Manuka Essential Oil Bibliography

Manuka Essential Oil Bibliography.
Leptospermum scoparium J.R. Forst & G. Forst.

Manuka Oil Anti-Microbial Activity.

Christolph F., Kaulfers P.M. & Stahl-Biskup E. (2000). "A comparitive study of the in vitro anti-microbial activity of tea tree oils s.l. with special reference to the activity of b-triketones". Planta Med. 66(6), 556-60. Abstract. The in vitro antibacterial and antifungal activities of Australian tea tree oil, cajuput oil, niaouli oil, kanuka oil and manuka oil as well as of a b-triketone complex isolated from manuka oil were investigated in a constituent-oriented study. The compositions of the oils were analysed by capillary GLC and GLC-MS. The MICs for sixteen different microorganisms were determined applying the broth dilution method. Australian tea tree oil showed the best overall antimicrobial effect. The best inhibitory effects on Gram-positive bacteria and dermatophytes were achieved with manuka oil due to its b-triketone content.

Christolph F., Kaulfers P.M. & Stahl-Biskup E. (2001). "In vitro evaluation of the antibactericidal activity of **b-triketones admixed to Melaleuca** oils." **Planta Med. 67(8), 768-771. Abstract.The in vitro antibacterial properties of mixtures of Australian tea tree oil and niaouli oil after adding the b-triketone complex isolated from manuka oil were tested. MIC and MBC values for four different bacteria were determined applying the broth dilution method. Both Melaleuca oil mixtures showed good antimicrobial effects against Staphylococcus aureus and Moraxella catarrhalis, exceeding the effectiveness of myrtol, which is well established in the treatment of acute and chronic bronchitis and sinusitis. The death kinetics of S. aureus were determined to draw subtle comparisons between the mixtures. The kill rate data indicated that both Melaleuca oil mixtures achieved a complete kill within 240 min.**

Christolph F. & Stahl-Biskup E. (2001) "Death kinetics of **Staphlococcus aureus exposed to commercial tea tree oils s.**l." **J. Essen. Oil Res. 13, 98-102. Abstract. Staphyloccus aureus cells were exposed to increasing concentrations of Australian tea-tree oil, cajuput oil, niaouli oil, Lema oil, kanuka oil, and manuka oil as well as of a b-triketone complex isolated from manuka oil. The death kinetics were determined by calculation of $\log_{10}$ reduction factors after increasing exposure periods. Niaouli oil turned out to be highly active, followed by Lema (this is a registered trademark), tea tree & cajuput oils. Kill rate data indicated that 1.0% (v/v) were lethal to the stationary phase cells in the assay conditions used. At 2.0% (v/v) niaouli oil and Lema oil yielded a complete 6.8 $\log_{10}$ reduction of cell numbers in suspensions within 60 min, whereas cells treated with tea tree & cajuput oils were inactivated more slowly within 120 & 240 min. respectively. Kanuka & manuka oils as well as the b-triketone complex, the active principle of manuka oil, lacked any bactericidal properties. Their high effectiveness against Gram-positive bacteria can be explained by bacteriostatic effects. The results obtained with Lema oil, a blend of tea tree and a polar fraction of manuka oil (mainly b-triketones), gave cause to discuss synergistic effects.**

Cooke & Cooke M.D. (1994) "An investigation into the antimicrobial properties of manuka & kanuka oils" Cawthron Report No 263, New Zealand.

Harkenthal M., Reichling J., Geiss H.K. & Saller R. (1999) "Comparative study on the in vitro antibacterial activity of Australian tea tree oil, cajuput oil, niaouli oil, manuka oil, kanuka oil, and eucalyptus oil." Pharmazie 54(6), 460-463. Abstract. To compare the antibacterial activity of the Australian tea tree oil (TTO) with various other medicinally and commercially important essential myrtaceous oils (cajuput oil, niaouli oil, kanuka oil, manuka oil, and eucalyptus oil) the essential oils were first analysed by GC-MS and then tested against various bacteria using a broth microdilution method. The highest activity was obtained by TTO, with MIC values of 0.25% for Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Salmonella choleraesuis, Shigella flexneri, Bacillus subtilis, Listeria monocytogenes, Staphylococcus aureus, S.

saprophyticus, and S. xylosus. It is noteworthy that manuka oil exhibited a higher activity than TTO against gram-positive bacteria, with MIC values of 0.12%. Both TTO and manuka oil also demonstrated a very good antimicrobial efficacy against various antibiotic-resistant Staphylococcus species. Pseudomonas aeruginosa was resistant to all essential oils tested, even at the highest concentration of 4%.

