Essential Oil Research

Eucalyptus

Stimulatory effect of Eucalyptus essential oil on innate cell-mediated immune response.

BMC Immunol. 2008 Apr 18; Serafino A, Vallebona PS, Andreola F, Zonfrillo M, Mercuri L, Federici M, Rasi G, Garaci E, Pierimarchi P.
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BACKGROUND: Besides few data concerning the antiseptic properties against a range of microbial agents and the anti-inflammatory potential both in vitro and in vivo, little is known about the influence of Eucalyptus oil (EO) extract on the monocytic/macrophagic system, one of the primary cellular effectors of the immune response against pathogen attacks. The activities of this natural extract have mainly been recognized through clinical experience, but there have been relatively little scientific studies on its biological actions. Here we investigated whether EO extract is able to affect the phagocytic ability of human monocyte derived macrophages (MDMs) in vitro and of rat peripheral blood monocytes/granulocytes in vivo in absence or in presence of immuno-suppression induced by the chemotherapeutic agent 5-fluorouracil (5-FU). METHODS: Morphological activation of human MDMs was analysed by scanning electron microscopy. Phagocytic activity was tested: i) in vitro in EO treated and untreated MDMs, by confocal microscopy after fluorescent beads administration; ii) in vivo in monocytes/granulocytes from peripheral blood of immuno-competent or 5-FU immuno-suppressed rats, after EO oral administration, by flow cytometry using fluorescein-labelled E. coli. Cytokine release by MDMs was determined using the BD Cytometric Bead Array human Th1/Th2 cytokine kit. RESULTS: EO is able to induce activation of MDMs, dramatically stimulating their phagocytic response. EO-stimulated internalization is coupled to low release of pro-inflammatory cytokines and requires integrity of the microtubule network, suggesting that EO may act by means of complement receptor-mediated phagocytosis. Implementation of innate cell-mediated immune response was also observed in vivo after EO administration, mainly involving the peripheral blood monocytes/granulocytes. The 5-FU/EO combined treatment inhibited the 5-FU induced myelotoxicity and raised the phagocytic activity of the granulocytic/monocytic system, significantly decreased by the chemotherapic. CONCLUSION: Our data, demonstrating that Eucalyptus oil extract is able to

implement the innate cell-mediated immune response, provide scientific support for an additional use of this plant extract, besides those concerning its antiseptic and anti-inflammatory properties and stimulate further investigations also using single components of this essential oil. This might drive development of a possible new family of immuno-regulatory agents, useful as adjuvant in immuno-suppressive pathologies, in infectious disease and after tumour chemotherapy.

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Juniper

Antibacterial and Antifungal
In our study we estimated the antibacterial and antifungal activity of three different juniper berry oils and their main components. All the micro-organisms used in this experiment were isolated from patients, and some of them showed resistance against commonly used antibiotics. Only one of the oils revealed good antimicrobial properties. None of the single oil components was a stronger antibacterial and antifungal inhibitor than the oil itself. Our data suggest that the antimicrobial activity of juniper oil is the result of either the specific composition of the oil (highest concentration of (-)-alpha-pinene, p-cymene and beta-pinene) or activity of a single non-identified compound. (Antibacterial and antifungal activity of juniper berry oil and its selected components. Filipowicz N, Kaminski M, Kurlenda J, Asztemborska M, Ochocka JR. Department of Biology and Pharmaceutical Botany, Medical University of Gdansk, Gdansk, Poland.)

Insecticidal
Extracts of woods commonly used for animal bedding were tested for antimicrobial activity. Extracts of Alaska cedar and western juniper showed significant antimicrobial activity against each of the microbes tested. The major chemical components of western juniper (cedrol and alpha- and beta-cedrene) were also tested. In western juniper, alpha- and beta-cedrene were found to be active components.
(Antimicrobial activity of some Pacific Northwest woods against anaerobic bacteria and yeast. Johnston WH, Karchesy JJ, Constantine GH, Craig AM. College of Veterinary Medicine, 105 Magruder Hall, Oregon State University, Corvallis, Oregon 97331, USA.)

Food preservative
In this work, the chemical compositions and antimicrobial properties of Juniperus essential oils and of their main components were determined. The antimicrobial activities of the oils and their components against food spoilage and pathogenic microorganisms were determined. The oils extracted from J. turbinata specimens were active against fungi, particularly against a strain of Aspergillus flavus (an aflatoxin B1 producer). Of the single compounds tested, delta-3-carene was found to possess the broadest spectrum of activity and appeared to contribute significantly to the antifungal activity observed for J. turbinata oils. This activity may be helpful in the prevention of aflatoxin contamination for many foods.

(Composition and antimicrobial properties of Sardinian Juniperus essential oils against foodborne pathogens and spoilage microorganisms. Cosentino S, Barra A, Pisano B, Cabizza M, Pirisi FM, Palmas F.
Department of Experimental Biology, University of Cagliari, S.S. 554 Km. 4,500, 09042 Monserrato, CA, Sardinia, Italy)

Relationship between bone tissue and wood
The wood of Juniperus communis and bone possess similarities in microstructural elements. Moreover, the wood is strong, durable, dense and is impregnated with essential oil that has antiseptic properties. Hip prostheses were shaped from juniper wood to match the geometry of animal femurs. One femoral head was then replaced with the wooden substitute in each animal. Implant rejection arising from infection was not observed and at three months, connective tissue was found abutting the implant and open (wood) cell walls were filled with tissue. Foreign body giant cells were not observed. After six months, bone was seen adjacent to the wood and some outer wood cells appeared to be filled with bone. Three years after implantation, secondary Haversian bone had formed adjacent to the wood and a central hole in the wood (from the drilling operation in the femoral stem) contained bone that made continuous contact with all locations in the wood. There were no signs of degradation in the wood and this was attributed to its essential oil content.
(Juniper wood as a possible implant material. Gross K A, Ezerietis E; Journal of Biomedical Material Research)

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Tea Tree

The mode of antimicrobial action of the essential oil of Melaleuca alternifolia (tea tree oil).
J Appl Microbiol. 2000 Jan;
Cox SD, Mann CM, Markham JL, Bell HC, Gustafson JE, Warmington JR, Wyllie SG.
Centre for Biostructural and Biomolecular Research, University of Western Sydney, Hawkesbury, New South Wales, Western Australia. s.cox@uws.edu.au

The essential oil of Melaleuca alternifolia (tea tree) exhibits broad-spectrum antimicrobial activity. Its mode of action against the Gram-negative bacterium Escherichia coli AG100, the Gram-positive bacterium Staphylococcus aureus NCTC 8325, and the yeast Candida albicans has been investigated using a range of methods. We report that exposing these organisms to minimum inhibitory and minimum bactericidal/fungicidal concentrations of tea tree oil inhibited respiration and increased the permeability of bacterial cytoplasmic and yeast plasma membranes as indicated by uptake of propidium iodide. In the case of E. coli and Staph. aureus, tea tree oil also caused potassium ion leakage. Differences in the susceptibility of the test organisms to tea tree oil were also observed and these are interpreted in terms of variations in the rate of monoterpene penetration through cell wall and cell membrane structures. The ability of tea tree oil to disrupt the permeability barrier of cell membrane structures and the accompanying loss of chemiosmotic control is the most likely source of its lethal action at minimum inhibitory levels.

