessions at Post I ($p < 0.005$) and Post II ($p < 0.001$). Differences between the two sessions were significant (Tantum, $p < 0.001$; essential oil, $p < 0.001$) in the level of VSC and significantly lower in the essential oil session than Tantum at the Post II ($p < 0.05$).

These findings suggest that mouth care using an essential oil mixture of diluted tea tree, peppermint and lemon may be an effective method to reduce malodour and VSC in intensive care unit patients.

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Oral Microbiol Immunol. 2003 Dec;18(6):389-92.

Susceptibility of oral bacteria to Melaleuca alternifolia (tea tree) oil in vitro.

The in vitro activity of Melaleuca alternifolia (tea tree) oil against 161 isolates of oral bacteria from 15 genera was determined. Minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) ranged from 0.003 to 2.0% (v/v). MIC90 values were 1.0% (v/v) for Actinomyces spp., Lactobacillus spp., Streptococcus mitis and Streptococcus sanguis, and 0.1% (v/v) for Prevotella spp. Isolates of Porphyromonas, Prevotella and Veillonella had the lowest MICs and MBCs, and isolates of Streptococcus, Fusobacterium and Lactobacillus had the highest. Time kill studies with Streptococcus mutans and Lactobacillus rhamnosus showed that treatment with > or = 0.5% tea tree oil caused decreases in viability of >3 log colony forming units/ml after only 30 s, and viable organisms were not detected after 5 min. These studies indicate that a range of oral bacteria are susceptible to tea tree oil, suggesting that tea tree oil may be of use in oral healthcare products and in the maintenance of oral hygiene.

Aust Dent J. 2004 Jun;49(2):78-83.

The effects of a tea tree oil-containing gel on plaque and chronic gingivitis.

BACKGROUND: [corrected] This clinical study assessed the effects of topically applied tea tree oil (TTO)-containing gel on dental plaque and chronic gingivitis.

METHODS: This was a double-blind, longitudinal, non-crossover study in 49 medically fit non-smokers (24 males and 25 females) aged 18-60 years with severe chronic gingivitis. Subjects were randomly assigned to three groups and given either TTO-gel (2.5 per cent), chlorhexidine (CHX) gel (0.2 per cent), or a placebo gel to apply with a toothbrush twice daily. Treatment effects were assessed using the Gingival Index (GI), Papillary Bleeding Index (PBI) and plaque staining score (PSS) at four and eight weeks.

RESULTS: No adverse reactions to any of the gels were reported. The data were separated into subsets by tooth (anterior and posterior) and tooth surface (buccal and lingual). The TTO group had significant reduction in PBI and GI scores. However, TTO did not reduce plaque scores, which tended to increase over the latter weeks of the study period.

CONCLUSION: Although further studies are required, the anti-inflammatory properties of TTO-containing gel applied topically to inflamed gingival tissues may prove to be a useful non-toxic adjunct to chemotherapeutic periodontal therapy.

Schweiz Monatsschr Zahnmed. 2003;113(9):985-96.

[Effect of mouthwashing with tea tree oil on plaque and inflammation].

[Article in French, German]

The tea tree oil (melaleuca alternifolia) has antiseptic, fungicide and bactericide effects. The efficiency against oral bacteria was also evident. Xylitol is known for counterattacking the cariogenic effect caused by the streptococcus mutans. Less plaque was developed during the time of the study.

Schweiz Monatsschr Zahnmed. 2000;110(11):125-30.

[Antimicrobial effects of tea tree oil (Melaleuca alternifolia) on oral microorganisms].

[Article in German]

The essential oil of Melaleuca alternifolia (tea tree oil) exhibits antimicrobial activity against a wide range of Gram-positive and Gram-negative bacteria, yeasts and fungi. In this study the bacteriostatic and bacteriocidal/fungicidal activity of a tea tree oil solution, of a new tea tree oil (Tebodont) and the respective placebo-gel, of a chlorhexidindigluconate-solution and of PlakOut was tested in vitro against ten different oral microorganisms. Minimum inhibitory concentrations were in the range from 0.0293% to

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1.25% for the tea tree oil solution and from 0.0082% to 1.25% for the tea tree oil gel. The values for minimum bacteriocidal/fungicidal concentrations were in the range from 0.0521% to 2.5% for the tea tree oil solution and from <0.0098% to 3.33% for the tea tree oil gel. The most susceptible microorganisms were Actinobacillus actinomycetemcomitans, Fusobacterium nucleatum, and Porphyromonas gingivalis, whereas Streptococcus mutans and Prevotella intermedia were the least susceptible ones. Both for the chlorhexidindigluconate solution and for PlakOut the values for the minimal inhibitory concentration and for the minimal cidal concentration were between <0.0002% and 0.0125%.

Clin Lab. 2015;61(1-2):61-8.

Antimicrobial effect of Australian antibacterial essential oils as alternative to common antiseptic solutions against clinically relevant oral pathogens.

BACKGROUND: The aim of the study was to examine the in vitro antibacterial activity of different oils in comparison to antiseptics against oral microorganisms.

METHODS: The antimicrobial effect of tea tree oil (TTO), eucalyptus oil (EO), lemon grass oil (LGO), and a eucalyptus-based oil mixture (MXT) were tested in comparison to chlorhexidine digluconate (CHX), povidone-iodine (BTA), and octenidine dihydrochloride (OCT). Oral bacterial strains and candida species using the agar diffusion test were used for the antimicrobial study.

RESULTS: All tested oils showed antimicrobial potency against the tested biological indicators. In comparison of all tested substances the largest effective zones were measured for LGO, followed from MXT and CHX. TTO and EO were less effective against the tested microorganisms followed from BTA.

CONCLUSIONS: The results of this study show that some essential oils have better antimicrobial properties than standard oral antiseptics. In a follow-up step, the ideal concentrations, the composition of essential oils, and the mode of application will be evaluated. The antibacterial efficacy of essential oils might be promising for use in clinical and oral hygiene applications. The cost reduction and availability particularly in rural areas with easy access to the originating plants might be advantageous factors to be considered.

J Indian Soc Periodontol. 2014 May;18(3):316-20.

A comparative study of antiplaque and antigingivitis effects of herbal mouthrinse containing tea tree oil, clove, and basil with commercially available essential oil mouthrinse.

BACKGROUND: The relatively safe nature and cost-effectiveness of herbal extracts have led to a resurgent interest in their utility as therapeutic agents. Therefore, this prospective, double-blind, randomly controlled clinical trial was designed to compare the antiplaque and antigingivitis effects of newly formulated mouthrinse containing tea tree oil (TTO), clove, and basil with those of commercially available essential oil (EO) mouthrinse.

MATERIALS AND METHODS: Forty patients were selected for a 21-day study period and randomly divided into two groups. The test group patients were given newly formulated herbal mouthrinse and the control group patients were given commercially available EO mouthrinse. The Plaque Index (PI), Gingival Index (GI), and Papillary Marginal Attachment (PMA) Index were recorded at baseline, 14 days, and 21 days. The microbial colony forming units (CFU) were assessed at baseline and 21 days.

RESULTS: Test group patients using herbal mouthrinse showed significant improvement in GI (0.16), PI (0.57), and PMA (0.02) scores. These improvements were comparable to those achieved with commercially available EO mouthrinse. However, the aerobic and anaerobic CFU of microbiota were reduced with the herbal mouthrinse (P = 0.0000).

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CONCLUSION: The newly formulated herbal mouthrinse and commercially available mouthrinse were beneficial clinically as antiplaque and antigingivitis agents. Newly formulated mouthrinses showed significant reduction in microbial CFU at 21 days. So, our findings support the regular use of herbal mouthrinse as an antiplaque, antigingivitis, and antimicrobial rinse for better efficacy.

Free PMC Article

Eur J Dent. 2013 Sep;7(Suppl 1):S71-7.

Antimicrobial efficacy of five essential oils against oral pathogens: An in vitro study.

OBJECTIVES: This study was aimed to find out the minimum inhibitory concentration (MIC) of five essential oils against oral pathogens and to find out the minimum bactericidal concentration (MBC) and minimum fungicidal concentration (MFC) of five essential oils against oral pathogens.

MATERIALS AND METHODS: The antimicrobial activities by detecting MIC and MBC/MFC of five essential oils such as tea tree oil, lavender oil, thyme oil, peppermint oil and eugenol oil were evaluated against four common oral pathogens by broth dilution method. The strains used for the study were *Staphylococcus aureus* ATCC 25923, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922 and *Candida albicans* ATCC 90028.

RESULTS: Out of five essential oils, eugenol oil, peppermint oil, tea tree oil exhibited significant inhibitory effect with mean MIC of 0.62 ± 0.45 , 9.00 ± 15.34 , 17.12 ± 31.25 subsequently. Mean MBC/MFC for tea tree oil was 17.12 ± 31.25 , for lavender oil 151.00 ± 241.82 , for thyme oil 22.00 ± 12.00 , for peppermint oil 9.75 ± 14.88 and for eugenol oil 0.62 ± 0.45 . *E. faecalis* exhibited low degree of sensitivity compared with all essential oils.

CONCLUSION: Peppermint, tea tree and thyme oil can act as an effective intracanal antiseptic solution against oral pathogens.

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Rheumatoid Arthritis

Pharmacogn Mag. 2015 May;11(Suppl 1):S190-208.

The potential of selected Australian medicinal plants with anti-Proteus activity for the treatment and prevention of rheumatoid arthritis.

BACKGROUND: A wide variety of herbal medicines are used in indigenous Australian traditional medicinal systems to treat rheumatoid arthritis (RA) and inflammation. The current study was undertaken to test the ability of a panel of Australian plants with a history of the ethnobotanical usage in the treatment of inflammation for the ability to block the microbial trigger of RA.

MATERIALS AND METHODS: One hundred and six extracts from 40 plant species were investigated for the ability to inhibit the growth of the bacterial trigger of RA (*Proteus mirabilis*). The extracts were tested for toxicity in the *Artemia nauplii* bioassay. The most potent inhibitor of *P. mirabilis* growth was further analyzed by reversed-phase high performance liquid chromatography (RP-HPLC) coupled to high accuracy time-of-flight (TOF) mass spectroscopy.

RESULTS: Sixty-five of the 106 extracts tested (61.3%) inhibited the growth of *P. mirabilis*. The *Aleurites moluccanus*, *Datura leichardtii*, *Eucalyptus major*, *Leptospermum bracteata*, *L. juniperium*, *Macadamia integriflora* nut, *Melaleuca alternifolia*, *Melaleuca quinquenervia*, *Petalostigma pubescens*, *P. trilocolae*, *P. augustifolium*, *Scaevola spinescens*, *Syzygium australe*, and *Tasmania lanceolata* extracts were determined to be the most effective inhibitors of *P. mirabilis* growth, with minimum inhibitory

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concentration (MIC) values generally significantly below 1000 µg/ml. *T. lanceolata* fruit extracts were the most effective *P. mirabilis* growth inhibitors, with a MIC values of 11 and 126 µg/ml for the methanolic and aqueous extracts, respectively. Subsequent analysis of the *T. lanceolata* fruit extracts by RP-HPLC coupled to high-resolution TOF mass spectroscopy failed to detect resveratrol in either *T. lanceolata* fruit extract. However, the resveratrol glycoside piceid and 2 combretastatin stilbenes (A-1 and A-4) were detected in both *T. lanceolata* fruit extracts. With the exception of the *Eucalyptus* and *Syzygium* extracts, all extracts exhibiting *Proteus* inhibitory activity were also shown to be nontoxic, or of low toxicity in the *Artemia nauplii* bioassay.