Kim, E. H. & Rhee G.J. (1999). "Activities of ketonic fraction from **Leptospermum scoparium alone and synergism in combination with some antibiotics agai**nst various bacterial strains and fungi." **Yakhak Hoeji (J. - Pharmaceutical Society of Korea). 43(6), 716-728.**

Malone M.A., Gatehouse H.S. & Treqidqa E.L. (2001) "Effects of time, temperature & honey on **Nosema apis (Microsporidia: Nosematidae), a parasite of the honeybee Apis mellifera (Hymenoptera: Apidae). J. Invertebrate Pathol 77(4), 258-68. Abstract.Newly emerged adult bees were fed with Nosema apis spores subjected to various treatments, and their longevity, proportions of bees infected, and spores per bee recorded. Spores lost viability after 1, 3, or 6 months in active manuka or multifloral honey, after 3 days in multifloral honey, and after 21 days in water or sugar syrup at 33 degrees C. Air-dried spores lost viability after 3 or 5 days at 40 degrees, 45 degrees, or 49 degrees C. Increasing numbers of bees became infected with increasing doses of spores, regardless of their subsequent food (active manuka honey, thyme honey, or sugar syrup). Final spore loads were similar among bees receiving the same food, regardless of dose. Bees fed with either honey had lighter infections than those fed with syrup, but this may have been due to reductions in their longevity. Bees fed with manuka honey were significantly shorter lived, whether infected or not.**

Reichling J., Koch C., Stahl-Biskup E., Sojka C., Schnitzler P. (2005) "Virucidal activity of beta**-triketone-rich essential oil of Leptospermum scoparium (Manuka Oil) against HSV-1 & HSV-**2 in cell culture." **Planta Med 71(12), 1123-7. Abstract.The inhibitory activity of manuka oil against Herpes simplex virus type 1 (HSV-1) and Herpes simplex virus type 2 (HSV-2) was tested in vitro on RC-37 cells (monkey kidney cells) using a plaque reduction assay. In order to determine the mode of antiviral action of the essential oil, manuka oil was added at different times to the cells or viruses during the infection cycle. Both HSV types were significantly inhibited when the viruses were pretreated with manuka oil 1 h prior to cell infection. At non-cytotoxic concentrations of the essential oil, plaque formation was significantly reduced by 99.5 % and 98.9 % for HSV-1 and HSV-2, respectively. The 50 % inhibitory concentration (IC (50)) of manuka oil for virus plaque formation was determined at 0.0001 % v/v (= 0.96 microg/mL) and 0.00006 % v/v (= 0.58 microg/mL) for HSV-1 and HSV-2, respectively. On the other hand, pretreatment of host cells with the essential oil before viral infection did not affect plaque formation. After virus penetration into the host cells only replication of HSV-1 particle was significantly inhibited to about 41 % by manuka oil. Flavesone and leptospermone, two characteristic ss-triketones of manuka oil, inhibited the virulence of HSV-1 in the same manner as the essential oil itself. When added at non-cytotoxic concentrations to the virus 1 h prior to cell infection, plaque formation was reduced by 99.1 % and 79.7 % for flavesone and leptospermone, respectively.**

Rhee G.J., Chung K.S., Klim E.H., Suh H.J., Hong N.D. (1997) "Anti**-microbial activities of a steam distillate of Leptospermum scoparium**." **Yakhak Hoeji 41, 132-138.**

Russell, K. M.; Molan, P. C.; Wilkins, A. L.; Holland, P. T. (1988) "The identification of some antibacterial constituents of New Zealand Manuka honey." Journal of Agricultural and Food Chemistry 38: 10-13.

Takarada K., Kimizuka R., Takahashi N., Honma K., Okuda K. & Kato T. (2004) "A comparison of the anti-bacterial efficacies of essential oils against oral pathogens." **Oral Microbiol. Immunol. 19(1), 61-64. Abstract. Cariogenic bacteria and periodontopathic bacteria are present in dental plaque as biofilms. In this study, we investigated the antibacterial effects of essential oils on the following oral bacteria: Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, Fusobacterium nucleatum, Streptococcus mutans, and Streptococcus sobrinus. We tested manuka oil, tea tree oil, eucalyptus oil, lavandula oil, and rosmarinus oil and determined their minimum inhibitory concentration and minimum**

bactericidal concentration. The essential oils inhibited the growth of the bacteria tested, manuka oil being the most effective. Minimum bactericidal concentration values showed that lavandula oil acts bacteriostatically, and the remaining oils, bactericidally. Periodontopathic bacterial strains tested were killed completely by exposure for 30 s to 0.2% manuka oil, tea tree oil or eucalyptus oil. Tea tree oil and manuka oil showed significant adhesion-inhibiting activity against P. gingivalis. All the essential oils tested inhibited the adhesion of S. mutans. This study showed that, among the essential oils tested, manuka oil and tea tree oil in particular had strong antibacterial activity against periodontopathic and cariogenic bacteria. From the viewpoint of safety, we also examined the effects of these essential oils on cultured human umbilical vein endothelial cells and found that, at a concentration of 0.2%, they had little effect on cultured cells.