Mechanism of action of Melaleuca alternifolia (tea tree) oil on Staphylococcus aureus determined by time-kill, lysis, leakage, and salt tolerance assays and electron microscopy.

Antimicrob Agents Chemother. 2002 Jun; Carson CF, Mee BJ, Riley TV.
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The essential oil of Melaleuca alternifolia (tea tree) has broad-spectrum antimicrobial activity. The mechanisms of action of tea tree oil and three of its components, 1,8-cineole, terpinen-4-ol, and alpha-terpineol, against Staphylococcus aureus ATCC 9144 were investigated. Treatment with these agents at their MICs and two times their MICs, particularly treatment with terpinen-4-ol and alpha-terpineol, reduced the viability of S. aureus. None of the agents caused lysis, as determined by measurement of the optical density at 620 nm, although cells became disproportionately sensitive to subsequent autolysis. Loss of 260-nm-absorbing material occurred after treatment with concentrations equivalent to the MIC, particularly after treatment with 1,8-cineole and alpha-terpineol. S. aureus organisms treated with tea tree oil or its components at the MIC or two times the MIC showed a significant loss of tolerance to NaCl. When the agents were tested at one-half the MIC, only 1,8-cineole significantly reduced the tolerance of S. aureus to NaCl. Electron microscopy of terpinen-4-ol-treated cells showed the formation of mesosomes and the loss of cytoplasmic contents. The predisposition to lysis, the loss of 260-nm-absorbing material, the loss of tolerance to NaCl, and the altered morphology seen by electron microscopy all suggest that tea tree oil and its components compromise the cytoplasmic membrane.

Acaricidal activity of Melaleuca alternifolia (tea tree) oil: in vitro sensitivity of sarcoptes scabiei var hominis to terpinen-4-ol.

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OBJECTIVE: To compare the acaricidal activity of Melaleuca alternifolia (tea tree) oil (TTO) and some of its individual active components on the itch mite Sarcoptes scabiei var hominis. DESIGN: In vitro acaricide sensitivity assessment. SETTING: The Menzies School of Health Research laboratory, located near the Infectious Diseases Ward of the Royal Darwin Hospital, Australia, where patients are admitted and treated for crusted scabies. PARTICIPANTS: Scabies mites (S scabiei var hominis) were collected from a 20-year-old Aboriginal woman admitted to the Royal Darwin Hospital with crusted scabies.Interventions Within 3 hours of collection, scabies mites were placed in continuous direct contact with the TTO products and control acaricides and were observed at regular intervals. MAIN OUTCOME MEASURES: Percentage of mites dead at regular observation intervals between 5 minutes and 24 hours during continuous exposure to the TTO products and acaricides. RESULTS: The 5% TTO and active component terpinen-4-ol were highly effective in reducing mite survival times. Statistically significant differences in mite survival curves were observed for 5% TTO, 2.1% terpinen-4-ol, 5% permethrin, and ivermectin

(100 microg/g of Emulsifying Ointment British Pharmacopoeia 88). In vivo effectiveness was also observed. CONCLUSIONS: Documentation of resistance against antiectoparasitic compounds is increasing. Reported S scabiei treatment failures with lindane, crotamiton, and benzyl benzoate, as well as likely emerging resistance to 5% permethrin and oral ivermectin, are of concern and advocate for the identification and development of novel acaricidal drugs. Tea tree oil is a membrane-active biocide extracted from the tree M alternifolia. It is a principal antimicrobial in a wide range of pharmaceuticals sold in Australia, with the main active component being oxygenated terpenoids. The results suggest that TTO has a potential role as a new topical acaricide and confirm terpinen-4-ol as the primary active component.

Free Radic Res. 2004 Aug;38(8):805-11.

Anti-inflammatory effects of Melaleuca alternifolia essential oil on human polymorphonuclear neutrophils and monocytes.

Caldefie-Chezet F, **Guerry M**, **Chalchat JC**, **Fusillier C**, **Vasson MP**, **Guillot J**.
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OBJECTIVE AND DESIGN: The fungicidal and bactericidal actions of the essential oil (EO) of Melaleuca alternifolia seem well established, but their anti-inflammatory and anti-oxidative effects remain unclear. In this study, we investigated in vitro the possible role of whole M. alternifolia EO as a modulator of the oxidative response, i.e. reactive oxygen species (ROS) production, of leukocytes (monocytes and polymorphonuclear neutrophils (PMNs)) in humans. METHODS: Whole blood leukocytes from healthy human volunteers (n = 7), isolated from erythrocytes by haemolytic shock, were incubated for 30 min with M. alternifolia EO (0-0.1%) to determine their ROS production by flow cytometry with or without stimulation of cells. We compared the effects of 3 different stimulating agents acting differently on transductional pathways to stimulate the ROS production: a phorbol ester (PMA), formyl-methionyl-leucyl-phenylalanine (fMLP) and opsonised zymosan (OZ). RESULTS: As attested by the Kruskall-Wallis test, M. alternifolia EO at 0.1% directly stimulated ROS production by PMNs (x 8.7 vs. 0% EO, $p < 0.05$) and increased the intracellular ROS produced by monocytes. Whichever the stimulating agent used (PMA, fMLP or OZ), M. alternifolia EO decreased the intracellular ROS production at the dilution of 0.1% by PMNs and monocytes, more so with PMNs. CONCLUSION: M. alternifolia EO may be both a direct active mediator of the bactericidal action of the circulating leukocytes and may be efficient in protecting the organism from an excess of ROS, through an anti-oxidant and radical scavenging activity.

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

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

Vazquez JA, **Arganoza MT**, **Boikov D**, **Akins RA**, **Vaishampayan JK**.
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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 alternafolia 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.

Vet Parasitol. 2005 Apr 20;129(1-2):173-6.
Acaricidal properties of the essential oil of Melaleuca alternifolia Cheel (tea tree oil) against nymphs of Ixodes ricinus.
Iori A, **Grazioli D**, **Gentile E**, **Marano G**, **Salvatore G**.
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The aim of the study was to examine the acaricidal effect of essential oil of Melaleuca alternifolia (tea tree oil, TTO) at different doses (4, 6, 8 and 10 microl) and for different exposure times (30, 60, 90 and 120 min) on nymphs of Ixodes ricinus. A dose of 8 microl TTO was lethal for more than 70% of ticks when inhaled and this effect was enhanced when the dose was increased to 10 microl (> 80%). The effect was correlated with the duration of exposure of ticks to TTO, with a significant effect being observed after 90 min exposure. The findings show that TTO has acaricidal properties and could be extremely useful in controlling ticks that are efficient vectors of pathogens.