CONCLUSIONS: The low toxicity of these extracts and their inhibitory bioactivity against *Proteus* spp. indicate their potential in blocking the onset of rheumatoid arthritis.

Free PMC Article

Toxicity

Food Chem Toxicol. 2006 May;44(5):616-25. Epub 2005 Oct 21.

A review of the toxicity of *Melaleuca alternifolia* (tea tree) oil.

The essential oil of *Melaleuca alternifolia*, also known as tea tree or melaleuca oil, is widely available and has been investigated as an alternative antimicrobial, anti-inflammatory and anti-cancer agent. While these properties are increasingly well characterised, relatively limited data are available on the safety and toxicity of the oil. Anecdotal evidence from almost 80 years of use suggests that the topical use of the oil is relatively safe, and that adverse events are minor, self-limiting and occasional. Published data indicate that TTO is toxic if ingested in higher doses and can also cause skin irritation at higher concentrations. Allergic reactions to TTO occur in predisposed individuals and may be due to the various oxidation products that are formed by exposure of the oil to light and/or air. Adverse reactions may be minimised by avoiding ingestion, applying only diluted oil topically and using oil that has been stored correctly. Data from individual components suggest that TTO has the potential to be developmentally toxic if ingested at higher doses, however, TTO and its components are not genotoxic. The limited ecotoxicity data available indicate that TTO is toxic to some insect species but more studies are required.

Pediatr Emerg Care. 2003 Jun;19(3):169-71.

Ingestion of tea tree oil (*Melaleuca* oil) by a 4-year-old boy.

A 4-year-old boy ingested a small quantity of tea tree oil. Within 30 minutes, he became ataxic and shortly thereafter progressed to unresponsiveness; he was endotracheally intubated by paramedics. His neurologic status improved gradually over 10 hours, and he remains well on follow-up. Tea tree oil is an increasingly popular topical antiseptic that is available in a wide variety of products, often without warning labels. Healthcare providers should be aware of the common uses of tea tree oil, as well as its potential toxicity.

Vet Hum Toxicol. 1994 Apr;36(2):139-42.

Toxicity of melaleuca oil and related essential oils applied topically on dogs and cats.

Cases of melaleuca oil toxicosis have been reported by veterinarians to the National Animal Poison Control Center when the oil was applied dermally to dogs and cats. In most cases, the oil was used to treat dermatologic conditions at inappropriate high doses. The typical signs observed were depression, weakness, incoordination and muscle tremors. The active ingredients of commercial melaleuca oil are

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predominantly cyclic terpenes. Treatment of clinical signs and supportive care has been sufficient to achieve recovery without sequelae within 2-3 d.

Antioxidant

J Agric Food Chem. 2004 May 19;52(10):2849-54.

Evaluation of antioxidant activity of Australian tea tree (*Melaleuca alternifolia*) oil and its components.

Antioxidant activity of Australian tea tree (*Melaleuca alternifolia*) oil (TTO) was determined using two different assays. In the 2,2-diphenyl-1-picrylhydrazyl assay, 10 microL/mL crude TTO in methanol had approximately 80% free radical scavenging activity, and in the hexanal/hexanoic acid assay, 200 microL/mL crude TTO exhibited 60% inhibitory activity against the oxidation of hexanal to hexanoic acid over 30 days. These results were equivalent to the antioxidant activities of 30 mM butylated hydroxytoluene in both tests at the same experimental conditions. This indicated that the TTO could be a good alternative antioxidant. Inherent antioxidants, i.e., alpha-terpinene, alpha-terpinolene, and gamma-terpinene, in the crude TTO were separated and identified chromatographically using silica gel open chromatography, C(18)-high-pressure liquid chromatography, and gas chromatography-mass spectrometry. Their antioxidant activities decreased in the following order in both assays: alpha-terpinene > alpha-terpinolene > gamma-terpinene.

Inflammation

Exp Biol Med (Maywood). 2007 Mar;232(3):420-6.

Mechanisms involved in the anti-inflammatory action of inhaled tea tree oil in mice.

Tea tree oil (TTO) is well known as an antimicrobial and immunomodulatory agent. In the present study we confirmed the anti-inflammatory properties of TTO and investigated the involvement of the hypothalamic-pituitary-adrenal (HPA) axis in the immunomodulatory action of TTO administered by inhalation. Sexually mature, 6-8-week-old, C(57)BI(10) x CBA/H (F(1)) male mice were used. One group of animals was injected intra-peritoneally (ip) with Zymosan to elicit peritoneal inflammation and was then submitted to four sessions of TTO inhalation (15 mins each). Some of the mice were simultaneously injected ip with Antalarmin, a CRH-1 receptor antagonist, to block HPA axis functions. Twenty-four hours after the injections the mice were killed by CO(2) asphyxia, and peritoneal leukocytes (PTLs) were isolated and counted. Levels of reactive oxygen species (ROS) and cyclooxygenase (COX) activity in PTLs were assessed by fluorimetric and colorimetric assays, respectively. The results obtained show that sessions of TTO inhalation exert a strong anti-inflammatory influence on the immune system stimulated by Zymosan injection, while having no influence on PTL number, ROS level, and COX activity in mice without inflammation. The HPA axis was shown to mediate the anti-inflammatory effect of TTO; Antalarmin abolished the influence of inhaled TTO on PTL number and their ROS production in mice with experimental peritonitis, but it had no effect on these parameters in mice without inflammation.

Handwashing

J Hosp Infect. 2005 Mar;59(3):220-8.

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Effectiveness of hand-cleansing formulations containing tea tree oil assessed ex vivo on human skin and in vivo with volunteers using European standard EN 1499.

The efficacy of formulations containing tea tree oil (TTO) has been assessed in vitro in previous studies. Products that passed the European suspension test guidelines were investigated further in this study, in vivo with volunteers using the European handwashing method (EN 1499) and ex vivo using freshly excised human skin samples. The activity of 5% TTO in 0.001% Tween 80, in a hygienic skin wash (HSW) and in an alcoholic hygienic skin wash (AHSW) was investigated and compared with that of a non-medicated soft soap (SS, control). These formulations were assessed against Escherichia coli K12 as recommended by the European standard. In-vivo results showed that 5% TTO in Tween 80 and the AHSW were significantly more active than the SS after 1 min of handwashing. When assessed ex vivo, these two products were also significantly more active than the reference soap after 1 min of rubbing. Both methods showed that 5% TTO in Tween 80 was generally, although not always, more active than a handwash formulation, and that the AHSW was generally more active than the HSW, although this difference was not significant. The formulations tested, as well as the SS, were more active when assessed in vivo than ex-vivo against E. coli, although only the SS and the HSW were significantly more active in vivo. There appeared to be a pattern in the comparison between ex vivo and in vivo results. The antiseptics tested were, on average, 1.28+/-0.06 times more active when assessed in-vivo than when assessed ex vivo. Nevertheless, the main outcome of the European handwashing method is for the formulation tested to be significantly more active than the SS; both 5% TTO in Tween 80 and the AHSW achieved this both in-vivo and ex-vivo. TTO in Tween 80 and in formulations met the European in-vivo method requirements.

Rev Lat Am Enfermagem. 2013 Nov-Dec;21(6):1212-9.

Comparison of hand hygiene antimicrobial efficacy: Melaleuca alternifolia essential oil versus triclosan.

OBJECTIVE: this study aimed to evaluate the efficacy of hand hygiene performed with two different soap formulations: 0.3% Melaleuca alternifolia essential oil versus 0.5% triclosan, and to compare them with two reference hygiene procedures: the official methodology procedure (soft soap) versus the draft version of the procedure (soft soap + propan-2-ol).

METHOD: using the European EN 1499 method, logarithmic reduction factors were determined for the number of colony forming units of Escherichia coli K12 before and after hand hygiene of 15 volunteer subjects, and compared using the one-tailed Wilcoxon test.

RESULTS: referring to the soft soap, there was no difference between the performance of soap with 0.3% M. alternifolia and soap containing 0.5% triclosan. The soft soap + propan-2-ol proved to be more effective than the other hand hygiene procedures.

CONCLUSION: studies to verify the therapeutic efficacy of essential oil in hand hygiene can improve adherence to this practice.

Free full text

Anti-Fungal

J Appl Microbiol. 2003;95(4):853-60.

Antifungal activity of the components of Melaleuca alternifolia (tea tree) oil.

AIMS: To investigate the in vitro antifungal activity of the components of Melaleuca alternifolia (tea tree) oil.

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METHODS AND RESULTS: Activity was investigated by broth microdilution and macrodilution, and time kill methods. Components showing the most activity, with minimum inhibitory concentrations and minimum fungicidal concentrations of $<$ or $=0.25\%$, were terpinen-4-ol, alpha-terpineol, linalool, alpha-pinene and beta-pinene, followed by 1,8-cineole. The remaining components showed slightly less activity and had values ranging from 0.5 to 2%, with the exception of beta-myrcene which showed no detectable activity. Susceptibility data generated for several of the least water-soluble components were two or more dilutions lower by macrodilution, compared with microdilution.

CONCLUSIONS: All tea tree oil components, except beta-myrcene, had antifungal activity. The lack of activity reported for some components by microdilution may be due to these components becoming absorbed into the polystyrene of the microtitre tray. This indicates that plastics are unsuitable as assay vessels for tests with these or similar components.

SIGNIFICANCE AND IMPACT OF THE STUDY: This study has identified that most components of tea tree oil have activity against a range of fungi. However, the measurement of antifungal activity may be significantly influenced by the test method.

Int J Environ Res Public Health. 2015 Jun 2;12(6):6319-32.

An evaluation of antifungal agents for the treatment of fungal contamination in indoor air environments.

Fungal contamination in indoor environments has been associated with adverse health effects for the inhabitants. Remediation of fungal contamination requires removal of the fungi present and modifying the indoor environment to become less favourable to growth. This may include treatment of indoor environments with an antifungal agent to prevent future growth. However there are limited published data or advice on chemical agents suitable for indoor fungal remediation. The aim of this study was to assess the relative efficacies of five commercially available cleaning agents with published or anecdotal use for indoor fungal remediation. The five agents included two common multi-purpose industrial disinfectants (Cavicide® and Virkon®), 70% ethanol, vinegar (4.0%-4.2% acetic acid), and a plant-derived compound (tea tree (*Melaleuca alternifolia*) oil) tested in both a liquid and vapour form. Tea tree oil has recently generated interest for its antimicrobial efficacy in clinical settings, but has not been widely employed for fungal remediation. Each antifungal agent was assessed for fungal growth inhibition using a disc diffusion method against a representative species from two common fungal genera, (*Aspergillus fumigatus* and *Penicillium chrysogenum*), which were isolated from air samples and are commonly found in indoor air. Tea tree oil demonstrated the greatest inhibitory effect on the growth of both fungi, applied in either a liquid or vapour form. Cavicide® and Virkon® demonstrated similar, although less, growth inhibition of both genera. Vinegar (4.0%-4.2% acetic acid) was found to only inhibit the growth of *P. chrysogenum*, while 70% ethanol was found to have no inhibitory effect on the growth of either fungi. There was a notable inhibition in sporulation, distinct from growth inhibition after exposure to tea tree oil, Virkon®, Cavicide® and vinegar. Results demonstrate that common cleaning and antifungal agents differ in their capacity to inhibit the growth of fungal genera found in the indoor air environment. The results indicate that tea tree oil was the most effective antifungal agent tested, and may have industrial application for the remediation of fungal contamination in residential and occupational buildings.

Med Mycol. 2015 Apr 1;53(3):285-94.

In Vitro activity of *Melaleuca alternifolia* (tea tree) oil on filamentous fungi and toxicity to human cells.