Williams L.R., Stockley J.K., Yan W. & Home V.N. (1998) IJA 8(4), 30-40. Abstract. After a comparison of the antimicrobial activity of the essential oils of Australian tea tree oil, Australian lavender, New Zealand manuka, lemongrass oil, and eucalyptus oil it was found that the relative antimicrobial activity varied depending upon the micro-organism under test. Lavender has useful antimicrobial properties and a product was formulated containing a combination of tea tree oil and lavender for the treatment of burns. A selected New Zealand manuka oil had strong antimicrobial activity against Staphylococcus aureus. The use of tea tree oil and combinations of tea tree oil and manuka are being investigated for therapeutic use against Methicillin Resistant Staphylococcus aureus (MRSA) and other antibiotic resistant bacteria such as Enterococci (VRE) which is resistant to Vancomycin. For therapeutic use as an antimicrobial active in formulated products the essential oil must have a broad spectrum of activity with the additional properties of being stable and non irritant to sensitive or damaged skin. Overall tea tree oil had the best combination of useful properties including strong antimicrobial activity. Australian Tea Tree Management Limited has assisted in the selection and breeding of superior plants of Melaleuca alternifolia and M. linariifolia which provide a tea tree oil high in terpinen-4-ol. By the end of 1997 over 2 million clones of these selections will have been planted. The use of tea tree oil in pharmaceutical products will be boosted by the production of commercial quantities of highly active oil with a broad spectrum of antimicrobial activity suitable for use in formulations for vaginal thrush, tinea, acne and dandruff.

Manuka Botany.

Anon (1956) “Manuka Blight” **Rep. Dep. Sci. Indust. Res N.Z. 1955/56 1956 p12. Abstract. Whereas Leptospermum scoparium has been almost wiped out in some areas by the scale insect Eriococcus orariensis, L. ericoides |(kanuka) is immune. The difference is apparently due to a difference in bark, that of manuka being rough & affording harbourage to large populations, while the smoother bark of kanuka limits the period for crawlers to become fixed. Surviving manuka was found to be smooth-barked like kanuka.**

Bicknell R. (1965) “Breeding cut-**flower cultivars of Leptospermum scoparium using interspecific** hybridisation.” **N.Z. Inst.Crop & Horticultural Sci 23(4), 415-421.**

Bray J.R., Burke W.D. et al. (1999) “Propagule dispersion & nitrogen distribution & accumulation **in Leptospermum scoparium (manuka): L. ericoides (kanuka) forests flowing fires in Golden Bay, New** Zealand.” **N Z Natural Sciences Nov 24: 34-52.**

Cook J.M., Mark A.F. & Shore B.F. (1980) "Responses of Leptospermum scoparium & L. ericoides (Myrtaceae) to water-logging." New Zealand J. Botany 18, 233-246. Abstract.Field observations of the contrasting tolerance & adaptations to permanently waterlogged habitats of the two widespread indigenous spp. of Leptospermum (Myrtaceae) were tested experimenatally. Seedlings of two populations of manuka, L. scoparium (inland semi-arid & coastal regions of Otago) and one of kanuka L. ericoides (coastal), were partly submerged in either stagnant or running fresh water. Anatomical & morphological responses of the submerged portions were followed and compared between species, populations & treatments.

Greer D.H. & Robinson L.A. (1995) "Temperature control of the development of frost hardiness in two populations of Leptospermum scoparium." Tree Physiol. 15(6), 399-404. Abstract. Seedlings of Leptospermum

scoparium J.R. et G. Forst (manuka) originating from seed from a low altitude coastal site (Auckland) and from a high altitude inland site (Desert Road) were grown for 96 days in four controlled environments to compare the relationship between growth temperature and frost hardening. Day/night temperature treatments were 12/6, 12/3, 12/0 and 12/-3 degrees C. Frost hardiness was determined at 14-day intervals by exposing whole seedlings to temperatures ranging from -2 to -8 degrees C. Frost damage differed significantly between the two populations: Desert Road seedlings were less affected than Auckland seedlings. At all growth temperatures, the time courses of frost hardiness of both populations followed curvilinear relationships reaching a maximum hardiness at about Day 50, after which the seedlings spontaneously dehardened. The rate of frost hardening increased linearly with decreasing temperature from 6 to 0 degrees C, but thereafter, no further increase occurred with decreasing temperature to -3 degrees C. The frost hardening process was more sensitive to temperature in the Desert Road seedlings than in the Auckland seedlings, and this difference may account for the intraspecific variation in frost hardening capacity of this species. Comparisons with Pinus radiata D. Don and Lolium perenne L. indicated that interspecific variation in frost hardening capacity can also be accounted for by differences in the sensitivity of the hardening process to temperature.

Malcock A.P. (1954) "A disease of manuka, **Leptospermum scoparium** Forst." **Transactions of the Royal Society of New Zealand, Wellington 82(1), 115-118.**
Abstract. A description is given of the disease caused by the joint effects of Eriococcus & the fungus Capnodium walteri feeding on the honey-dew. The fungus was isolated & cultured & details are given of morphology & measurements. The disease was reproduced on a host plant free from insects by spraying the plants with a 1% honeydew solution after inoculation with a culture of the fungus.