Dis Aquat Organ. 2005 Aug 9;66(1):29-32.
Effect of Australian tea tree oil on Gyrodactylus spp. infection of the three-spined stickleback Gasterosteus aculeatus.
Steverding D, **Morgan E**, **Tkaczynski P**, **Walder F**, **Tinsley R**.
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Gyrodactylus spp. infections of commercially farmed fishes are responsible for significant economic losses. Existing treatments have proved uneconomic, stressful to the fishes, and ecologically damaging. Essential oils are naturally occurring compounds that exhibit a wide range of anti-microbial and anti-fungal activities. This study explored the possibility of using Australian tea tree (Melaleuca alternifolia) oil (TTO) to treat Gyrodactylus spp. infection on the three-spined stickleback Gasterosteus aculeatus. In the presence of 0.01 % Tween 80 as an emulsifier, TTO treatments at concentrations between 3 and 30 ppmv (parts per million by volume) lowered the prevalence and significantly reduced the

parasite burden of sticklebacks naturally infected with Gyrodactylus spp. In addition, Tween 80 alone exhibited parasiticidal activity against Gyrodactylus spp. These findings show the potential of TTO in combination with Tween 80 as an effective treatment of Gyrodactylus spp. infection of fishes.

Phytother Res. 2006 May;20(5):364-70.
Potential anti-inflammatory effects of Melaleuca alternifolia essential oil on human peripheral blood leukocytes.
Caldefie-Chezet F, **Fusillier C**, **Jarde T**, **Laroye H**, **Damez M**, **Vasson MP**, **Guillot J**.
Laboratoire de Botanique, Cryptogamie et Microbiologie, CRNH Auvergne, Clermont-Ferrand, France.

The fungicidal and bactericidal actions of the essential oil (EO) of Melaleuca alternifolia seem well established, but their anti-inflammatory and antioxidative effects remain unclear. This study investigated in vitro the possible role of whole Melaleuca alternifolia EO as a modulator of the inflammatory/non-specific immune response by exploring the chemotaxis and kinetic radical oxygen species (ROS) production of leukocytes and cytokine secretion in peripheral blood mononuclear cells (PBMCs) in humans.The influence of Melaleuca alternifolia EO on the chemotaxis under agarose of isolated neutrophils (PMNs) was evaluated. The kinetics of ROS production by stimulated total circulating leukocytes was followed over 2 h by recording the fluorescence intensity of oxidized dihydrorhodamine 123. The effects of this EO on pro-(interleukin IL-2) and anti-(IL-4 and IL10) inflammatory cytokine secretions were determined by ELISA following incubation of PBMCs with the EO for 24 h.Melaleuca alternifolia EO was inefficient on the chemotaxis of PMNs. It exerted an antioxidant effect, reducing ROS production throughout the kinetic study. Melaleuca alternifolia EO inhibited PBMC proliferation, as revealed by a reduction in IL-2 secretion by stimulated lymphocytes. This EO at 0.1% directly increased the secretion of the anti-inflammatory cytokine IL-4 compared with IL-4 secretion without EO (18.5 +/- 10.0 vs 3.3 +/- 1, $p < 0.05$), and also increased IL-10 secretion at 0.01% (94.9 +/- 38.7 vs 44.1 +/- 18, ns). Melaleuca alternifolia EO may not only act as an anti-inflammatory mediator through its antioxidant activity but may also efficiently protect the organism by reducing the proliferation of inflammatory cells without affecting their capacity to secrete anti-inflammatory cytokines. Copyright (c) 2006 John Wiley & Sons, Ltd.

Oral Oncol. 2006 May;42(5):487-92. Epub 2006 Feb 20.
Susceptibility to Melaleuca alternifolia (tea tree) oil of yeasts isolated from the mouths of patients with advanced cancer.
Bagg J, **Jackson MS**, **Petrina Sweeney M**, **Ramage G**, **Davies AN**.
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Yeasts that are resistant to azole antifungal drugs are increasingly isolated from the mouths of cancer patients suffering from oral fungal infections. Tea tree oil is an agent possessing antimicrobial properties that may prove useful in the prevention and management of infections caused by these organisms. In this study, 301 yeasts isolated

from the mouths of 199 patients suffering from advanced cancer were examined by an in vitro agar dilution assay for susceptibility to tea tree oil. All of the isolates tested were susceptible, including 41 that were known to be resistant to both fluconazole and itraconazole. Clinical studies of tea tree oil as an agent for the prevention and treatment of oral fungal infections in immunocompromised patients merit consideration.

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.
Kim HJ, **Chen F**, **Wu C**, **Wang X**, **Chung HY**, **Jin Z**.
Department of Food Science, Clemson University, Clemson, South Carolina 29634, USA.

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.

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.
Calcabrini A, **Stringaro A**, **Toccacieli L**, **Meschini S**, **Marra M**, **Colone M**, **Salvatore G**, **Mondello F**, **Arancia G**, **Molinari A**.
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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 adriamicin-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 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.

Phytother Res. 2004 Jan;18(1):30-5.
Chemical and biological evaluation of the essential oils of different Melaleuca species.

M. ericifolia, M. leucadendron, M. armillaris and M. styphelioides were isolated by a hydrodistillation method and analysed by a gas chromatography/mass spectrometry (GC/MS) technique. The essential oil of M. ericifolia contained methyl eugenol (96.84%) as a major constituent, whereas M. leucadendron was rich in 1,8-cineole (64.30%). The essential oil of M. armillaris was rich in 1,8-cineole (33.93%) followed by terpinen-4-ol (18.79%), whereas M. styphelioides was rich in caryophyllene oxide (43.78%) and (-) spathulenol (9.65%). The essential oils of these species possessed antimicrobial and antifungal activities. M. ericifolia exhibited the highest inhibitory effects against Bacillus subtiles and Aspergillus niger. The antiviral activities of the essential oils against Herpes simplex virus type 1 (HSV-1) were studied in African green monkey kidney cells (Vero) by a plaque reduction assay. The volatile oil of M. armillaris was more effective as a virucidal (up to 99%) than that of M. leucadendron (92%) and M. ericifolia (91.5%). The effects of the essential oils on the antioxidant system status in carbon tetrachloride treated animals were studied. The essential oil of M. armillaris exhibited a marked antioxidant effect, it improved vitamin E, vitamin C and superoxide dismutase parameters so it can be used as a free radical suppressor. Copyright 2004 John Wiley & Sons, Ltd.

Lett Appl Microbiol. 2003;37(2):185-7.
Antimycotic activity of Melaleuca alternifolia essential oil and its major components.
Oliva B, **Piccirilli E**, **Ceddia T**, **Pontieri E**, **Aureli P**, **Ferrini AM**.
Department of Experimental Medicine, Section of Microbiology, University of L'Aquila, L'Aquila, Italy. oliva@univaq.it

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-olo were the most active compounds. CONCLUSIONS: The majority of the organisms were sensitive to the essential oil, with TTO and terpinen-4-olo 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-olo and suggests further studies for a possible therapeutic use.