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Invasive fungal wound infections (IFIs) are increasingly reported in trauma patients and cause considerable morbidity and mortality despite standard of care treatment in trauma centers by experienced medical personnel. Topical agents such as oil of melaleuca, also known as tea tree oil (TTO), have been proposed for adjunctive treatment of IFIs. We evaluated the activity of TTO against filamentous fungi associated with IFIs by testing 13 clinical isolates representing nine species via time-kill assay with seven concentrations of TTO (100%, 75%, 50%, 25%, 10%, 5%, and 1%). To ascertain the safety of topical application to wounds, cell viability assays were performed in vitro using human fibroblasts, keratinocytes, osteoblasts, and umbilical vein endothelial cells with 10 concentrations of TTO (75%, 50%, 25%, 10%, 5%, and 10-fold serial dilutions from 1 to 0.0001%) at five time points (5, 15, 30, 60, and 180 min). Compatibility of TTO with explanted porcine tissues was also assessed with eight concentrations of TTO (100%, 75%, 50%, 25%, 10%, 5%, 1%, and 0.1%) at the time points used for cellular assays and at 24 h. The time-kill studies showed that fungicidal activity was variable between isolates. The effect of TTO on cell viability was primarily concentration dependent with significant cytotoxicity at concentrations of = 10% and = 50% for cells lines and whole tissue, respectively. Our findings demonstrate that TTO possesses antifungal activity against filamentous fungi associated with IFIs; furthermore that negligible effects on whole tissues, in contrast to individual cells, were observed following exposure to TTO. Collectively, these findings indicate a potential use of TTO as topical treatment of IFIs.

Gerodontology. 2014 Dec 19.

Comparative evaluation of antifungal action of tea tree oil, chlorhexidine gluconate and fluconazole on heat polymerized acrylic denture base resin - an in vitro study.

OBJECTIVE: Candida albicans-associated denture stomatitis is the most common type of denture stomatitis seen in denture wearers. This study evaluates and compares the antifungal action of fluconazole, chlorhexidine gluconate and tea tree oil on heat-polymerised denture base resin, which has been previously contaminated with C. albicans grown in BHI broth.

MATERIAL AND METHODS: Seventy-five specimens were immersed in BHI broth previously inoculated with C. albicans and stored for 3 h at 37°C. They were divided into five groups (n = 15): G1: 2% chlorhexidine solution; G2: 100% pure pharmaceutical grade tea tree oil; G3: 65 µg/ml fluconazole solution; C1: specimens not disinfected; C2: specimens not contaminated with Candida. Each specimen was then transferred to individual tubes containing BHI broth and incubated for 24 h. Culture media turbidity was evaluated for absorbance over a period of 14 days using a microplate reader. It was observed that the lower the absorbance, the stronger the antimicrobial action. Statistical analysis was performed (two-way anova and Bonferroni test, p < 0.001).

RESULTS: Chlorhexidine and tea tree oil inhibited Candida up to the 14th day, whereas antifungal effect of fluconazole was not significant after the 7th day.

CONCLUSION: Tea tree oil and chlorhexidine gluconate are more effective than fluconazole in inhibiting C. albicans growth on heat-polymerised acrylic resin.

BMC Complement Altern Med. 2014 Dec 15;14:489.

Essential oil of Melaleuca alternifolia for the treatment of oral candidiasis induced in an immunosuppressed mouse model.

BACKGROUND: The search for alternative therapies for oral candidiasis is a necessity and the use of medicinal plants seems to be one of the promising solutions. The objective of this study was to evaluate the in vitro and in vivo effects of the essential oil of Melaleuca alternifolia on Candida albicans.

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METHODS: The minimum inhibitory concentration (MIC) and minimum biofilm eradication concentration (MBEC) of *M. alternifolia* were determined by the broth microdilution assay. For the in vivo study, twelve immunosuppressed mice with buccal candidiasis received topical applications of *M. alternifolia* with MBEC. After treatment, yeasts were recovered from the mice and quantified (CFU/mL). Mice were killed for morphologic analysis of the tongue dorsum by optical and scanning electron microscopy. Data were analyzed using Student's t test or Mann-Whitney test.

RESULTS: The MIC of *M. alternifolia* was 0.195% and the MBEC was 12.5%. Treatment with *M. alternifolia* achieved a 5.33 log reduction in *C. albicans* and reduced the microscopic lesions of candidiasis.

CONCLUSIONS: *M. alternifolia* oil at a 12.5% was effective to eradicate a *C. albicans* biofilm formed in vitro and to reduce yeasts of *C. albicans* in an immunosuppressed mouse model.

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Braz J Microbiol. 2012 Oct;43(4):1347-54.

Inhibitory effect of essential oils against *Trichosporon ovoides* causing Piedra Hair Infection.

Piedra, is an asymptomatic fungal infection of the hair shaft, resulting in the formation of nodules of different hardness on the infected hair. The infection also known as Trichomycosis nodularis is a superficial fungal infection arising from the pathogen being restricted to the stratum corneum with little or no tissue reaction. The nodules are a concretion of hyphae and fruiting bodies of the fungus. Two varieties of Piedra may be seen, Black Piedra and White Piedra. The fungus *Trichosporon ovoides* is involved in the occurrence of both types of Piedras. The purpose of this study was to examine the effectiveness of selected essential oils for the control of growth of the fungus and to determine whether the antifungal effect was due to the major compounds of the oils. Two screening methods viz. Agar well diffusion assay and Minimum Inhibitory Concentration were adopted for the study. MIC and MFC were determined by tube dilution method. Essential oils from Eucalyptus, Ocimum basilicum, Mentha piperita, Cymbopogon flexuosus, Cymbopogon winterians, Trachyspermum ammi, Zingiber officinalis, Citrus limon, Cinnamomum zeylanicum, Salvia sclarea, Citrus aurantifolia, Melaleuca alternifolia, Citrus aurantium, Citrus bergamia, Pogostemon pathchouli, Cedrus atlantica, Jasminum officinale, Juniperus communis, Abelmoschus moschatus, Cyperus scariosus, Palargonium graveolens, Boswellia carterii, Rosa damascene, Vetiveria zizanioides and Commiphora myrrha were evaluated. The essential oils of Cymbopogon winterians, Mentha piperita, Cinnamomum zeylanicum, Melaleuca alternifolia and Eucalyptus globulus were proved to be most effective against the fungus *Trichosporon ovoides*.

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J Environ Biol. 2013 Jan;34(1):17-22.

Screening of some essential oils against *Trichosporon* species.

White Piedra is a superficial mycoses characterized by nodules on the hair shaft, caused by the basidiomycetous yeast *Trichosporon* species. In this study 25 essential oils were extracted and screened against two *Trichosporon* species i.e. *Trichosporon asahii* and *Trichosporon cutaneum*. Both these fungi procured from MTCC Chandigarh were maintained on yeast malt agar plates and tubes at 25 degrees C. Two screening methods viz., agar well diffusion assay and minimum inhibitory concentration were adopted for the study. The results showed that the maximum anti-yeast activity against *T. asahii* and *T. cutaneum* was demonstrated by oil of Mentha piperita showing full inhibition of both the fungi, Melaleuca alternifolia with an inhibition zone of 45 and 40 mm, Cymbopogon winterians with inhibition zone of 45 and 45 mm and Cymbopogon flexuosus with 35 and 30 mm inhibition zones. The oil of Trachyspermum ammi exhibited 10 and 20 mm, Abelmoschus moschatus exhibited 30 and 20 mm, Salvia sclarea showed 20 and

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18 mm and *Jasminum officinale* exhibited 25 and 15 mm inhibition zones showing moderate activity. The oil of *Cyperus scariosus*, *Pogostemon patchouli* and *Rosa damascene* showed no inhibition zone against both the fungi while *Vetiveria zizanoides* exhibited no inhibition in case of *T. asahii* and inhibition zone of 10 mm in case of *T. cutaneum* demonstrating comparatively low activity against both the fungi. These results support that the essential oils can be used to cure superficial mycoses and these oils may have significant role as pharmaceuticals and preservatives.

Phytomedicine. 2009 Nov;16(11):1056-8.

Antifungal activity of tea tree oil from *Melaleuca alternifolia* against *Trichophyton equinum*: an in vivo assay.

Dermatophytes are a group of keratinophilic and keratinolytic molds, some of which are responsible for ringworm. Among them *Trichophyton equinum*, which mostly infects equids, can cause extensive outbreaks in stud farms. The conventional treatment of equine trichophytosis is topical, based upon medicated shampoos to reduce the spread of infection among the animals. Nevertheless the popularity of phytotherapy is at an all-time peak, and the interest for natural alternatives or complements to conventional drug therapy is challenging both in human and veterinary field. Among herbal remedies Tea Tree Oil (TTO) shows a wide range of antimicrobial activities. A randomized open clinical trial was carried out on 60 thoroughbred breeding horses affected by equine ringworm. The animals were randomly divided into 2 groups of 30 subjects. Diagnostic criteria were the presence of clinical signs and positive *T. equinum* culture. Specificity control using TTO mixture in 5 not dermatophyte affected animals was achieved also. The antimycotic activity against *T. equinum* of a mixture containing 25% TTO in sweet almond oil, was evaluated in vivo treating 30 subjects, the others were administered enilconazole 2% solution. The animals of both groups were topically treated twice a day for 15 days with a 25% mixture of TTO diluted in sweet almond oil and every 3 days, four times with enilconazole rinses, respectively. The clinical and mycological outcome were evaluated at day 30 from the start of the treatments. Data analysis was performed by chi square test. All the treated animals showed complete clinical and aetiological healing. Part of control subjects also, showed an improvement and none of them exacerbate the lesions. This therapeutic protocol appears to be effective and versatile, being applicable immediately after physical examination, prior to have the laboratory response. It could be an alternative for practitioners interested in herbal medicines, contributing to fulfill the gap existing between in vitro and clinical studies.

Lett Appl Microbiol. 2007 Jun;44(6):613-8.

In vitro antifungal activity of the tea tree (*Melaleuca alternifolia*) essential oil and its major components against plant pathogens.

AIMS: The aim of this study was to examine the effect of *Melaleuca alternifolia* essential oil (TTO) and its principal components on four cereal-pathogenic fungi.

METHODS AND RESULTS: The antimycotic properties of TTO and of terpinen-4-ol, gamma-terpinen and 1,8-cineole (eucalyptol) were evaluated in vitro on *Fusarium graminearum*, *Fusarium culmorum* and *Pyrenophora graminea*. Moreover, barley leaves infected with *Blumeria graminis* were treated with whole TTO. All the tested fungi were susceptible to TTO and its components.

CONCLUSIONS: TTO exerted a wide spectrum of antimycotic activity. Single TTO purified components were more active than the whole oil in reducing in vitro growth of fungal mycelium and, among the tested compounds, terpinen-4-ol was the most effective.

SIGNIFICANCE AND IMPACT OF THE STUDY: TTO and its components can be considered potential alternative natural fungicides.

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BMC Infect Dis. 2006 Nov 3;6:158.

In vivo activity of terpinen-4-ol, the main bioactive component of Melaleuca alternifolia Cheel (tea tree) oil against azole-susceptible and -resistant human pathogenic Candida species.

BACKGROUND: Recent investigations on the antifungal properties of essential oil of Melaleuca alternifolia Cheel (Tea Tree Oil, TTO) have been performed with reference to the treatment of vaginal candidiasis. However, there is a lack of in vivo data supporting in vitro results, especially regarding the antifungal properties of TTO constituents. Thus, the aim of our study was to investigate the in vitro and the in vivo anti-Candida activity of two critical bioactive constituents of TTO, terpinen-4-ol and 1,8-cineole.