Prior R.J., Davidson N.J. & Close D.C. (2006) "Waterlogging **duration: Interspecific comparison (Forst et Forst f.) Acaia melanoxylon (R.Br.) Nothofagus cunninghamii (Hook.) and Eucalyptus oblique** (l'Herit)". **Austral. Ecology 31(3), 408-416.**

Rongua Y., Mark A.F. & Wilson J.B. (1984) "Aspects of the ecology of the indigenous shrub Leptospermum scoparium (Myrtaceae) in New Zealand." New Zealand J. Botany 22, 483-507. Abstract. Geographic variation in leaf size and shape of the environmentally friendly-tolerant indigenous shrub Leptospermum scoparium (Myrtaceae) was determined from 82 herbarium specimens collected over much of its natural range. There were significant correlations with geographic & climatic factors of latitude, distance from the coast, annual & winter temperatures. Seventeen seedling populations raised in a uniform environment showed that this leaf variation had a significant genetic component as did the variation in form and the age at first flowering. Flowering phenology in four year old plants from seven widely spread sites also differed significantly when grown together. Ecotypic differentiation is therefore clearly indicated in L. scoparium and this is discussed in relation to previous claims & explanations. Sixteen communities dominated by L. scoparium and southern South Island differed in floristics. The density, basal area, age class distribution and height of the Leptospermum stems also vary and are correlated with environmental parameters. The eight climax or sub-climax stands of more extreme island locations are compared with the eight serai from moister control habitats. A plea is made for L. scoparium communities to be adequately represented in the New Zealand reserves system rather than ignored because of the often aggressive and serai characteristics of its dominant species.
Richard B., Primack R.B. & Lloyd D.G. (1980) "Andromonoecy in the New Zealand Montane Shrub Manuka, Leptospermum scoparium (Myrtaceae)."American J. Botany, 67(3), 361-368. Abstract. The ecological and evolutionary advantages of andromonoecy are considered by examining populations of a montane grasslands shrub. Manuka plants (Leptospermum scoparium, Myrtaceae) produce two kinds of flowers: male flowers having functional stamens and a non-functional pistil, and hermaphrodite flowers in which both the stamens and pistil are functional. Factors affecting the ratio of the two flower types were investigated at Cass, Canterbury, New Zealand. Stamens mature at the same rate in the two flower types. Individual plants within one population vary from having predominantly hermaphrodite flowers to having no hermaphrodite flowers. Individual variation within a population in the percentage of hermaphrodite flowers is correlated between seasons, indicating some stability in this character. In a particular season, variation among plants within a population in the

percentage of hermaphrodite flowers is negatively correlated with date of flowering, but it is not correlated with either the number of flowers or vegetative growth per plant. The hermaphrodite flowers tend to open in the first flush of flowering, and the proportion of hermaphrodite flowers subsequently declines in individual plants and in the population as a whole. The earlier anthesis of hermaphrodite flowers probably increases the frequency of outcrossing; it also provides more time for fruit to mature. The percentage of hermaphrodite flowers is greater toward the top of the plant and among terminal flowers on branchlets than among proximal flowers. The percentage of hermaphrodite flowers on a plant was progressively increased with increasing nutrient treatments. The flowers are visited by a wide range of insects. Fruit set was not increased by hand pollinations of flowers exposed to natural insect visits, indicating that pollinator activity does not limit natural fruit production. A considerable fraction of the variation between individuals in the proportions of male and hermaphrodite flowers is environmentally induced. Andromonoecy may have been selected for in manuka because it is advantageous for pollen to be presented in more flowers than the number of ovule- and seed-bearing flowers. Alternatively, andromonoecy may allow an individual plant to adjust its reproductive output to its immediate physiological condition. However, andromonoecy by itself is not an out-breeding mechanism.

Stephens J.M.C, Molan P.C. & Clarkson B.D. (2005). "A review of Leptospermum scoparium (Myrtaceae) in New Zealand." New Zealand Journal of Botany. 43(2),431-449. Abstract. Information about Leptospermum scoparium (Myrtaceae), the most widespread and important New Zealand indigenous shrub species, is reviewed. L. scoparium is a variable species, requiring more study of the genetically based differences between New Zealand populations and the affinity of these populations to Australian populations and other closely allied Australian species. Improved understanding of the species' variation will assist both its conservation roles and **economic uses, and the need to sustain genetically distinct varieties is emphasised. Ecologically, the species has a dominant role in infertile and poorly drained environments, and a wider occurrence as a seral shrub species in successions to forest where it may be regarded as a woody weed of pasture or a useful species for erosion control, carbon sesquestration, and vegetation restoration. The main economic products derived from the species** are ornamental shrubs, essential oils, and honey. The species' development as an ornamental plant and further **definition of the pharmacologically active components are recommended as priority areas for research.**

Watson A. & O'Laughlin C. (1985). "Morphology, strength & biomass of manuka roots & their influence on slope stability." **NZ J of Forestry Sci 15(3), 337-348.**