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Thyme

Thymus is a genus of around 350 species of woody-based, aromatic, evergreen perennials and shrubs found mainly on dry grassland throughout Europe and Asia.
Thymol is the primary constituent of some species, carvacrol of others, and borneol of others.

Strong Anti-microbial Effects
The extracts from thyme by water and ethanol, thyme essential oil, thymol and carvacrol were used as antimicrobial agents. The results show that all antimicrobial agents used have strong inhibition activity against Staphalococcus aureus, Bacillus subtilis, Escherichia coli.

[Studies on antimicrobial activity of extracts from thyme] Fan M, Chen J. School of Biology, Jiangsu University of Science and Technology, Zhenjiang 212013, China.

Review of strongest antimicrobial oils
In recent years (1987-2001), a large number of essential oils and their constituents have been investigated for their antimicrobial properties against some bacteria and fungi in more than 500 reports. Essential oils of spices and herbs (thyme, origanum, mint, cinnamon, salvia and clove) were found to possess the strongest antimicrobial properties among many tested.

Curr Med Chem. 2003 May;10(10):813-29.Antibacterial and antifungal properties of essential oils. Kalemba D, Kunicka A. Institute of General Food Chemistry, Technical University of Lodz, Poland

Spices and herbs inhibit Shigella
Cloves, thyme, oregano, allspice, basil, rosemary, and marjoram showed antimicrobial effects on Shigella flexneri and Shigella sonnei. It was established that basil or thyme can contribute to combination processing as a growth-inhibitory factor for Shigella spp.

J Food Prot. 2003 Apr;66(4):668-73.Antimicrobial effect of spices and herbs on Shigella sonnei and Shigella flexneri. Bagamboula CF, Uyttendaele M, Debevere J. Laboratory of Food Microbiology and Food Preservation, Faculty of Agricultural and Applied Biological Sciences, Ghent University, Coupure Links 653, B-9000 Ghent, Belgium.

Carvacrol and cymene demonstrate synergistic antimicrobial effects as food preservatives
The antimicrobial activity of carvacrol, a compound present in the essential oil fraction of oreganum and thyme, toward the foodborne pathogen Bacillus cereus on rice was studied. To decrease the input of carvacrol on the taste and flavor of the product, a combined treatment with the structure analog cymene was tested. A synergistic effect was observed when 0.30 mg/g carvacrol was combined with 0.27 mg/g cymene. Finally it was demonstrated that a common taste enhancer like soya sauce also increased the antimicrobial action of carvacrol toward B. cereus. The antimicrobial activity of carvacrol with cymene or soya sauce was influenced by the addition of NaCl.

J Food Prot. 2000 May;63(5):620-4.Antimicrobial activity of carvacrol toward Bacillus cereus on rice. Ultee A, Slump RA, Steging G, Smid EJ. Agrotechnological Research Institute (ATO-DLO), Wageningen, The Netherlands.

Spice oils have potent antibacterial effects against 25 genera of bacteria
The volatile oils of black pepper [Piper nigrum L. (Piperaceae)], clove [Syzygium aromaticum (L.) Merr. & Perry (Myrtaceae)], geranium [Pelargonium graveolens L'Herit (Geraniaceae)], nutmeg [Myristica fragrans Houtt. (Myristicaceae), oregano [Origanum vulgare ssp. hirtum (Link) Letsw. (Lamiaceae)] and thyme [Thymus vulgaris L. (Lamiaceae)] were assessed for antibacterial activity against 25 different genera of bacteria. These included animal and plant pathogens, food poisoning and spoilage bacteria. The volatile oils exhibited considerable inhibitory effects against all the organisms under test while their major components demonstrated various degrees of growth inhibition.

J Appl Microbiol. 2000 Feb;88(2):308-16.Antimicrobial agents from plants: antibacterial activity of plant volatile oils. Dorman HJ, Deans SG. Aromatic and Medicinal Plant Group, Scottish Agricultural College, Auchincruive, South Ayrshire, UK.

Carvacrol and thymol most effective against foodborne bacteria
Three essential oils obtained from different species of Thymus growing wild in Sardinia and a commercial sample of Thymus capitatus oil were analysed. The GC/MS analysis showed that the major constituents of the oils were monoterpene hydrocarbons and phenolic monoterpenes, but the concentration of these compounds varied greatly among the oils examined. The results of the antimicrobial assay showed that essential oils extracted from Sardinian Thymus species have an antimicrobial activity comparable to the one observed in other thyme oils. It seems also confirmed that the antimicrobial properties of thyme essential oils are mainly related to their high phenolic content. Among the single compounds tested carvacrol and thymol turned out to be the most efficient against both reference strains and food-derived bacteria. The results of this study confirmed the possibility of using thyme essential oils or some of their components in food systems to prevent the growth of foodborne bacteria and extend the shelf-life of processed foods.

Lett Appl Microbiol. 1999 Aug;29(2):130-5.In-vitro antimicrobial activity and chemical composition of Sardinian Thymus essential oils. Cosentino S, Tuberoso CI, Pisano B, Satta M, Mascia V, Arzedi E, Palmas F. Department of Experimental Biology, University of Cagliari, Sardinia, Italy.

Thyme oil from flowering stage has most antibacterial power, especially against Escherichia coli O157:H7

J Food Prot. 1999 Sep;62(9):1017-23.Antimicrobial activity of the essential oils of Thymus vulgaris L. measured using a bioimpedometric method. Marino M, Bersani C, Comi G. Dipartimento di Scienze degli Alimenti, Facolta di Agraria, Universita degli Studi di Udine, Italy.

Thyme oil the most potent of 52 oils against C. albicans and E. coli
52 plant oils and extracts were investigated for activity against Acinetobacter baumanii, Aeromonas veronii biogroup sobria, Candida albicans, Enterococcus faecalis, Escherichia col, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella enterica subsp. enterica serotype typhimurium, Serratia marcescens and Staphylococcus aureus, using an agar dilution method. The lowest minimum inhibitory concentrations were 0.03% (v/v) thyme oil against C. albicans and E. coli and 0.008% (v/v) vetiver oil against Staph. aureus. These results support the notion that plant essential oils and extracts may have a role as pharmaceuticals and preservatives.

J Appl Microbiol. 1999 Jun;86(6):985-90.Antimicrobial activity of essential oils and other plant extracts. Hammer KA, Carson CF, Riley TV. Department of Microbiology, The University of Western Australia, Nedlands, Western Australia.