METHODS: Oophorectomized, pseudoestrus rats under estrogen treatment were used for experimental vaginal infection with azole (fluconazole, itraconazole) -susceptible or -resistant strains of *C. albicans*. All these strains were preliminarily tested for in vitro susceptibility to TTO, terpinen-4-ol and 1,8-cineole for their antifungal properties, using a modification of the CLSI (formerly NCCLS) reference M27-A2 broth micro-dilution method.

RESULTS: In vitro minimal inhibitory concentrations (MIC90) values were 0.06% (volume/volume) for terpinen-4-ol and 4% (volume/volume) for 1,8-cineole, regardless of susceptibility or resistance of the strains to fluconazole and itraconazole. Fungicidal concentrations of terpinen-4-ol were equivalent to the candidastatic activity. In the rat vaginal infection model, terpinen-4-ol was as active as TTO in accelerating clearance from the vagina of all *Candida* strains examined.

CONCLUSION: Our data suggest that terpinen-4-ol is a likely mediator of the in vitro and in vivo activity of TTO. This is the first in vivo demonstration that terpinen-4-ol could control *C. albicans* vaginal infections. The purified compound holds promise for the treatment of vaginal candidiasis, and particularly the azole-resistant forms.

Rev Iberoam Micol. 2000 Jun;17(2):60-3.

In vitro susceptibilities of Candida and Aspergillus species to Melaleuca alternifolia (tea tree) oil.

Candida species are an important cause of opportunistic infection in the oral cavity of immunocompromised patients, especially HIV infected patients. Melaleuca oil obtained commercially was investigated since it is known to have broad antifungal properties. The in-vitro susceptibilities of *Aspergillus* and susceptible and resistant *Candida* species were performed utilizing serial dilutions in microtiter plates with Sabouraud dextrose agar and the commercial preparation of Melaleuca. As a comparator, in vitro susceptibilities to amphotericin B and fluconazole were also determined using the broth microdilution technique. The results demonstrate that Melaleuca inhibited the *Candida* species. However, the growth of *Aspergillus* was not inhibited at the concentrations tested. Thus, preparations containing Melaleuca alternifolia may be a useful alternative for superficial candidal infections. In fact, it may be a useful alternative regimen for advanced HIV-positive patients with oropharyngeal candidiasis refractory to fluconazole. However, controlled clinical studies to evaluate its efficacy are still needed.

J Antimicrob Chemother. 2004 Jun;53(6):1081-5. Epub 2004 May 12.

Antifungal effects of Melaleuca alternifolia (tea tree) oil and its components on Candida albicans, Candida glabrata and Saccharomyces cerevisiae.

OBJECTIVES: The aim of this study was to investigate the mechanism of action of tea tree oil and its components against *Candida albicans*, *Candida glabrata* and *Saccharomyces cerevisiae*.

METHODS: Yeast cells were treated with tea tree oil or components, at one or more concentrations, for up to 6 h. During this time, alterations in permeability were assessed by measuring the leakage of 260 nm absorbing materials and by the uptake of Methylene Blue dye. Membrane fluidity was measured by

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1,6-diphenyl-1,3,5-hexatriene fluorescence. The effects of tea tree oil on glucose-induced medium acidification were quantified by measuring the pH of cell suspensions in the presence of both tea tree oil and glucose.

RESULTS: The treatment of *C. albicans* with tea tree oil and components at concentrations of between 0.25 and 1.0% (v/v) altered both permeability and membrane fluidity. Membrane fluidity was also increased when *C. albicans* was cultured for 24 h with 0.016%-0.06% (v/v) tea tree oil, as compared with control cells. For all three organisms, glucose-induced acidification of the external medium was inhibited in a dose-dependent manner in the presence of 0.2%, 0.3% and 0.4% tea tree oil.

CONCLUSIONS: Data from this study support the hypothesis that tea tree oil and components exert their antifungal actions by altering membrane properties and compromising membrane-associated functions.

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Lett Appl Microbiol. 2003;37(2):185-7.

Antimycotic activity of *Melaleuca alternifolia* essential oil and its major components.

AIMS: The aim of this study was to analyse the antimycotic properties of *Melaleuca alternifolia* essential oil (tea tree oil, TTO) and its principal components and to compare them with the activity of 5-fluorocytosine and amphotericin B.

METHODS AND RESULTS: The screening for the antimycotic activity was performed by serial twofold dilutions in Roswell Park Memorial Institute medium with the inclusion of Tween-80 (0.5%). **TTO and terpinen-4-ol were the most active compounds.**

CONCLUSIONS: The majority of the organisms were sensitive to the essential oil, with TTO and terpinen-4-ol being the most active oils showing antifungal activity at minimum inhibitory concentration values lower than other drugs.

SIGNIFICANCE AND IMPACT OF THE STUDY: This study provides a sample large enough to determine the antifungal properties of TTO and terpinen-4-ol and suggests further studies for a possible therapeutic use.

Skin Pharmacol. 1996;9(6):388-94.

Antifungal activity of the essential oil of *Melaleuca alternifolia* (tea tree oil) against pathogenic fungi in vitro.

The in vitro antifungal activity of tea oil, the essential oil of *Melaleuca alternifolia*, has been evaluated against 26 strains of various dermatophyte species, 54 yeasts, among them 32 strains of *Candida albicans* and other *Candida* sp. as well as 22 different *Malassezia furfur* strains. Minimum inhibitory concentrations (MIC) of tea tree oil were measured by agar dilution technique. **Tea tree oil was found to be able to inhibit growth of all clinical fungal isolates.** For the investigated dermatophytes MIC values from 1,112.5 to 4,450.0 micrograms/ml with a geometric mean of 1,431.5 micrograms/ml were demonstrated. Both *C. albicans* strains and the other strains belonging to the genus *Candida* and *Trichosporon* appeared to be slightly less susceptible to tea tree oil in vitro. However, their MIC values, which varied from 2,225.0 to 4,450.0 micrograms/ml (geometric mean 4,080 micrograms/ml), indicated moderate susceptibility to the essential oil of *M. alternifolia*. The lipophilic yeast *M. furfur* seemed to be most susceptible to tea tree oil. MIC values between 556.2 and 4,450.0 micrograms/ml (geometric mean 1,261.5 micrograms/ml) were found against the tested *M. furfur* strains. However, when calculated as percentage tea tree oil of the agar, the above-mentioned concentrations correspond to 0.5-0.44% tea tree oil content. These values are far below the usual relatively high therapeutic concentrations of the agent; approximately 5-10% solution or even the concentrated essential oil are used for external treatment. In comparison with tea tree oil, in vitro susceptibility against miconazole, an established topical antifungal, was tested. As expected, very low MIC

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values for miconazole were found for dermatophytes (geometric mean 0.2 microgram/ml), yeasts (geometric mean 1.0 microgram/ml), and *M. furfur* (geometric mean 2.34 micrograms/ml). It is suggested that the in vivo effect of tea tree oil ointment in the therapy of fungal infections of the skin and mucous membranes as well as in the treatment of dandruff, a mild form of seborrheic dermatitis, may be at least partly due to an antifungal activity of tea tree oil.

Mycoses. 2004 Apr;47(3-4):87-92.

Herbal medicines for treatment of fungal infections: a systematic review of controlled clinical trials.

Traditional medicine has made use of many different plant extracts for treatment of fungal infections and some of these have been tested for in vitro antifungal activity. This systematic review evaluates antifungal herbal preparations that have been tested in controlled clinical trials. Four electronic databases were searched for controlled clinical trials of antifungal herbal medicines. Data were extracted in a standardized manner by two independent reviewers and are reviewed narratively. Seven clinical trials met our inclusion criteria. Tea tree oil preparations were tested in four randomized clinical trials and some positive outcomes were attributed to the intervention in all trials. Solanum species (two trials) and oil of bitter orange preparations (one trial) were compared with conventional treatments. In all cases encouraging results were reported. There are few controlled clinical trials of herbal antifungal medicines. The most thoroughly clinically tested is tea tree oil, which holds some promise. All herbal remedies require further investigation in rigorous clinical trials.

Anti-Bacterial

Can J Microbiol. 2015 Jan;61(1):82-8.

Effect of tea tree (*Melaleuca alternifolia*) oil as a natural antimicrobial agent in lipophilic formulations.

There has been increased interest surrounding the use of tea tree oil (TTO) as a natural antimicrobial. In this study, the antimicrobial activity of TTO and its components were investigated in vitro and in a predominantly lipid-based personal care formulation. In vitro, TTO showed minimal inhibitory concentrations of 0.2% (for *Saccharomyces cerevisiae* and *Pythium sulcatum*), 0.4% (for *Escherichia coli*, *Bacillus subtilis*, and *Rhizopus stolonifer*), and 0.8% (for *Botrytis cinerea*). TTO at 0.08%-0.8% was often as efficient as parabens. Comparison of the antimicrobial activities of TTO components showed that terpinen-4-ol and γ -terpinene were generally most effective in inhibiting microbial growth. TTO activity in a personal care product was evaluated through air and water exposure, artificial inoculation, and shelf life studies. While TTO did not increase shelf life of unopened products, it decreased microbial load in products exposed to water and air. Results from this study support that antimicrobial activity of TTO can be attributed to varying levels of its components and that low levels of TTO were effective in reducing microbial growth during the use of the product. This study showed that TTO can act as a suitable preservative system within an oil-based formulation.

J Microbiol Biotechnol. 2009 Dec;19(12):1590-5.

Activity of essential oils against *Bacillus subtilis* spores.

Alternative methods for controlling bacterial endospore contamination are desired in a range of industries and applications. Attention has recently turned to natural products, such as essential oils, which have sporicidal activity. In this study, a selection of essential oils was investigated to identify those with activity

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against *Bacillus subtilis* spores. Spores were exposed to thirteen essential oils, and surviving spores were enumerated. Cardamom, tea tree, and juniper leaf oils were the most effective, reducing the number of viable spores by 3 logs at concentrations above 1%. Sporicidal activity was enhanced at high temperatures (60 degrees C) or longer exposure times (up to one week). Gas chromatography-mass spectrometry analysis identified the components of the active essential oils. However, none of the major oil components exhibited equivalent activity to the whole oils. The fact that oil components, either alone or in combination, did not show the same level of sporicidal activity as the complete oils suggested that minor components may be involved, or that these act synergistically with major components. Scanning electron microscopy was used to examine spores after exposure to essential oils and suggested that leakage of spore contents was the likely mode of sporicidal action. Our data have shown that essential oils exert sporicidal activity and may be useful in applications where bacterial spore reduction is desired.
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J Appl Microbiol. 2010 Mar;108(3):936-44.

Inhibition of group A streptococcal infection by *Melaleuca alternifolia* (tea tree) oil concentrate in the murine model.

AIMS: To investigate the effect of a water-soluble *Melaleuca alternifolia* concentrate (MAC) on group A streptococcus (GAS; *Streptococcus pyogenes*)-induced necrotizing fasciitis.

METHODS AND RESULTS: MAC pretreatment (1% and 2% v/v) was able to protect mice from GAS infection in an air pouch model. GAS-induced mouse death and skin injury were inhibited dose dependently by MAC. Administration of MAC at 6 h post-GAS infection partially delayed mouse death. Surveys of the exudates of the air pouch of MAC-treated mice revealed that the survival of infiltrating cells was prolonged, the bacteria were eliminated, and the production of inflammatory cytokines was inhibited. MAC could directly inhibit the growth of GAS in vitro, and the minimal inhibitory concentration (MIC) of MAC for GAS was determined as 0.05% v/v using the time-kill assay. Furthermore, a sub-MIC dose of MAC not only enhanced the bactericidal activity of RAW264.7 macrophage cells against GAS but also increased susceptibility of GAS for blood clearance.