Whitehead D., Walcroft A.S., Scott N.A., Townsend J.A., Trotter CM. & Rogers G.N. (2004) "Characteristics of photosynthesis and stomatal conductance in the shrubland species manuka (Leptospermum scoparium) and kanuka (Kunzea ericoides) for the estimation of annual canopy carbon uptake."Tree Physiol. 24(7), 795-804. Abstract. Responses of photosynthesis to carbon dioxide (CO2) partial pressure and irradiance were measured on leaves of 39-year-old trees of manuka (Leptospermum scoparium J. R. Forst. & G. Forst.) and kanuka (Kunzea ericoides var. ericoides (A. Rich.) J. Thompson) at a field site, and on leaves of young trees grown at three nitrogen supply rates in a nursery, to determine values for parameters in a model to estimate annual net carbon uptake. These secondary successional species belong to the same family and commonly co-occur. Mean (+/- standard error) values of the maximum rate of carboxylation (hemi-surface area basis) (Vcmax) and the maximum rate of electron transport (Jmax) at the field site were 47.3 +/- 1.9 micromol m(-2) s(-1) and 94.2 +/- 3.7 micromol m(-2) s(-1), respectively, with no significant differences between species. Both Vcmax and Jmax were positively related to leaf nitrogen concentration on a unit leaf area basis, and the slopes of these relationships did not differ significantly between species or between the trees in the field and young trees grown in the nursery. Mean values of Jmax/Vcmax measured at 20 degrees C were significantly lower (P < 0.01) for trees in the field (2.00 +/- 0.05) than for young trees in the nursery with similar leaf nitrogen concentrations (2.32 +/- 0.08). Stomatal conductance decreased sharply with increasing air saturation deficit, but the sensitivity of the response did not differ between species. These data were used to derive parameters for a coupled photosynthesis-stomatal conductance model to scale estimates of photosynthesis from leaves to the canopy, incorporating leaf respiration at night, site energy and water balances, to estimate net canopy carbon uptake. Over the course of a year, 76% of incident irradiance (400-700 nm) was absorbed by the canopy, annual net

photosynthesis per unit ground area was 164.5 mol m(-2) (equivalent to 1.97 kg C m(-2)) and respiration loss from leaves at night was 37.5 mol m(-2) (equivalent to 0.45 kg m(-2)), or 23% of net carbon uptake. When modelled annual net carbon uptake for the trees was combined with annual respiration from the soil surface, estimated net primary productivity for the ecosystem (0.30 kg C m(-2)) was reasonably close to the annual estimate obtained from independent mensurational and biomass measurements made at the site (0.22 +/- 0.03 kg C m(-2)). The mean annual value for light-use efficiency calculated from the ratio of net carbon uptake (net photosynthesis minus respiration of leaves at night) and absorbed irradiance was 13.0 mmol C mol(-1) (equivalent to 0.72 kg C GJ(-1)). This is low compared with values reported for other temperate forests, but is consistent with limitations to photosynthesis in the canopy attributable mainly to low nitrogen availability and associated low leaf area index.

Zieslin N. & Gottesman V. (1986). "Environmental factors involved in growth, flowering & post**-harvest behaviour of flowers of Leptospermum scoparium J.R. & G. Forst. Israel J of Botany Basic & Applied Plant Sciences 35(2), 101-108.**

Manuka Oil chemical composition.

Briggs L.H., Penfold A.R. & Short W.F. (1938) "Leptospermone Part I" J. Chem Soc. 141(2), 1193-1195.

Briggs L.H., Hassall C.H. & Short W.F. (1945) "Leptospermone Part II" J. Chem Soc. 148, 706-709.

Cambie R.C. & Seelye R.N. (1959) "Note on the identification of manuka manna". **N.Z. J. Sci 2(4), 498. Abstract The colourless, crystalline water-soluble compound found on Leptospermum scoparium & associated with the nymphal form of Scolypopa australis & the larva of Aemona hirta has now been identified as d-mannitol.**

Douglas M.H., van Klink J.W., Bruce M., Smallfield B.M., Perry N.B., Anderson R.E., Johnstone P. & Weavers R.T. (2004) "Essential oils from New Zealand manuka: triketone and other chemotypes o**f Leptospermum scoparium.**" **Phytochemistry 65(9) May 2004, pp1255-1264. Abstract:The triketone chemotype of manuka, Leptospermum scoparium(Myrtaceae), is commercially important because of its antimicrobial activity. Oils from 36 individual plants on the East Cape of New Zealand all showed similar high triketone contents (>20% total triketones) with little seasonal variation. Analyses of oils from 261 individual manuka plants collected from 87 sites throughout New Zealand showed that the high triketone chemotype was localised on the East Cape, although oils with triketone levels up to 20% were found in the Marlborough Sounds area of the South Island. Cluster analysis revealed other chemotypes localised on other areas. Ten further chemotypes are described: a-pinene; sesquiterpene-rich with high myrcene; sesquiterpene-rich with elevated caryophyllene and humulene; sesquiterpene-rich with an unidentified sesquiterpene hydrocarbon; high geranyl acetate; sesquiterpene-rich with high g-ylangene + a-copaene and elevated triketones; sesquiterpene-rich with no distinctive components; sesquiterpene-rich with high trans-methyl cinnamate; high linalol; and sesquiterpene-rich with elevated elemene and selinene. Some of the chemotypes contained aroma compounds at relatively high levels, with a geranyl acetate-rich oil being most notable. Possible origins for this complex array of chemotypes are proposed.**