Monoterpenes of thyme oil more effective mosquito repellant than deet
Five monoterpenes (carvacrol, p-cymene, linalool, alpha-terpinene, and thymol) derived from the essential oil of thyme (Thymus vulgaris) were examined for their repellency against the mosquito Culex pipiens pallens. All 5 monoterpenes effectively repelled mosquitoes based on a human forearm bioassay. Alpha-terpinene and carvacrol showed significantly greater repellency than a commercial formulation, N,N-diethyl-m-methylbenzamide (deet), whereas thymol showed similar repellency to that of deet. The duration of repellency after application for all these monoterpenes was equal to or higher than that of deet. These findings indicate that a spray-type solution containing 2% alpha-terpinene may serve as an alternative mosquito repellent.

(Thymus vulgaris) as potential mosquito repellents. Park BS, Choi WS, Kim JH, Kim KH, Lee SE. School of Agricultural Biotechnology, Seoul National University, Suwon 441-744, Korea.

Antibacterial food preservative
Thyme oil has been found to be strongly antibacterial against Listeria monocytogenes, and is being considered as a possible food preservative to prevent Listeriosis food poisoning.

Int J Infect Dis. 2006 May;10(3):236-41. Epub 2006 Jan 10.Ultrastructural studies on antimicrobial efficacy of thyme essential oils on Listeria monocytogenes. Rasooli I, Rezaei MB, Allameh A. Department of Biology, Shahed University, PO Box 18151-159, Tehran, Iran.

Antifungal, potentiates antifungal drugs
Oil of Thymus vulgaris thymol chemotype potentiates the antifungal action of amphotericin B suggesting a possible utilization of this essential oil in addition to antifungal drugs for the treatment of mycoses.

Phytother Res. 2004 Dec;18(12):990-5.Antifungal effect of various essential oils against Candida albicans. Potentiation of antifungal action of amphotericin B by essential oil from Thymus vulgaris. Giordani R, Regli P, Kaloustian J, Mikail C, Abou L, Portugal H.

Laboratoire de Botanique, Cryptogamie et Biologie Cellulaire, Faculte de Pharmacie, Universite de la Mediterranee, 27 Bd Jean Moulin, 13385 Marseille Cedex 05, France.

Feedlot Disinfectant
Weekly applications of thymol on corncobs to feedlots reduced the total colifoms by 89% and E. coli by 91%, and reduced odor emissions.

J Anim Sci. 2006 Feb;84(2):481-7.Incorporation of thymol into corncob granules for reduction of odor and pathogens in feedlot cattle waste. Varel VH, Miller DN, Berry ED. USDA-ARS, US Meat Animal Research Center, Clay Center, NE 68933, USA.

Wastes generated from the production of cattle and swine in confined facilities create the potential for surface and groundwater pollution, emission of greenhouse gases, transmission of pathogens to food and water sources, and odor.

Thymol and eugenol at 0.2% stopped all production of gas and volatile fatty acids, and eliminated all fecal coliform bacteria. Eugenol stimulated lactate formation in cattle and swine wastes. Thus, eugenol may offer a distinct advantage over thymol, because lactate accumulation in the wastes causes the pH to drop more rapidly, further inhibiting microbial activity and nutrient emissions. We conclude that plant oils may offer solutions to controlling various environmental problems associated with livestock wastes, assuming that they are cost-effective.

Water Sci Technol. 2004;50(4):207-13.Plant oils thymol and eugenol affect cattle and swine waste emissions differently. Varel VH, Miller DN, Lindsay AD. USDA-ARS, US Meat Animal Research Center, Clay Center, NE 68933, USA.

Alternatives to Synthetic Fungicides for Plant Diseases
Volatile phase effect of oregano and thyme oils at 0.3 microg/ml air was found to completely inhibit the growth of Phytophthora infestans (tomato late blight disease). Complete growth inhibition of pathogen by essential oil of fennel, rosemary, lavender and laurel was observed at 0.4-2.0 microg/ml air concentrations. Light and scanning electron microscopic (SEM) observation on pathogen hyphae, exposed to both volatile and contact phase of oil, revealed considerable morphological alterations in hyphae such as cytoplasmic coagulation, vacuolations, hyphal shrivelling and protoplast leakage.

Mycopathologia. 2006 Feb;161(2):119-28.Antimicrobial activities of the essential oils of various plants against tomato late blight disease agent Phytophthora infestans. Soylu EM, Soylu S, Kurt S. Department of Plant Protection, Faculty of Agriculture, Mustafa Kemal University, 31034, Antakya-Hatay, Turkey.

Potentiates Antibiotics
Baicalein (5, 6, 7-trihydroxyflavone), is a compound isolated from the leaves of Thymus vulgaris. It has been found to greatly reduce the minimum inhibitory concentration (MIC) of tetracycline against MRSA methicillin-resistant Staphylococcus aureus.

Microbiol Immunol. 2005;49(4):391-6.Remarkable synergies between baicalein and tetracycline, and baicalein and beta-lactams against methicillin-resistant Staphylococcus aureus. Fujita M, Shiota S, Kuroda T, Hatano T, Yoshida T, Mizushima T, Tsuchiya T. Department of Microbiology, Faculty of Pharmaceutical Sciences, Okayama University, Okayama, Japan.

Assists Healing of Burns

Thyme oil applied with olive oil may serve as a protective agent to burn damaged tissues by decreasing the nitric oxide level, an important mediator in numerous physiologic and pathophysiologic events. Thyme oil increased the formation of new tissue after burns.

J Burn Care Rehabil. 2003 Nov-Dec;24(6):395-9.Role of thymus oil in burn wound healing. Dursun N, Liman N, Ozyazgan I, Gunes I, Saraymen R. Department of Physiology, Faculty of Medicine, University of Erciyes, Kayseri, Turkey.

J Ethnopharmacol. 2006 Feb 20;103(3):413-9. Epub 2005 Oct 10.

Preliminary study on immunological and behavioural effects of Thymus broussonetii Boiss., an endemic species in Morocco.

Elhabazi K, **Dicko A**, **Desor F**, **Dalal A**, **Younos C**, **Soulimani R**.

Neurosciences, FSSM, Cadi Ayyad University, Marrakech, Morocco.

In the present work, we had tried to evaluate the immunotropic and behavioural effects of Thymus broussonetii Boiss. So, we tested the neurostimulant effects of four extracts. This preliminary study allowed to identify both the immunostimulant and the neurotropic antistress effects of the studied extracts. Among the four extracts, only the aqueous and ethyl acetate ones showed an apparent effect on the tested biological activities, whereas the butanolic extract and the essential oil did not show any interesting effect (data not shown). These results showed that the aqueous and ethyl extracts of this endemic species are of interest for two reasons: stimulation of the immunizing system and protection against the stress by a neurotropic activity. Thyme extracts increased in vivo the number of leucocyte categories studied including polynuclears, total lymphocytes, TCD4+, TCD8+ and NK cells. These data suggest that the intraperitoneal administration of Thymus broussonetii extract has a potent direct effect on leucocytes in vivo. The elevation of leucocyte and thrombocyte counts produced by thyme in the peripheral blood was already reported in the literature. These results could be of practical importance in the field of phytotherapy in the treatment of some cases of human immunodeficiency such as cancer, leukaemia and AIDS.