CONCLUSIONS: These results suggest that MAC may inhibit GAS-induced skin damage and mouse death by directly inhibiting GAS growth and enhancing the bactericidal activity of macrophages.

SIGNIFICANCE AND IMPACT OF THE STUDY: Our results provide scientific data on the use of MAC for the treatment of GAS-induced necrotizing fasciitis in the murine model.

Int J Antimicrob Agents. 2009 Apr;33(4):343-7.

Effects of tea tree (*Melaleuca alternifolia*) oil on *Staphylococcus aureus* in biofilms and stationary growth phase.

Tea tree oil (TTO) is known for its antimicrobial activity. In this study, we determined whether TTO is effective against *Staphylococcus aureus* in biofilms and how TTO activity is affected by the *S. aureus* growth phase. All clinical strains tested were killed by TTO both as planktonic cells and as biofilms. The minimum biofilm eradication concentration was usually two times higher than the minimum bactericidal concentration, yet it was never higher than 1% v/v. The fastest killing of biofilm occurred during the first 15min of contact with TTO and was not influenced by increasing TTO concentration above 1% v/v. Planktonic stationary phase cells exhibited decreased susceptibility to TTO compared with exponential phase cells. The killing rate for stationary phase cells was also less affected by increasing TTO concentration than that for exponential phase cells. These data show that TTO efficiently kills *S. aureus* in

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the stationary growth phase and within biofilms and is therefore a promising tool for *S. aureus* eradication.

Int J Immunopathol Pharmacol. 2006 Jul-Sep;19(3):539-44.

Melaleuca alternifolia essential oil possesses potent anti-staphylococcal activity extended to strains resistant to antibiotics.

Melaleuca alternifolia Cheel essential oil (TTO) and its major component terpinen-4-ol were examined against a large number of clinical isolates of Staphylococcus aureus to establish their anti-staphylococcal activities. Classic and established procedures were used to study M.I.C., time-kill curves, synergism and mutational frequency. The anti-staphylococcal activity of terpinen-4-ol and TTO were superior to those of antibiotics belonging to the major families (all the tested drugs are for topical use or included in ointments, eye drops or used during surgery); terpinen 4-ol and TTO were active against strains resistant to mupirocin, fusidic acid, vancomycin, methicillin and linezolid. TTO and terpinen-4-ol were bactericidal as revealed by time-kill curves; the frequency of mutational frequency to TTO was $< 2.9 \times 10^{-9}$. The study demonstrates good anti-staphylococcal activity of TTO and terpinen-4-ol against a large number of *S.aureus* isolates and suggests the possible application of these agents for topical treatment of staphylococcal infections. This is the first extensive study on the anti-staphylococcal activity of TTO. The results suggest that this compound may have application as a topical agent for the control of superficial staphylococcal infections, including activity against organisms resistant to antibiotics which can be used, or are specific, for topical use.

J Antimicrob Chemother. 2006 Aug;58(2):449-51. Epub 2006 May 30.

Susceptibility of pseudomonads to Melaleuca alternifolia (tea tree) oil and components.

OBJECTIVES: Thirty isolates of *Pseudomonas aeruginosa*, 15 isolates of *Pseudomonas putida* and 11 isolates of *Pseudomonas fluorescens* were tested for susceptibility to tea tree oil (TTO), the essential oil of *Melaleuca alternifolia*, and the components terpinen-4-ol, alpha-terpineol, cineole, gamma-terpinene and rho-cymene.

METHODS: MICs were determined by broth microdilution in Mueller-Hinton medium supplemented with 0.002% (v/v) Tween 80.

RESULTS: The MIC₉₀ of TTO for all isolates tested was 4% (v/v) or less. Susceptibility to components tested varied between species.

CONCLUSIONS: *Pseudomonas* spp. are susceptible to TTO and some of its components although they are less susceptible than many other bacteria tested previously.

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Clin Microbiol Rev. 2006 Jan;19(1):50-62.

Melaleuca alternifolia (Tea Tree) oil: a review of antimicrobial and other medicinal properties.

Complementary and alternative medicines such as tea tree (*Melaleuca*) oil have become increasingly popular in recent decades. This essential oil has been used for almost 100 years in Australia but is now available worldwide both as neat oil and as an active component in an array of products. The primary uses of tea tree oil have historically capitalized on the antiseptic and anti-inflammatory actions of the oil. This review summarizes recent developments in our understanding of the antimicrobial and anti-inflammatory activities of the oil and its components, as well as clinical efficacy. Specific mechanisms of antimicrobial and anti-inflammatory action are reviewed, and the toxicity of the oil is briefly discussed.

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J Laryngol Otol. 2005 Mar;119(3):198-201.

Tea tree oil: in vitro efficacy in otitis externa.

OBJECTIVE: The purpose of this study was to determine the susceptibility of organisms causing otitis externa (OE) to the essential oil of *Melaleuca alternifolia*, or tea tree oil (TTO).

METHODS: Fifty-seven swabs were taken from the ears of 52 patients with OE for culture and sensitivity. A broth microdilution method was used to determine the minimum inhibitory concentration (MIC) of TTO for each organism.

RESULTS: In 51 percent of the swabs taken, pathogenic organisms were cultured. Of these cultures 71 percent, both bacteria and yeast, were susceptible to TTO 2 percent or less. The only organism showing resistance to TTO was *Pseudomonas aeruginosa*; however 25 percent of these bacteria were sensitive.

CONCLUSION: Tea tree oil may have a role to play in the treatment of OE. However, more work needs to be done to enhance the anti-pseudomonal effect and to assess ototoxicity.

Pharmazie. 2005 Mar;60(3):208-11.

Formulation and evaluation of an effective pH balanced topical antimicrobial product containing tea tree oil.

The effect of pH on the antimicrobial activity of *Melaleuca alternifolia* essential oil formulations was studied. Microemulsions, liposomal dispersions, multiple emulsions and a colloidal bed of sterile clay were formulated using 5% w/w of tea tree oil. A number of formulations were prepared at various pH values (5.0, 5.5, 6.0, 6.5, and 7.0). Thermal stability studies showed that the formulations were stable for more than eight months. Agar dilution tests showed MICs of 1.0% v/v *S. aureus* and *S. epidermidis*. In the broth dilution test, MBC of the oil for *P. acnes* was 0.5% v/v. MIC and MBC values were comparable to those of non-formulated tea tree oil, indicating that tea tree oil retained its activity in the above-mentioned formulations. The microbiological evaluation showed that the formulations containing 5% w/w tea tree oil had a maximum effect at pH 5.5.

J Antimicrob Chemother. 1995 Mar;35(3):421-4.

Susceptibility of methicillin-resistant *Staphylococcus aureus* to the essential oil of *Melaleuca alternifolia*.

All 66 isolates of *Staphylococcus aureus* tested were susceptible to the essential oil of *Melaleuca alternifolia*, or tea tree oil, in disc diffusion and modified broth microdilution methods. Of the isolates tested, 64 were methicillin-resistant *S. aureus* (MRSA) and 33 were mupirocin-resistant. The MIC and MBC for 60 Australian isolates were 0.25% and 0.50%, respectively. Comparable results were obtained by co-workers in Britain using similar methods. These in-vitro results suggest tea tree oil may be useful in the treatment of MRSA carriage.

J Appl Bacteriol. 1995 Mar;78(3):264-9.

Antimicrobial activity of the major components of the essential oil of *Melaleuca alternifolia*.

Tea tree oil, or the essential oil of *Melaleuca alternifolia*, is becoming increasingly popular as a naturally occurring antimicrobial agent. The antimicrobial activity of eight components of tea tree oil was evaluated using disc diffusion and broth microdilution methods. Attempts were also made to overcome methodological problems encountered with testing compounds which have limited solubility in aqueous media. After assessing media with and without solubilizing agents, the disc diffusion method was used to determine the susceptibility of a range of micro-organisms to 1,8-cineole, 1-terpinen-4-ol, rho-cymene, linalool, alpha-terpinene, gamma-terpinene, alpha-terpineol and terpinolene. While the disc diffusion

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method lacked reproducibility, it was considered useful as a procedure for screening for antimicrobial activity. Terpinen-4-ol was active against all the test organisms while rho-cymene demonstrated no antimicrobial activity. Linalool and alpha-terpineol were active against all organisms with the exception of *Pseudomonas aeruginosa*. Minimum inhibitory and minimum cidal concentrations of each component against *Candida albicans*, *Escherichia coli* and *Staphylococcus aureus* were determined using a broth microdilution method. Modifications to this method overcame solubility and turbidity problems associated with the oil components and allowed the antimicrobial activity of each of the components to be quantified reproducibly. There was reasonable agreement between minimum inhibitory concentrations and zones of inhibition. **These results may have significant implications for the future development of tea tree oil as an antimicrobial agent.**

Ann Agric Environ Med. 2011 Jun;18(1):139-44.

Antimicrobial activity of two essential oils.

The aim of the study was to evaluate the antimicrobial activity of essential oils in vitro for possible application to reduce the content of microorganisms in the air of animal houses. The essential oils of *Cymbopogon citratus* L. and *Malaleuca alternifolia* L. were screened against bacteria *Staphylococcus aureus*, *Enterococcus faecium*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus mirabilis* and yeast *Candida albicans*. The minimal inhibitory concentration of the active essential oils was tested using broth dilution assay. The essential oils concentrations ranged from 0.1-50.0%. The combined effects of essential oils were tested for *Malaleuca alternifolia* L. and *Cymbopogon citratus* L. concentrations ranged from 0.005-50.0%. The oils showed a wide spectrum of antibacterial activity. Concentrations of 0.1-0.5% of *Cymbopogon citratus* L. and *Malaleuca alternifolia* L. reduced total microorganisms count of *Proteus mirabilis* and *Candida albicans*. High antibacterial activity was also revealed for *Cymbopogon citratus* L. with bactericidal concentrations of 0.8% for *Escherichia coli*, 5.0% for *Enterococcus faecium*, 5.0% for *Pseudomonas aeruginosa* and 8.0% for *Staphylococcus aureus*. Bactericidal concentrations of *Malaleuca alternifolia* L. were 5.0% for *Pseudomonas aeruginosa* and *Enterococcus faecium*, and 8.0% for *Staphylococcus aureus*. The essential oils of *Cymbopogon citratus* and *Malaleuca alternifolia* may be a promising alternative of air disinfection in animal houses.

Free full text

BMJ Clin Evid. 2011 Jan 17;2011. pii: 0923.

MRSA colonisation (eradicating colonisation in people without active/invasive infection).

INTRODUCTION: Methicillin-resistant *Staphylococcus aureus* (MRSA) has a gene that makes it resistant to methicillin as well as to other beta-lactam antibiotics, including flucloxacillin, beta-lactam/beta-lactamase inhibitor combinations, cephalosporins, and carbapenems. MRSA can be part of the normal body flora (colonisation), especially in the nose, but it can cause infection. Until recently, MRSA has primarily been a problem associated with exposure to the healthcare system, especially in people with prolonged hospital admissions, with underlying disease, or after antibiotic use. In many countries worldwide, a preponderance of *S aureus* bloodstream isolates are resistant to methicillin.

METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of treatment for MRSA nasal or extra-nasal colonisation? We searched: Medline, Embase, The Cochrane Library, and other important databases up to January 2010 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA).

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RESULTS: We found 9 systematic reviews, RCTs, or observational studies that met our inclusion criteria.
CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: antiseptic body washes, chlorhexidine-neomycin nasal cream, mupirocin nasal ointment, systemic antimicrobials, tea tree oil preparations, and other topical antimicrobials.
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J Craniomaxillofac Surg. 2009 Oct;37(7):392-7.