Flynn T.M., Lassak E.V., & Smyth M.P. (1979). "The volatile leaf oils of three species **of Leptospermum**." **Phytochemistry 18, 2030-2031.**

Gardner R. (1924). "The essential oil of Manuka (**Leptospermum scoparium). J. Soc. Chem. Ind. 43, 34-35.**

Gardner R. (1924). "The essential oil of Manuka (**Leptospermum scoparium). J. Soc. Chem. Ind. 44, 528-530.**

Gardner R. (1924). "The **essential oil of Manuka (Leptospermum scoparium). J. Soc. Chem. Ind. 45, 96-98.**

Haeberlein, H. & K. P. Tschiersch (1998). "On the occurrence of methylated and methoxylated flavonoids **in Leptospermum scoparium**." **Biochemical Systematics and Ecology26(1), 97-103. Abstract. Samples of Leptospermum scoparium, collected from climatically and geologically different locations, were examined for**

their external leaf flavonoids. HPLC fingerprint analyses of dichloromethane extracts revealed different compositions and amounts of methylated and methoxylated flavonoids. In the area of Auckland, Coromandel, Whangaruru North, and Rawhiti plants have been found which possess high amounts of pharmacologically active 5,7-dimethoxyflavone, 5-hydroxy-7-methoxy-6-methylflavone, and 5-hydroxy-7-methoxy-6,8-dimethylflavan-3-one.

Haberlein, H. & K. P. Tschiersch (1994). "2,5-**Dihydroxy-7-methoxy-6,8-dimethylflavan-3-one a novel flavonoid from Leptospermum scoparium: In vitro affinity to the benzodiazepine binding site of the GABA-A receptor-**chloride channel complex." **Pharmazie 49(11), 860.**

Haberlein, H., K. P. Tschiersch, et al. (1994). "Flavonoids from **Leptospermum scoparium with affinity to the benzodiazepine receptor characterized by structure activity relationships and in vivo studies of a plant** extract." **Pharmazie 49(12), 912-922. Abstract.The New Zealand Myrtacea Leptospermum scoparium Forst. contains lipophilic flavonoids which interact specifically with benzodiazepine receptors. For an indepth characterization of their binding behavior, structure activity relationships were delineated which are in accord with results obtained by quantum-chemical and spectroscopic methods. Inhibition experiments have been performed by a radio receptor assay with [3H]flunitrazepam and IC50-values of 2.1 microM for 5,7-dimethoxyflavone (1), 45 microM for 5,7-dimethoxy-6-methylflavone (2), 3.3 microM for 5-hydroxy-7-methoxy-6-methylflavone (3) and 40 microM for 5-hydroxy-7-methoxy-6,8-dimethylflavone (4) have been measured. Flavanones 5 to 8, however, at concentrations < or = 0.1 mM, did not show a 50% inhibition of the binding radiolignand. The agonistic profile of the flavones was determined indirectly by TBPS-shift experiments which revealed a negative cooperation with the TBPS/picrotoxinin-binding site. To characterize the biologically active conformations, energy minima were calculated using the semiempirical method AM1. The steric arrangement of the substituents for all global minima calculated were in accord with homonuclear NOE-experiments. A correlation of the geometry of the lowest energy conformers with corresponding IC50-values reveals an increase of the affinity towards the benzodiazepine receptor, when the substituents at the flavones are coplanar to the aromatic system and R3 represents a sterically demanding methylgroup. Analyses of the global minima of 5,7-Dimethoxyflavone and diazepam showed one conformer each, in which the methoxy substituent in R3 and the N-methyl on the one hand and the corresponding carbonyl oxygens as well as the unsubstituted phenyl rings on the other were nearly superimposable. The flavanones lacking the double bond between C-2 and C-3 have angular structures, whereby the loss of affinity to the receptor can be explained. From the locomotion study with rats, an in vivo sedating, possibly even anxiolytic effect of the dry extract of the tincture prepared from Leptospermum scoparium by use of 70% ethanol, could be concluded. At doses of 50 mg and 250 mg of the dry extract per kg of body weight, an unequivocal but not linear dose-activity relationship in respect to the moving activities of the animals was determined. Upon an application of 500 mg of this extract per kg body weight, by contrast, only a negligible reduction of the moving activity was found in relation to a control group. We suppose that at higher doses, activating compounds of the extract come to the fore pharmacologically neutralizing the primarily sedating effect.**

Haberlein, H. & K. P. Tschiersch (1994). "Triterpenoids and flavonoids from **Leptospermum scoparium**." **Phytochemistry Oxford 35(3), 765-768. Abstract.An investigation of the dichloromethane extract of Leptospermum scoparium afforded seven 3-substituted triterpenoid acids, four of which were novel, and eight methylated flavonoids including one new flavone. The new compounds were identified by their spectroscopic** data as 3β-**O-trans-ferulyl-**2α-**hydroxy-urs-12-en-28-**oic acid, 3β-**O-cis-ferulyl-**2α-**hydroxy-urs-12-en-28-oic acid,** 2α-**O-trans-ferulyl-**3β-**hydroxy-urs-12-en-28-**oic acid, 3β-**O-cis-coumaroyl-**2α-**hydroxy-urs-12-en-28-oic acid and 5,7-dimethoxy-6-methylflavone.**

Hellyer R.O. (1968) "The occurrence of beta-triketones in the steam volatile oils of some myrtaceous Australian plants." Australian Journal of Chemistry 21, 2825-2828.