J Agric Food Chem. 2004 Dec 29;52(26):8261-7.

Essential oils of Satureja, Origanum, and Thymus species: chemical composition and antibacterial activities against foodborne pathogens.

Chorianopoulos N, **Kalpoutzakis E**, **Aligiannis N**, **Mitaku S**, **Nychas GJ**, **Haroutounian SA**.

Agricultural University of Athens, Iera odos 75, Athens 11855, Greece.

The chemical composition of the essential oils obtained from the species restricted to Greece and the eastern Mediterranean region, Satureja spinosa L. and Thymus longicaulis L.; species endemic to central and south Greece, Satureja parnassica ssp. parnassica Heldr. and Sart ex Boiss.; species endemic to the island of Crete, Origanum dictamnus L.; and species widely distributed in the Mediterranean region, Satureja thymbra L. and Origanum vulgare L. subsp. hirtum, were determined by gas chromatography (GC) and GC/mass spectrometry (MS) analysis. The in vitro antibacterial activities of the essential oils were evaluated against a panel of five foodborne bacteria (Escherichia coli 0157:H7 NCTC 12900, Salmonella enteritidis PT4, Staphylococcus aureus ATCC 6538, Listeria monocytogenes ScottA, and Bacillus cereus FSS 134). The analytical data indicated that various monoterpene hydrocarbons and phenolic monoterpenes constitute the major components of the oils, but their concentrations varied greatly among the oils examined. The antibacterial assay results showed that 5 muL doses of the essential oils extracted from the endemic Satureja species in Greece possess remarkable bactericidal properties, which are clearly superior as compared to those of Origanum and Thymus species essential oils. Therefore, they represent an inexpensive source of natural mixtures of antibacterial compounds that exhibit potentials for use in food systems to prevent the growth of foodborne bacteria and extend the shelf life of the processed food.

J Agric Food Chem. 2004 Aug 25;52(17):5418-24.
Thymus zygis subsp. Gracilis: watering level effect on phytomass production and essential oil quality.
Sotomayor JA, **Martinez RM**, **Garcia AJ**, **Jordan MJ**.
Murcian Institute of Investigation and Agricultural Development, C./Mayor s/n, 30150 La Alberca (Murcia), Spain.

Thymus zygis subsp. gracilis (chemotype thymol) was evaluated on the basis of its phytomass production and essential oil quality. Three different watering levels were assayed to achieve 63, 44, and 30% of the local potential evapotranspiration (Eto). According to the statistical analysis, a water supplement equivalent to 44% Eto in this cultivation area was optimal for maximum plant dry matter production and essential oil yield. Capillary GC-MS analysis of the essential oil allowed the identification of 86 volatile components. Among them, 30 are described for the first time as volatile constituents of the essential oil in this thyme subspecies and chemotype. The watering level effect on essential oil composition was noticeable, because the application of a water supplement equivalent to the 63% Eto favored the production of an essential oil richer in low molecular weight components. However, the greatest thymol concentrations were obtained under the 30 and 44% Eto watering levels.

Pest Manag Sci. 2004 Feb;60(2):173-7.
Insecticidal effects of essential oils from various plants against larvae of pine processionary moth (Thaumetopoea pityocampa Schiff) (Lepidoptera: Thaumetopoeidae).

Kanat M, **Alma MH**.
Department of Forest Engineering, Faculty of Forestry, Kahramanmaras Sutcu Imam University, 46060 Kahramanmaras, Turkey. mkanat@ksu.edu.tr

Along with sulfate turpentine, the essential oils obtained by steam distillation from nine plant species naturally grown in Turkish forests were tested at three different concentrations to evaluate their effectiveness against the larvae of pine processionary moth (Thaumetopoea pityocampa Schiff). The results indicated that the essential oils from the nine species and sulfate turpentine were effective against the larvae of T pityocampa. The most effective essential oil in the control of the larvae was steam-distilled wood turpentine, followed by thyme herb oil, juniper berry oil, laurel leaf oil, lavender flower oil, eucalyptus leaf oil, lavender leaf oil, cypress berry oil, essential oil of styrax and sulfate turpentine, respectively, in terms of mean mortality time. It is therefore feasible to use these essential oils as environment-friendly insecticides in the control of T pityocampa.

Oils for respiratory tract infections
J Infect Chemother.Screening of the antibacterial effects of a variety of essential oils on respiratory tract pathogens, using a modified dilution assay method. Inouye S, Yamaguchi H, Takizawa T. Teikyo University Institute of Medical Mycology, 259 Otsuka, Hachioji, Tokyo 192-0395, Japan.

Haemophilus influenzae was most susceptible to the essential oils, followed by Streptococcus pneumoniae and Streptococcus pyogenes. Staphylococcus aureus was less susceptible. Essential oils containing aldehyde or phenol as a major component showed the highest antibacterial activity, followed by the essential oils containing terpene alcohols. Other essential oils, containing terpene ketone, or ether, had much weaker activity, and an oil containing terpene hydrocarbon was inactive. Based on these findings, thyme (wild, red, and geraniol types), cinnamon bark, lemongrass, perilla, and peppermint oils were selected for further evaluation.

Lett Appl Microbiol. 1999 Aug;29(2):130-5.
In-vitro antimicrobial activity and chemical composition of Sardinian Thymus essential oils.
Cosentino S, **Tuberoso CI**, **Pisano B**, **Satta M**, **Mascia V**, **Arzedi E**, **Palmas F**.
Department of Experimental Biology, University of Cagliari, Sardinia, Italy. scosenti@vaxcal.unica.it

Essential oils and their components are becoming increasingly popular as naturally occurring antimicrobial agents. In this work the chemical composition and the antimicrobial properties of Thymus essential oils and of their main components were determined. Three essential oils obtained from different species of Thymus growing wild in Sardinia and a commercial sample of Thymus capitatus oil were analysed. The essential oil components were identified by GC/MS analysis. The antimicrobial activity of the oils and components was determined against a panel of standard reference strains and multiple strains of food-derived spoilage and pathogenic bacteria, using a broth microdilution

method. The GC/MS analysis showed that the major constituents of the oils were monoterpene hydrocarbons and phenolic monoterpenes, but the concentration of these compounds varied greatly among the oils examined. The results of the antimicrobial assay showed that essential oils extracted from Sardinian Thymus species have an antimicrobial activity comparable to the one observed in other thyme oils. It seems also confirmed that the antimicrobial properties of thyme essential oils are mainly related to their high phenolic content. Among the single compounds tested carvacrol and thymol turned out to be the most efficient against both reference strains and food-derived bacteria. The results of this study confirmed the possibility of using thyme essential oils or some of their components in food systems to prevent the growth of foodborne bacteria and extend the shelf-life of processed foods.