The battle against multi-resistant strains: Renaissance of antimicrobial essential oils as a promising force to fight hospital-acquired infections.

Hospital-acquired infections and antibiotic-resistant bacteria continue to be major health concerns worldwide. Particularly problematic is methicillin-resistant *Staphylococcus aureus* (MRSA) and its ability to cause severe soft tissue, bone or implant infections. First used by the Australian Aborigines, Tea tree oil and Eucalyptus oil (and several other essential oils) have each demonstrated promising efficacy against several bacteria and have been used clinically against multi-resistant strains. Several common and hospital-acquired bacterial and yeast isolates (6 *Staphylococcus* strains including MRSA, 4 *Streptococcus* strains and 3 *Candida* strains including *Candida krusei*) were tested for their susceptibility for Eucalyptus, Tea tree, Thyme white, Lavender, Lemon, Lemongrass, Cinnamon, Grapefruit, Clove Bud, Sandalwood, Peppermint, Kunzea and Sage oil with the agar diffusion test. Olive oil, Paraffin oil, Ethanol (70%), Povidone iodine, Chlorhexidine and hydrogen peroxide (H₂O₂) served as controls. Large prevailing effective zones of inhibition were observed for Thyme white, Lemon, Lemongrass and Cinnamon oil. The other oils also showed considerable efficacy. Remarkably, almost all tested oils demonstrated efficacy against hospital-acquired isolates and reference strains, whereas Olive and Paraffin oil from the control group produced no inhibition. As proven in vitro, essential oils represent a cheap and effective antiseptic topical treatment option even for antibiotic-resistant strains as MRSA and antimycotic-resistant *Candida* species.

In Vivo. 2007 Nov-Dec;21(6):1027-30.

Antibacterial effect of tea-tree oil on methicillin-resistant *Staphylococcus aureus* biofilm formation of the tympanostomy tube: an in vitro study.

The antibacterial effects of tea-tree oil against the formation of methicillin-resistant *Staphylococcus aureus* (MRSA) biofilm on the surface of the tympanostomy tubes was evaluated.

MATERIALS AND METHODS: Silicone tympanostomy tubes were pretreated with normal saline for 12 hours, the control group (n=4), with 100% tea-tree oil, experimental group A (n=3), or with 50% tea-tree oil, experimental group B (n=3). All the tubes were incubated in a MRSA solution for 2 days and then processed for evaluation using scanning electron microscopy.

RESULTS: The development of the biofilm mode of growth of MRSA was observed in the saline-treated control group. In contrast, only focal biofilms were present on the tube surface in experimental group A and considerable reduction of biofilm with destruction of the MRSA cells was shown in experimental group B.

CONCLUSION: From these results, the antimicrobial effect of tea-tree oil against biofilm formation on tympanostomy tubes in vitro has been verified.

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Pharmazie. 2000 May;55(5):380-4.

Effect of Australian tea tree oil on the viability of the wall-less bacterium *Mycoplasma pneumoniae*.

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In vitro assays using a variety of essential oils revealed a particularly high antibacterial effect of Australian tea tree oil (TTO) on a great number of gram-negative and gram-positive bacteria of unrelated phylogenetic origin. In the present study, the susceptibility of cell wall-less bacteria such as the human pathogenic bacterium *Mycoplasma pneumoniae* to Australian tea tree oil was examined. The minimum inhibitory concentration (MIC) was determined to be 0.006% (v/v) TTO for the wild type and to 0.003% (v/v) TTO for mutants of *M. pneumoniae* which lost the ability to adhere to host cells (cytadherence-negative). The MIC and the MBC (minimum bactericidal concentration) for *M. pneumoniae* are 100 times lower than those for all other eubacteria tested. Electron microscopy with negatively stained cells as well as with ultrathin sections revealed a tendency to ovoid or round cells after oil treatment whereas the untreated cells of the wild type exhibit a flask-shaped morphology with a tip-like structure at one pole of the cell. The integrity of the mycoplasmal membrane seems not to be affected by TTO since no leakage of the *Mycoplasma* cell was observed after oil treatment. In the HET-CAM test TTO did not show any visible signs of irritation in concentrations less than 25%. Although the active component in TTO that has anti-mycoplasmal activity is not known, it seems very promising to use TTO tentatively for mouth washing and inhalation in case of *Mycoplasma-pneumoniae*-infection.

J Antimicrob Chemother. 2003 Feb;51(2):241-6.

Herbal medicines for treatment of bacterial infections: a review of controlled clinical trials.

OBJECTIVES: Many hundreds of plant extracts have been tested for in vitro antibacterial activity. This review is a critical evaluation of controlled clinical trials of herbal medicines with antibacterial activity.

METHODS: Four electronic databases were searched for controlled clinical trials of antibacterial herbal medicines. Data were extracted and validated in a standardized fashion, according to predefined criteria, by two independent reviewers.

RESULTS: Seven clinical trials met our inclusion criteria. Four of these studies were randomized. Three trials of garlic and cinnamon treatments for *Helicobacter pylori* infections reported no significant effect. Bacterial infections of skin were treated in four trials. Positive results were reported for an ointment containing tea leaf extract in impetigo contagiosa infections. Two trials of tea tree oil preparations used for acne and methicillin-resistant *Staphylococcus aureus*, and one trial of *Ocimum gratissimum* oil for acne, reported results equivalent to conventional treatments.

CONCLUSIONS: Few controlled clinical trials have been published and most are methodologically weak. The clinical efficacy of none of the herbal medicines has so far been demonstrated beyond doubt. This area seems to merit further study through rigorous clinical trials.

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Lett Appl Microbiol. 1995 Oct;21(4):242-5.

Antimicrobial effects of tea-tree oil and its major components on *Staphylococcus aureus*, *Staph. epidermidis* and *Propionibacterium acnes*.

Major components of two tea-tree oil samples were identified using thin layer and gas-liquid chromatography (TLC and GLC). Using a TLC-bioautographic technique, the tea-tree oils, terpinen-4-ol, alpha-terpineol and alpha-pinene were found to be active against *Staphylococcus aureus*, *Staph. epidermidis* and *Propionibacterium acnes* whereas cineole was inactive against these organisms. The MIC values of the three active compounds increased in the order alpha-terpineol < terpinen-4-ol < alpha-pinene for all three micro-organisms. MIC values of the tea-tree oils and terpinen-4-ol were lower for *P. acnes* than for the two staphylococci. This study supports the use of tea-tree oil in the treatment of acne, and demonstrates that terpinen-4-ol is not the sole active constituent of the oil.

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J Infect Dev Ctries. 2015 Jul 4;9(6):650-4.

Essential oils in ocular pathology: an experimental study.

INTRODUCTION: The antimicrobial activity of essential oils (EOs) has been known for ages; in particular, the EOs of *Melaleuca alternifolia*, *Thymus vulgaris*, *Mentha piperita*, and *Rosmarinus officinalis* have been used for the treatment of fungal and bacterial infections.

METHODOLOGY: This study focused on the in vitro cytotoxicity to normal human conjunctiva cells and antimicrobial activity of 20 EOs.

RESULTS: The oils tested showed no cytotoxic effect at very low concentrations. *Rosmarinus officinalis*, *Melaleuca alternifolia*, and *Thymus vulgaris* L. red thyme geraniol sel oils had good antimicrobial activity against Gram-positive and Gram-negative strains.

CONCLUSIONS: The results of this study are of great interest and may have a major impact on public health, providing useful tips to optimize the therapeutic use of some natural drugs.

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Anti-Viral

Molecules. 2013 Aug 9;18(8):9550-66.

Melaleuca alternifolia concentrate inhibits in vitro entry of influenza virus into host cells.

Influenza virus causes high morbidity among the infected population annually and occasionally the spread of pandemics. *Melaleuca alternifolia* Concentrate (MAC) is an essential oil derived from a native Australian tea tree. Our aim was to investigate whether MAC has any in vitro inhibitory effect on influenza virus infection and what mechanism does the MAC use to fight the virus infection. In this study, the antiviral activity of MAC was examined by its inhibition of cytopathic effects. In silico prediction was performed to evaluate the interaction between MAC and the viral haemagglutinin. We found that when the influenza virus was incubated with 0.010% MAC for one hour, no cytopathic effect on MDCK cells was found after the virus infection and no immunofluorescence signal was detected in the host cells. Electron microscopy showed that the virus treated with MAC retained its structural integrity. By computational simulations, we found that terpinen-4-ol, which is the major bioactive component of MAC, could combine with the membrane fusion site of haemagglutinin. Thus, we proved that MAC could prevent influenza virus from entering the host cells by disturbing the normal viral membrane fusion procedure.

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Lett Appl Microbiol. 2009 Dec;49(6):806-8.

In vitro antiviral activity of Melaleuca alternifolia essential oil.

AIMS: To investigate the in vitro antiviral activity of *Melaleuca alternifolia* essential oil (TTO) and its main components, terpinen-4-ol, alpha-terpinene, gamma-terpinene, p-cymene, terpinolene and alpha-terpineol.

METHODS AND RESULTS: The antiviral activity of tested compounds was evaluated against polio type 1, ECHO 9, Coxsackie B1, adeno type 2, herpes simplex (HSV) type 1 and 2 viruses by 50% plaque reduction assay. The anti-influenza virus assay was based on the inhibition of the virus-induced cytopathogenicity. Results obtained from our screening demonstrated that the TTO and some of its components (the terpinen-4-ol, the terpinolene, the alpha-terpineol) have an inhibitory effect on influenza A/PR/8 virus subtype H1N1 replication at doses below the cytotoxic dose. The ID(50) value of the TTO was found to be 0.0006% (v/v) and was much lower than its CD(50) (0.025% v/v). All the compounds

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were ineffective against polio 1, adeno 2, ECHO 9, Coxsackie B1, HSV-1 and HSV-2. None of the tested compounds showed virucidal activity. Only a slight virucidal effect was observed for TTO (0.125% v/v) against HSV-1 and HSV-2.

CONCLUSIONS: These data show that TTO has an antiviral activity against influenza A/PR/8 virus subtype H1N1 and that antiviral activity has been principally attributed to terpinen-4-ol, the main active component.

SIGNIFICANCE AND IMPACT OF THE STUDY: TTO should be a promising drug in the treatment of influenza virus infection.

J Antimicrob Chemother. 2001 Sep;48(3):450-1.

Melaleuca alternifolia (tea tree) oil gel (6%) for the treatment of recurrent herpes labialis.

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HNO. 2011 Dec;59(12):1176-84.

[Efficacy of plant products against herpetic infections].

[Article in German]

Essential oils from various aromatic medicinal plants are highly active against some viral infections, e.g. labial herpes caused by herpes simplex virus type 1. Balm oil, tea tree oil and peppermint oil demonstrate in vitro a significant antiherpetic activity, mainly related to a direct drug-virus particle interaction, some essential oils also act directly virucidal. Interestingly, these essential oils are also highly active against acyclovir-resistant herpes simplex virus strains. In clinical studies, tea tree oil has been shown to possess antiherpetic, anti-inflammatory and pain-relieving properties, as well as to accelerate the healing process of herpes labialis. Applying diluted essential oils three to four times daily for the antiherpetic treatment of affected areas is recommended. Some companies have marketed plant products, e.g. from Melissa, for the treatment of recurrent herpetic infections.

Phytother Res. 2010 May;24(5):673-9.

Comparative study on the antiviral activity of selected monoterpenes derived from essential oils.