Joulain D. (1996). "Investigating new oils: rationale, results, limitations." **Perfumer & Flavourist 21(2),1.**

van Klink J.W., Brophy J.J. Perry N.B & Weavers R.T. (1999) "b-**Triketones from the Myrtaceae: Isoleptospermone from Leptospermum scoparium & papuanone from Corymbia dallachiana**." **J. Nat. Products 62, 487-489. Abstract. Naturally occurring beta-triketones, isoleptospermone [3,5-hydroxy-4-(2-methyl-**

1-oxopentyl)-2,2,6,6-tetramethyl-4-cyclohexene-1,3-dione) from Leptospermum scoparium] and papuanone [6,5-hydroxy-4-(1-oxohexyl)-2,2,6,6-tetramethyl-4-cyclohexene-1,3-dione from Corymbia dallachiana] have been synthesised. Full spectra data are reported for the first time. The 13C NMR spectra of 3,6 and the other triketones flavescone (2), leptospermone (4) and grandiflorone (5) found in Myrtaceous plants are fully assigned.

Maddocks-Jennings W., Wilkinson J.M., Shillington D. & Cavanagh H. (2005). " A Fresh Look at Manuka and Kanuka Essential Oils from New Zealand." **International Journal of Aromatherapy 15(3), 141-146. Summary:Essential oil is obtained from manuka, Leptospermum scoparium and kanuka, Kunzea ericoides, which are indigenous plants to New Zealand. The oil from these plants has been commercially available to aromatherapists for more than a decade. In this time, attention has been given to the antiseptic and antimicrobial actions of the oils. Of most interest to researchers and aromatherapists is the presence of beta-triketones, present in the manuka oil. These triketones are believed to significantly contribute to the antimicrobial action. More recently, it has emerged that there are significant geographical variations affecting the composition of these oils. Whilst a full understanding of the therapeutic implications is some way off, it is important for aromatherapists to appreciate that these differences exist and the oils selected may match the intended therapeutic purpose.**

Mayer, R. (1996). Three lupane derivatives from Leptospermum scoparium. Archiv der Pharmazie Weinheim 329(10), 447-450.

Mayer, R. (1993). "A **b-hydroxychalcone from Leptospermum scoparium**." **Planta Medica 59(3), 269-271.**

Mayer, R. (1990). "Flavonoids from **Leptospermum scoparium**." **Phytochemistry 29(4), 1340-1342.**

Melching S., Bülow N., Wihstutz K., Jung S. & König W.A. (1998?) "Natural occurrence of both enantiomers of **cadina-3,5-diene and & d-**amorphene." **Phytochemistry 44, 1291-1296. Abstract: The labile sesquiterpene hydrocarbon (-)-(1R,7S,10R)-cadina-3,5-diene was isolated from manuka oil (Leptospermum scoparium) by preparative gas chromatography, while its enantiomer is present in a chemotype of the liverwort Conocephalum conicum collected in southern Germany. The structure and absolute configuration was derived by NMR investigations, enantioselective gas chromatography and by conversion into a series of products of known stereochemistry by acid catalysed rearrangement, e.g. (-)-(7S,10R)-trans-calamenene, (-)-(7S,10R)-cadina-1(6),4,diene, (-)-(1R,7S,10R)-bicyclosesquiphellandrene and (-)-(1R,10R)-zonarene. In addition, (+)-d-amorphene was identified as a constituent of L. scoparium, whilst (-)-d-amorphene is present in vetiver oil. Both enantiomers of this sesquiterpene, which has not been described as a natural product so far, were prepared by rearrangement of an enantiomeric mixture of germacrene D isolated from Solidago canadensis.**

Perry, N. B., Brennan N.J., van Klinck J.W., Harris W., Douglas M.H., McGimpsey J.A., Smallfield B.M. & Anderson R.E. (1997). "Essential oils from New Zealand manuka and kanuka: Chemotaxonomy **of Leptospermum**." **Phytochemistry Oxford 44(8), 1485-1494. Abstract.A standardized analytical GC method has been used to analyse essential oils from selected Australian and New Zealand Kunzea species, grown from seed at a single site. The distillation yields and analyses are reported for oils from 26 populations of K. ericoides (kanuka) and from single populations of each of K. flavescens, K. pauciflora, K. sinclairii and x Kunzspermum hirakimata (a Kunzea x Leptospermum cross). Principal components analyses of 37 GC peaks in these oils were used to distinguish compositional patterns. Oils from K. flavescens, K. pauciflora and x Kunzspermum hirakimata had chemical compositions distinct from K. sinclairii and K. ericoides. Oils front New Zealand K. ericoides** were mainly **α-pinene (mean 68%), but some oils had high p-cymene contents, particularly oils from one Marlborough provenance (mean 31%). A wild population of K. ericoides var. linearis gave oils with similar composition to other K. ericoides. Two K. ericoides oils showed weak antifungal activity.**