Phytochemistry. 2005 Nov;66(22):2668-73. Epub 2005 Nov 9.

Essential oil composition is related to the natural habitats: Coridothymus capitatus and Satureja thymbra in NATURA 2000 sites of Crete.

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Laboratory of Systematic Botany and Phytogeography, Department of Botany, School of Biology, Aristotle University of Thessaloniki, Thessaloniki 541 24, Greece.
karousou@bio.auth.gr

The study of essential oils obtained from Coridothymus capitatus and Satureja thymbra collected from different natural habitat types of 11 NATURA 2000 sites scattered all over Crete has shown that they are characterized either by a high amount of carvacrol (up to 75.7%) or thymol (up to 65.6%) or by a more or less equal amount of the two phenols. The results of a discriminant analysis with predefined groups the natural habitat types wherefrom the plants were collected have shown that the oils of both species collected from the dry dwarf-shrub formations of the lowland have a high carvacrol content whereas those collected from the more mesic timber or highland formations have a high thymol content. Furthermore, the results of this study introduce the use of natural habitat unit as a tool for the assessment of essential oil variation.

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Tulsi

Evaluation of in vitro antimicrobial activity of Thai basil oils and their micro-emulsion formulas against Propionibacterium acnes.

Int J Cosmet Sci. 2006 Apr;28(2); Viyoch J, Pisutthanan N, Faikreua A, Nupangta K, Wangtorpol K, Ngokkuen J.
Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, Naresuan University, 65000 Phitsanulok, Thailand.

The aim of this study was to evaluate the efficacy of Thai basil oils and their micro-emulsions, on in vitro activity against Propionibacterium acnes. An agar disc diffusion method was employed for screening antimicrobial activity of the essential oils of

Ocimum basilicum L. (sweet basil), Ocimum sanctum L. (holy basil) and Ocimum americanum L. (hoary basil) against P. acnes. Minimum inhibitory concentration (MIC) values of the basil oils were determined using an agar dilution assay. The obtained results indicated that the MIC values of sweet basil and holy basil oils were 2.0% and 3.0% v/v, respectively, whereas hoary basil oil did not show activity against P. acnes at the highest concentration tested (5.0% v/v). Gas chromatography-mass spectrometry analysis revealed that methyl chavicol (93.0%) was the major compound in sweet basil oil, and eugenol (41.5%), gamma-caryophyllene (23.7%) and methyl eugenol (11.8%) were major compounds in holy basil oil. Hoary basil oil contained high amounts of geraniol (32.0%) and neral (27.2%) and small amounts of methyl chavicol (0.8%). The Oil-in-water (o/w) micro-emulsions of individual basil oils with concentrations corresponding to their MIC values were formulated. The stable o/w micro-emulsion system for basil oil consisted of 55.0% v/v water phase, 10.0% v/v oil phase (2.0 or 3.0% v/v sweet basil or 3.0% v/v holy basil oil plus 7.0% v/v isopropyl myristate), 29.2% v/v polysorbate 80 and 5.8% v/v 1,2-propylene glycol. Hydroxyethylcellulose at a concentration of 0.5% w/v was used as thickening agent. According to the disc diffusion assay, the formulations containing sweet basil oil exhibited higher activity against P. acnes than those containing holy basil oil, and the thickened formulations tended to give a lower activity against P. acnes than the non-thickened formulations. The prepared micro-emulsions were stable after being tested by a heat-cool cycling method for five cycles. These findings indicate the possibility to use Thai sweet and holy basil oil in suitable formulations for acne skin care.

Therapeutic uses of Ocimum sanctum Linn (Tulsi) with a note on eugenol and its pharmacological actions: a short review.

Indian J Physiol Pharmacol. 2005 Apr; Prakash P, Gupta N.
Department of Biochemistry, Seema Dental College & Hospital, Barrage Road, Rishikesh, Dehradoon - 249 203, Uttranchal.

The medicinal plants are widely used by the traditional medical practitioners for curing various diseases in their day to day practice. In traditional systems of medicine, different parts (leaves, stem, flower, root, seeds and even whole plant) of Ocimum sanctum Linn (known as Tulsi in Hindi), a small herb seen throughout India, have been recommended for the treatment of bronchitis, bronchial asthma, malaria, diarrhea, dysentery, skin diseases, arthritis, painful eye diseases, chronic fever, insect bite etc. The Ocimum sanctum L. has also been suggested to possess antifertility, anticancer, antidiabetic, antifungal, antimicrobial, hepatoprotective, cardioprotective, antiemetic, antispasmodic, analgesic, adaptogenic and diaphoretic actions. Eugenol (1-hydroxy-2-methoxy-4-allylbenzene), the active constituent present in Ocimum sanctum L., has been found to be largely responsible for the therapeutic potentials of Tulsi. Although because of its great therapeutic potentials and wide occurrence in India the practitioners of traditional systems of medicine have been using Ocimum sanctum L. for curing various ailments, a rational approach to this traditional medical practice with modern system of medicine is, however, not much available. In order to establish the therapeutic uses of Ocimum sanctum L. in modern medicine, in last few decades several Indian scientists and researchers have studied the pharmacological effects of steam distilled, petroleum ether and benzene extracts of various

parts of Tulsi plant and eugenol on immune system, reproductive system, central nervous system, cardiovascular system, gastric system, urinary system and blood biochemistry and have described the therapeutic significance of Tulsi in management of various ailments. These pharmacological studies have established a scientific basis for therapeutic uses of this plant.

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MRSA

Comparison of the cidal activity of tea tree oil and terpinen-4-ol against clinical bacterial skin isolates and human fibroblast cells.
Lett Appl Microbiol. 2008 Apr; Loughlin R, Gilmore BF, McCarron PA, Tunney MM.
School of Pharmacy, Medical Biology Centre, Queen's University Belfast, Belfast, UK.

AIMS: The aim of this study was to compare both the antimicrobial activity of terpinen-4-ol and tea tree oil (TTO) against clinical skin isolates of meticillin-resistant Staphylococcus aureus (MRSA) and coagulase-negative staphylococci (CoNS) and their toxicity against human fibroblast cells. METHODS AND RESULTS: Antimicrobial activity was compared by using broth microdilution and quantitative in vitro time-kill test methods. Terpinen-4-ol exhibited significantly greater bacteriostatic and bactericidal activity, as measured by minimum inhibitory and bactericidal concentrations, respectively, than TTO against both MRSA and CoNS isolates. Although not statistically significant, time-kill studies also clearly showed that terpinen-4-ol exhibited greater antimicrobial activity than TTO. Comparison of the toxicity of terpinen-4-ol and TTO against human fibroblasts revealed that neither agent, at the concentrations tested, were toxic over the 24-h test period. CONCLUSIONS: Terpinen-4-ol is a more potent antibacterial agent against MRSA and CoNS isolates than TTO with neither agent exhibiting toxicity to fibroblast cells at the concentrations tested. SIGNIFICANCE AND IMPACT OF THE STUDY: Terpinen-4-ol should be considered for inclusion as a single agent in products formulated for topical treatment of MRSA infection. However, further work would initially be required to ensure that resistance would not develop with the use of terpinen-4-ol as a single agent.