Essential oils are complex natural mixtures, their main constituents, e.g. terpenes and phenylpropanoids, being responsible for their biological properties. Essential oils from eucalyptus, tea tree and thyme and their major monoterpene compounds alpha-terpinene, gamma-terpinene, alpha-pinene, p-cymene, terpinen-4-ol, alpha-terpineol, thymol, citral and 1,8-cineole were examined for their antiviral activity against herpes simplex virus type 1 (HSV-1) in vitro. These essential oils were able to reduce viral infectivity by >96%, the monoterpenes inhibited HSV by about >80%. The mode of antiviral action has been determined, only moderate antiviral effects were revealed by essential oils and monoterpenes when these drugs were added to host cells prior to infection or after entry of HSV into cells. However, both essential oils and monoterpenes exhibited high anti-HSV-1 activity by direct inactivation of free virus particles. All tested drugs interacted in a dose-dependent manner with herpesvirus particles thereby inactivating viral infection. Among the analysed compounds, monoterpene hydrocarbons were slightly superior to monoterpene alcohols in their antiviral activity, alpha-pinene and alpha-terpineol revealed the highest selectivity index. However, mixtures of different monoterpenes present in natural tea tree essential oil revealed a ten-fold higher selectivity index and a lower toxicity than its isolated single monoterpenes.

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Bacterial Antibiotic Resistance as Result of Chemical Biocide Exposure

Microbiology. 2010 Jan;156(Pt 1):30-8.

Effect of subinhibitory concentrations of benzalkonium chloride on the competitiveness of *Pseudomonas aeruginosa* grown in continuous culture.

This study investigates the link between adaptation to biocides and antibiotics in *Pseudomonas aeruginosa*. An enrichment continuous culture of *P. aeruginosa* NCIMB 10421 (MIC 25 mg BKC l(-1)) was operated (D=0.04 h(-1), 792 h) with added benzalkonium chloride (BKC). A derivative, PA-29 (696 h), demonstrated a >12-fold decrease in sensitivity to the biocide (MIC >350 mg BKC l(-1)). The variant demonstrated a 256-fold increase in resistance to ciprofloxacin, with a mutation in the *gyrA* gene (Thr-83-->Ile). Similarly, culturing of the original strain in a continuous-culture system with ciprofloxacin selection pressure led to the evolution of BKC-adapted populations (MIC 100 mg BKC l(-1)). Efflux pump activity predominantly contributed to the developed phenotype of PA-29. An amino acid substitution (Val-51-->Ala) in *nfxB*, the Mex efflux system regulator gene, was observed for PA-29. Overexpression of both MexAB-OprM and MexCD-OprJ was recorded for PA-29. Similarly, *mexR*, a repressor of the Mex system, was downregulated. Competition studies were carried out in continuous culture between PA-29 and the original strain (in the presence of subinhibitory concentrations of BKC). The outcome of competition was influenced by the concentration of biocide used and the nature of limiting nutrient. The inclusion of 1 mg BKC l(-1) in the medium feed was sufficient to select (S=0.011) for the BKC-adapted strain in magnesium-limited culture. Conversely, the presence of 10 mg BKC l(-1) in the medium supply was insufficient to select for the same organism (S=-0.017) in the glucose-limited culture. These results indicate the importance of environmental conditions on selection and maintenance of biocide adaptation.

Dairy Cow Hoof Dermatitis

J Dairy Sci. 2014 Apr;97(4):2498-501.

Effect of a tea tree oil and organic acid footbath solution on digital dermatitis in dairy cows.

Copper sulfate is the industry gold standard footbath ingredient for controlling dairy cow digital dermatitis. However, when used footbath solutions are deposited on soil, high levels of copper in the soil may result, which can have toxic and negative effects on plant growth. An alternative to copper sulfate is Provita Hoofsure Endurance (Provita Eurotech Ltd., Omagh, UK), which is a biodegradable solution containing organic acids, tea tree oil, and wetting agents. The objective of this study was to quantify changes in digital dermatitis frequency when using Provita Hoofsure Endurance and copper sulfate in a split footbath in 3 commercial dairy herds. This study was conducted from January 5, 2012, to March 19, 2012, in 3 commercial Kentucky dairies with 120, 170, and 200 milking Holstein cows. None of the herds was using a footbath for digital dermatitis control before the study. Footbath solutions were delivered using a split footbath. During the study, a 3% Hoofsure Endurance solution for the left hooves and a 5% copper sulfate solution for the right hooves was used. Digital dermatitis was scored every 3wk using the M0 to M4 system, where M0=a claw free of signs of digital dermatitis; M1=a lesion <2cm that is not painful; M2=the ulcerative stage, with lesion diameter of >2cm, and painful to the touch; M3=the healing stage and covered by a scab; and M4=the chronic stage and characterized by dyskeratosis or proliferation of the surface that is generally not painful. McNemar's test statistic suggested that a statistically significant difference existed in the proportions of M1 and M2 lesions between the beginning and end of the study for both treatments. This indicates that each solution was effective in decreasing the proportion of M1 or M2 lesions from

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baseline to the last time point. A chi-square test calculated using PROC FREQUENCY of SAS (SAS Institute Inc., Cary, NC) indicated that no statistically significant relationship existed between the treatments among changes in digital dermatitis frequency from the baseline to the end of the study.

Performance of the 2 footbath solutions was comparable throughout the study. No significant differences were observed between the copper sulfate and Provita Hoofsure Endurance.

Repelling Flies on Pastured Dairy Cows

Med Vet Entomol. 2014 Jun;28(2):193-200.

Repellent effectiveness of seven plant essential oils, sunflower oil and natural insecticides against horn flies on pastured dairy cows and heifers.

Plant essential oils (basil, geranium, balsam fir, lavender, lemongrass, peppermint, pine and tea tree), mixed with either sunflower oil or ethyl alcohol, were applied at 5% concentrations to the sides of Holstein cattle. Pastured cattle treated with essential oils diluted in sunflower oil had less flies than the untreated control for a 24-h period. However, the essential oil treatments were not significantly different than the carrier oil alone. Barn-held heifers treated with essential oils and sunflower oil alone had significantly less flies than the untreated control for up to 8 h after treatment. Basil, geranium, lavender, lemongrass and peppermint repelled more flies than sunflower oil alone for a period ranging from 1.5 to 4 h after treatments applied to heifers. All essential oils repelled > 75% of the flies on the treated area for 6 and 8 h on pastured cows and indoor heifers, respectively. Geranium, lemongrass and peppermint stayed effective for a longer duration. Essential oils mixed with ethyl alcohol demonstrated less repellence than when mixed with the carrier oil. Safer's soap, natural pyrethrins without piperonyl butoxide and ethyl alcohol alone were not efficient at repelling flies. Essential oils could be formulated for use as fly repellents in livestock production.

Animal Parasites

J Helminthol. 2015 Jun 22:1-6. [Epub ahead of print]

In vitro activity of essential oils of free and nanostructured Melaleuca alternifolia and of terpinen-4-ol on eggs and larvae of Haemonchus contortus.

Haemonchus contortus is one of the major gastrointestinal nematodes responsible for significant economic and production losses of sheep. Diseases caused by this species lack effective anthelmintic products, and the search for new compounds to replace synthetic anthelmintics has been extensive. The present investigation assesses the in vitro activity of the essential oil of melaleuca (Melaleuca alternifolia), both free (TTO) and nanostructured (nanoTTO), and terpinen-4-ol (terp-4-ol) on eggs and larvae of H. contortus. Tests of egg hatching (EHT) and inhibition of larval migration (LMIT) were used to assess the in vitro efficacy of TTO, nanoTTO and terp-4-ol. Using EHT, at a concentration of 3.5 mg/ml, 100% inhibition occurred using TTO and terp-4-ol, with LC50 values of 0.43 and 0.63 mg/ml, and LC90 values of 1.75 mg/ml and 3.12 mg/ml, respectively. NanoTTO had lower activity, with 82.6% inhibition at the same concentration. Using LMIT, TTO and nanoTTO had a similar activity with 88.0% and 84.8% inhibition, respectively, at a concentration of 56 mg/ml. Terp-4-ol had a greater effect on larvae, with 85.7% inhibition at a concentration of 56 mg/ml and 82.4% at 3.5 mg/ml, demonstrating high activity at the lowest concentration tested. Therefore, the results indicate that all substances tested showed ovicidal and larvicidal activity against H. contortus. TTO, terp-4-ol and, mainly, nanoTTO may be targeted in vivo

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studies, besides being a promising line of research into the control and treatment of veterinary important helminths.

Biomed Res Int. 2014;2014:549510.

Activity of tea tree (*Melaleuca alternifolia*) essential oil against L3 larvae of *Anisakis simplex*.

Nematicidal activity of *Melaleuca alternifolia* essential oil, commonly known as tea tree oil (TTO), was assayed in vitro against L3 larvae of *Anisakis simplex*. The results showed a mortality of 100% for concentrations between 7 and 10 $\mu\text{L}/\text{mL}$ after 48 h of incubation, obtaining an LD50 value of 4.53 $\mu\text{L}/\text{mL}$ after 24 hours and 4.27 $\mu\text{L}/\text{mL}$ after 48 hours. Concentration-dependent inhibition of acetylcholinesterase was observed for tea tree essential oil showing inhibition values of 100% at 100 $\mu\text{L}/\text{mL}$. This fact suggests that TTO may act as an AChE inhibitor. Terpinen-4-ol was discarded as main larvicide compound as it did not show larvicidal or anticholinesterase activity. The data obtained suggest that the essential oil of *Melaleuca alternifolia* may have a great therapeutic potential for the treatment of human anisakiasis.

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Insecticidal / Insect Repellent Activity

Trop Biomed. 2015 Mar;32(1):160-6.

In vitro repellent effect of tea tree (*Melaleuca alternifolia*) and andiroba (*Carapa guianensis*) oils on *Haemotobia irritans* and *Chrysomya megacephala* flies.

This study aimed to evaluate the repellent effect of tea tree (*Melaleuca alternifolia*) and andiroba (*Carapa guianensis*) essential oils on two species of flies (*Haemotobia irritans* and *Chrysomya megacephala*). For the in vitro studies, free-living adult flies were captured and reared in the laboratory. To verify the repellency effect, an apparatus was constructed where *H. irritans* and *C. megacephala* were exposed to andiroba and tea tree oils (5.0%), as well as to a known repellent (citronella, 5.0%) to validate the test. The study demonstrated that all three oils used showed in vitro repellent effect against both species of flies. It is possible to conclude that the essential oils (tea tree and andiroba) have repellent effect on these species of flies used in this study.

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Vet Parasitol. 2012 Mar 23;184(2-4):271-8.

Insecticidal and repellent effects of tea tree (*Melaleuca alternifolia*) oil against *Lucilia cuprina*.

Laboratory studies were conducted to assess the effect of tea tree oil (TTO) from *Melaleuca alternifolia* (terpinen-4-ol chemotype) against different stages of the Australian sheep blowfly *Lucilia cuprina*. When applied to wool, 3% TTO formulation repelled gravid female *L. cuprina* and prevented oviposition for six weeks. Formulations containing 1% TTO caused 100% mortality of *L. cuprina* eggs and 1st instar larvae and 2.5% TTO caused mortality of most second and third instar larvae in agar feeding assays. In experiments where third instar larvae were dipped in TTO formulations for 60s, concentrations of up to 50% TTO gave less than 50% kill. TTO at concentrations of 0.5%, 2% and 5% was strongly repellent to third instar larvae and caused them to evacuate treated areas. Inclusion of TTO in formulations with diazinon, ivermectin and boric acid reduced mortality in comparison with the larvicides used alone, at least partially because of avoidance behaviour stimulated by the TTO. Addition of TTO to wound treatments may aid in wound protection and myiasis resolution by preventing oviposition by *L. cuprina* adults.