Susceptibility of methicillin-resistant Staphylococcus aureus to the essential oil of Melaleuca alternifolia.
J Antimicrob Chemother. 1995 Mar; Carson CF, Cookson BD, Farrelly HD, Riley TV.
Department of Microbiology, University of Western Australia, Queen Elizabeth II Medical Centre, Nedlands.

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.

The effect of essential oils on methicillin-resistant Staphylococcus aureus using a dressing model.
Burns. 2004 Dec;
Edwards-Jones V, Buck R, Shawcross SG, Dawson MM, Dunn K.
Department of Biological Sciences, the Manchester Metropolitan University, Chester Street, Manchester, M15GD, UK. v.e.jones@mmu.ac.uk

Patchouli, tea tree, geranium, lavender essential oils and Citricidal (grapefruit seed extract) were used singly and in combination to assess their anti-bacterial activity against three strains of Staphylococcus aureus: Oxford S. aureus NCTC 6571 (Oxford strain), Epidemic methicillin-resistant S. aureus (EMRSA 15) and MRSA (untypable). The individual essential oils, extracts and combinations were impregnated into filter paper discs and placed on the surface of agar plates, pre-seeded with the appropriate strain of Staphylococcus. The effects of the vapours of the oils and oil combinations were also assessed using impregnated filter paper discs that were placed on the underside of the Petri dish lid at a distance of 8mm from the bacteria. The most inhibitory combinations of oils for each strain were used in a dressing model constructed using a four layers of dressings: the primary layer consisted of either Jelonet or TelfaClear with or without Flamazine; the second was a layer of gauze, the third a layer of Gamgee and the final layer was Crepe bandage. The oil combinations were placed in either the gauze or the Gamgee layer. This four-layered dressing was placed over the seeded agar plate, incubated for 24h at 37 degrees C and the zones of inhibition measured. All experiments were repeated on three separate occasions. No anti-bacterial effects were observed when Flamazine was smeared on the gauze in the dressing model. When Telfaclear was used as the primary layer in the dressing model compared to Jelonet, greater zones of inhibition were observed. A combination of Citricidal and geranium oil showed the greatest-anti-bacterial effects against MRSA, whilst a combination of geranium and tea tree oil was most active against the methicillin-sensitive S. aureus (Oxford strain). This study demonstrates the potential of essential oils and essential oil vapours as antibacterial agents and for use in the treatment of MRSA infection.

Comparison of the effects in vitro of tea tree oil and plaunotol on methicillin-susceptible and methicillin-resistant strains of Staphylococcus aureus.
Microbios. 2001; Hada T, Furuse S, Matsumoto Y, Hamashima H, Masuda K, Shiojima K, Arai T, Sasatsu M.
Department of Microbiology, Showa Pharmaceutical University, Machida, Tokyo, Japan.

The effects in vitro of tea tree oil (TTO) and plaunotol were examined by monitoring the growth of a standard strain of Staphylococcus aureus FDA 209P and of fourteen methicillin-susceptible strains of S. aureus (MSSA), together with twenty methicillin-resistant strains (MRSA). The minimum inhibitory concentrations (MIC) and the doses for 50% inhibition of growth (ID50) were determined by the micro-broth dilution (MD) method, and the broth dilution with shaking (BDS) method, respectively. The

MIC of plaunotol for 50 and 90% of the MSSA and MRSA were assessed by the MD method, as 16 microg/ml and > or = 1,024 microg/ml, respectively. No antibacterial effects of TTO on MSSA and MRSA were detected by the MD method. The growth-inhibitory effects of TTO on S. aureus by the BDS method were examined, and it appeared that TTO was effective over a lower range of concentrations than previously reported. It seems that TTO is very effective in vitro against MSSA and MRSA at high concentrations but less effective below 40 microg/ml of TTO.

Antibacterial effect of tea-tree oil on methicillin-resistant Staphylococcus aureus biofilm formation of the tympanostomy tube: an in vitro study.
In Vivo. 2007 Nov-Dec; Park H, Jang CH, Cho YB, Choi CH.
College of Natural Science, Chosun University, Gwangju, South Korea.
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.

Is tea tree oil effective at eradicating MRSA colonization? A review.
Br J Community Nurs. 2005 Mar;
Flaxman D, Griffiths P.
Queen Mary's Hospital, Sidcup, Kent. debbie.flaxman@qms.nhs.uk

In vitro studies show that tea tree oil is capable of killing methicillin-resistant Staphylococcus aureus (MRSA) in a laboratory setting. This review of randomized controlled trials (RCTs) was undertaken to find out whether it is effective at eradicating MRSA colonization compared to standard mupirocin-based regimens in colonized patients. A wide range of databases and internet sources were searched to identify published and unpublished studies. Two RCTs were found that researched the effectiveness of tea tree oil preparations against MRSA. One small RCT (n = 30) showed a large but non-significant improvement at eradicating MRSA compared to traditional treatment, whereas a larger study (n = 224) demonstrated little difference in rates of eradication overall (41% for tea tree and 49% for mupirocin, p = 0.286). However, the larger study found that those with nasal colonization receiving a tea tree regimen were more likely to remain colonized with MRSA in the nose (absolute risk increase 31%, p<0.001). Currently there is insufficient evidence to support the routine use of tea tree oil in clinical practice for eradication of MRSA colonization.

A randomized, controlled trial of tea tree topical preparations versus a standard topical regimen for the clearance of MRSA colonization.

J Hosp Infect. 2004 Apr;

Dryden MS, Dailly S, Crouch M.
Department of Microbiology and Communicable Disease, Royal Hampshire County Hospital, Romsey Road, Winchester, Hampshire SO22 5DG, UK.
matthew.dryden@weht.swest.nhs.uk

Two topical MRSA eradication regimes were compared in hospital patients: a standard treatment included mupirocin 2% nasal ointment, chlorhexidine gluconate 4% soap, silver sulfadiazine 1% cream versus a tea tree oil regimen, which included tea tree 10% cream, tea tree 5% body wash, both given for five days. One hundred and fourteen patients received standard treatment and 56 (49%) were cleared of MRSA carriage. One hundred and ten received tea tree oil regimen and 46 (41%) were cleared. There was no significant difference between treatment regimens (Fisher's exact test; P = 0.0286). Mupirocin was significantly more effective at clearing nasal carriage (78%) than tea tree cream (47%; P = 0.0001) but tea tree treatment was more effective than chlorhexidine or silver sulfadiazine at clearing superficial skin sites and skin lesions. The tea tree preparations were effective, safe and well tolerated and could be considered in regimens for eradication of MRSA carriage.