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insecticidal action against *L. cuprina* eggs and larvae, stimulating larvae to leave the wound and through antimicrobial and anti-inflammatory properties that aid in wound healing.

Med Vet Entomol. 2014 Aug;28 Suppl 1:33-9.

Insecticidal and repellent effects of tea tree and andiroba oils on flies associated with livestock.

This study aimed to evaluate the insecticidal and repellent effects of tea tree, *Melaleuca alternifolia* (Myrtales: Myrtaceae), and andiroba, *Carapa guianensis* (Sapindales: Meliaceae), essential oils on two species of fly. For in vitro studies, free-living adult flies were captured and reared in the laboratory. To evaluate the insecticidal effects of the oils, adult flies of *Haematobia irritans* (L.) and *Musca domestica* L. (both: Diptera: Muscidae) were separated by species in test cages (n=10 per group), and subsequently tested with oils at concentrations of 1.0% and 5.0% using a negative control to validate the test. Both oils showed insecticidal activity. Tea tree oil at a concentration of 5.0% was able to kill *M.domestica* with 100.0% efficacy after 12h of exposure. However, the effectiveness of andiroba oil at a concentration of 5.0% was only 67.0%. The insecticidal efficacy (100.0%) of both oils against *H.irritans* was observed at both concentrations for up to 4h. The repellency effects of the oils at concentrations of 5.0% were tested in vivo on Holstein cows naturally infested by *H.irritans*. Both oils demonstrated repellency at 24h, when the numbers of flies on cows treated with tea tree and andiroba oil were 61.6% and 57.7%, respectively, lower than the number of flies on control animals. It is possible to conclude that these essential oils have insecticidal and repellent effects against the species of fly used in this study.

Exp Appl Acarol. 2014 May;63(1):77-83.

Influence of tea tree oil (*Melaleuca alternifolia*) on the cattle tick *Rhipicephalus microplus*.

The aim of this study was to verify the influence of tea tree oil (TTO) (*Melaleuca alternifolia*) tested in its pure and nanostructured (TTO nanoparticles) forms on the reproduction of female *Rhipicephalus microplus*. For our purpose, female ticks were collected from naturally infected animals and treated in vitro with TTO (1, 5, and 10 %) and TTO nanoparticles (0.075, 0.375, and 0.75 %). In order to validate the tests, they were performed in triplicate using positive (amitraz) and negative (untreated) controls. It was possible to observe that pure TTO (5 and 10 %) and TTO nanoparticles (0.375 and 0.75 %) showed 100 % reproductive inhibition on female ticks. Additionally, pure TTO (1 %) also showed an acaricide effect (70 %), similarly to the positive control (78.3 %). This is the first study demonstrating the activity of pure TTO and TTO nanoparticles on female ticks. Therefore, based on these results, we were able to show that both forms and all concentrations of *M. alternifolia* affected tick reproduction by inhibiting egg laying and hatching. We were also able to show that TTO nanoparticles potentiated the inhibitor effect of pure TTO on the reproduction of *R. microplus*.

Med Vet Entomol. 2013 Dec;27(4):408-13.

Control of the chewing louse *Bovicola (Werneckiella) ocellatus* in donkeys, using essential oils.

Infestations by lice can be a significant clinical and welfare issue in the management of large animals. The limited range of commercial pediculicides available and the development of resistance have led to the need to explore alternative louse management approaches. The results of in vitro and in vivo trials undertaken to control populations of the donkey chewing louse, *Bovicola ocellatus* (Piaget) (Phthiraptera: Trichodectidae) using the essential oils of tea tree (*Melaleuca alternifolia*) and lavender (*Lavandula angustifolia*) are reported here. Results of contact and vapour bioassays showed that 5% (v/v) tea tree and lavender oils resulted in >80% louse mortality after 2h of exposure. On farms, separate groups of 10 donkeys sprayed with 5% (v/v) tea tree and lavender oil as part of their usual grooming regime showed

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significant reductions in louse numbers compared with a control group (0.2% polysorbate 80 in water). These findings indicate that tea tree and lavender essential oils can provide clinically useful levels of control of *B. ocellatus* when used as part of a grooming routine and suggest that with further development could form the basis of an easy to apply and valuable component of a louse management programme for donkeys.

Parasitol Res. 2008 Sep;103(4):889-98.

Medicinal plant treatments for fleas and ear problems of cats and dogs in British Columbia, Canada.

Research conducted in 2003/2004 documented and validated (in a non-experimental way) ethnoveterinary medicines used by small-scale, organic livestock farmers in British Columbia (BC), Canada. Interviews were conducted with 60 participants who were organic farmers or holistic medicinal/veterinary practitioners. A workshop was held with selected participants to discuss the plant-based treatments. This paper reports on the medicinal plants used for fleas in cats and dogs. Fleas and flies are treated with *Artemisia vulgaris* L. (Asteraceae), *Citrus x limon* (L.), *Juniperus communis* L. var. *depressa* Pursh. (Cupressaceae), *Lavandula officinalis* L. (Labiatae), *Melissa officinalis* L. (Lamiaceae), and *Thuja plicata* Donn ex D. Don (Cupressaceae). All of the plants used have insecticidal activity. Ear problems are treated with *Achillea millefolium* L., *Calendula officinalis* L., and *Helichrysum angustifolium* (Roth.) G. Don. (Asteraceae), *Allium sativum* L. (Alliaceae), *Berberis aquifolium* Pursh./*Mahonia aquifolium* (Berberidaceae), *Glycyrrhiza glabra* L. (Fabaceae), *Lobelia inflata* L. (Campanulaceae), *Matricaria recutita* L., *Melaleuca alternifolia* L. (Myrtaceae), *Origanum vulgare* L. (Labiatae), *Ricinus communis* L. (Euphorbiaceae), *Syzygium aromaticum* (L.) Merr. & L. M. Perry (Myrtaceae), *Thymus vulgaris* L. (Lamiaceae), and *Verbascum thapsus* L. (Scrophulariaceae).

Vet Parasitol. 2012 Oct 26;189(2-4):338-43.

Dipping and jetting with tea tree (*Melaleuca alternifolia*) oil formulations control lice (*Bovicola ovis*) on sheep.

The in vivo pediculicidal effectiveness of 1% and 2% formulations of tea tree (*Melaleuca alternifolia*) oil (TTO) against sheep chewing lice (*Bovicola ovis*) was tested in two pen studies. Immersion dipping of sheep shorn two weeks before treatment in both 1% and 2% formulations reduced lice to non detectable levels. No lice were found on any of the treated sheep despite careful inspection of at least 40 fleece partings per animal at 2, 6, 12 and 20 weeks after treatment. In the untreated sheep louse numbers increased from a mean (\pm SE) of 2.4 (\pm 0.7) per 10 cm fleece part at 2 weeks to 12.3 (\pm 4.2) per part at 20 weeks. Treatment of sheep with 6 months wool by jetting (high pressure spraying into the fleece) reduced louse numbers by 94% in comparison to controls at two weeks after treatment with both 1% and 2% TTO formulations. At 6 and 12 weeks after treatment reductions were 94% and 91% respectively with the 1% formulation and 78% and 84% respectively with the 2% formulation. TTO treatment also appeared to reduce wool damage in infested sheep. Laboratory studies indicated that tea tree oil 'stripped' from solution with a progressive reduction in concentration as well as volume as more wool was dipped, indicating that reinforcement of active ingredient would be required to maintain effectiveness when large numbers of sheep are treated. The results of these studies suggest significant potential for the development of ovine lousicides incorporating TTO.

Vet Parasitol. 2012 Jul 6;187(3-4):498-504.

Bioactivity of tea tree oil from *Melaleuca alternifolia* against sheep lice (*Bovicola ovis* Schrank) in vitro.

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Tea tree oil (TTO) from the Australian native plant *Melaleuca alternifolia* has wide ranging bio-active properties, including insecticidal and repellent activity against arthropods. Furthermore, composition of commercially available Australian TTO is specified under an International Organization for Standardization standard (ISO 4730), reducing the potential for variable effects often noted with botanical pesticides. The effect of TTO, meeting the ISO standard for terpinen-4-ol chemotype, was tested against sheep lice (*Bovicola ovis* Schrank) in a series of laboratory studies. Immersion of wool for 60s in formulations containing concentrations of 1% TTO and above caused 100% mortality of adult lice and eggs. Exposure to vapours from TTO, delivered as droplets in fumigation chambers and when applied to wool also caused high mortality in both lice and eggs. The main active component of TTO in the fumigant tests was terpinen-4-ol. Treated surface assays and tests with wool where the formulation was allowed to dry before exposure of lice indicated low persistence. These studies demonstrate that TTO is highly toxic to sheep lice and active at concentrations that suggest potential for the development of TTO-based ovine lousicides.

Res Vet Sci. 2012 Oct;93(2):831-5.

Toxicity of essential and non-essential oils against the chewing louse, *Bovicola* (*Werneckiella*) *ocellatus*.

The toxicity of six plant essential oils to the chewing louse, *Bovicola* (*Werneckiella*) *ocellatus* collected from donkeys, was examined in laboratory bioassays. The oils examined were: tea-tree (*Melaleuca alternifolia*), lavender (*Lavandula angustifolia*), peppermint (*Mentha piperita*), eucalyptus (*Eucalyptus globulus* Labillardiere), clove bud (*Eugenia caryophyllata*) and camphor (*Cinnamomum camphora*). All except camphor oil showed high levels of toxicity, with significant dose-dependent mortality and an LC(50) at concentrations of below 2% (v/v). Hundred percent mortality was achieved at concentrations of 5-10% (v/v). Two essential oil components: eugenol and (+)-terpinen-4-ol showed similar levels of toxicity. The data suggest that these botanical products may offer environmentally and toxicologically safe, alternative veterinary pediculicides for the control of ectoparasitic lice.

Pathogenic Plant Fungus/Mold

Commun Agric Appl Biol Sci. 2014;79(3):439-49.

ACTIVITY OF NATURAL PRODUCTS AGAINST SOME PHYTOPATHOGENIC FUNGI.

The requirement of environmental protection and food safety is perceived with always major interest by public opinion and it is consistent with European Union legislation on the sustainable use of pesticides (Directive 2009/128/EC). This directive requires member states to promote low pesticide-input, giving priority to non-chemical methods and low risk plant protection products. In order to contribute to the achievement of these objectives antifungal activity of natural substances, characterized by a good toxicological and ecotoxicological profile, was tested. Essential oil of *Melaleuca alternifolia*, essential oil of *Syzygium aromaticum* and extract from *Mimosa tenuiflora* were tested against *Alternaria alternata*, *Botrytis cinerea* and *Fusarium oxysporum* f. sp. *lycopersici* (races 1 and 2). In vitro tests involved determination of radial growth of the colonies of fungi in the presence of varying concentrations of tested products in agar media and determination of germination percentage in the presence of tested product at various concentrations. The products based on essential oil of *M. alternifolia* were also tested in vivo on tomato fruits wounded and artificially inoculated with *A. alternata* or with *B. cinerea*. The in vitro tests showed the antifungal activity of both essential oils instead the extract from *M. tenuiflora* exhibited poor antifungal activity and only against *A. alternata* and *B. cinerea*. The results on tomato fruits showed

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inhibition of grey mould and black mould by essential oil of *M. alternifolia*. The antifungal activity increased with increasing concentrations. In conclusion, the obtained results in the present study showed promising prospects for the utilisation of investigated products to reduce the using of antifungal chemicals and to achieve a more sustainable use of pesticides.