Porter, N. G., Smale P. E., Nelson M.E., Hay A.J., van Klink J.W. & Dean C.M. (1998). "Variability in essential oil **chemistry and plant morphology within a Leptospermum scoparium**population." **New Zealand Journal of**

Botany 36(1), 125-133. Abstract Essential oil composition and plant morphology were observed over four years in individual plants raised from seed of a wild population of Leptospermum scoparium (Myrtaceae) collected at a single site in New Zealand. Principal component analyses of data from young and mature plants showed no significant grouping of plants on the basis of oil composition, but identified differences between the essential oil components contributing most to variation in oil composition in both young and mature plants. The dominant variables were six sesquiterpene components in young plants, and three monoterpenes and two sesquiterpenes in mature plants. Levels of these components differed significantly at the population level between young and mature plants and also within and between seasons. Levels of all these components varied markedly within and between individual plants at all sample times. The habit, leaf size and density, and stem and foliage colour also varied markedly between individual plants. The variation observed indicates the need for more extensive sampling and statistical analysis over more than one growing season if sufficiently reliable data on essential oil compositions in individual plants or populations are to be obtained for chemotaxonomic or plant selection purposes.

Porter N.G. & Wilkins A.L. (1999) "Chemical, physical and antimicrobial properties of essential oils **of Leptospermum scoparium and Kunzea ericoides." Phytochemistry Oxford50(3), 407-415. Abstract: The major components of commercial New Zealand essential oils of Leptospermum scoparium (manuka) and Kunzea ericoides (kanuka) are identified. In the manuka oil, monoterpenes are present at low levels (£3%). Sesquiterpene hydrocarbons are predominant (³60%) and include groups possessing cubebene/copaene, elemene, gurjunene/aromadendrene, farnesene/caryophyllene, selinene, calamenene and cadinene skeletons. Oxygenated sesquiterpenes and triketones are present (³30%). The antimicrobial activity of the manuka oil was associated with a fraction containing three major and three trace triketones, two of the latter were previously unreported. Kanuka oil was characterized by high levels of a-pinene (>50%) and lower levels (<10%) of viridiflorol and viridiflorene. GC-MS and GC-FID detector responses to the same components were noticeably different for some major components, including the triketones. Non-commercial manuka oils from different sites differed widely in composition and could be separated into four groups by the presence and levels of distinctive components. The density and refractive index of manuka and kanuka oils were closely correlated with the total sesquiterpene levels. The density of the commercial manuka oil was closely correlated with the level of the triketones. Simple density measurements enabled discrimination between the commercial oil and oils from other sites, and prediction of antimicrobial activity.**

Short W.F. (1926) "The essential oil of Manuka (Leptospermum scoparium)." J. Soc. Chem. Ind. 45, 96-98.

Tschiersch, K.-P.Dissertationes botanicae, Vol. 241. Leptospermum scoparium J. R. & G. Forst.: "Isolation, structural explanation, and analysis of flavonoids and resin esters with in vitro affinity to GABAA receptor chloride channel complex." Gebr. Bor**nträger Verlagsbuchhandlung, Stuttgart, 1995.**

Wilkins L. (1997). "Chemical & compositional analyses of New Zealand manuka & kanuka oils." Proceedings of Pacific Oils 2000 Conference Nov 1997, Auckland.

Manuka Dissertation.

Chistoph F. (2001)"Chemische Zusammensetzung und antimikrobielle Eigenschaften der ätherischen Öle von Leptospermum scoparium J. R. et G. Forst. und anderer Teebaumöle der Gattungen Kunzea, Leptospermum und Melaleuca unter besonderer Berücksichtigung von Handelsölen" Univ. Hamburg 2001 - see http://www.sub.uni-hamburg.de/opus/volltexte/2001/448/pdf/Dissertation.pdf

Manuka Miscellaneous Reports.

Porter N. (2001) "Manuka: the good oil from New Zealand." Herbalgram 53, 26-30.

Manuka Oil Pesticidal Activity.

Watanabe Keisuke & Sugano Masayo (2003) "Agent for controlling harmful arthropod containing oil of Leptospermum scoparium." Patent No: JP2003055123 dated 26-02-2003. Abstract: PROBLEM TO BE SOLVED: To obtain a new agent for controlling a harmful arthropod, derived from a natural product because the new agent derived from the natural product is required in a field of the agent for controlling the harmful arthropod in connection with the enhancement of health consciousness and naturalism consciousness of human beings in recent years. SOLUTION: This agent for controlling the harmful arthropod contains an oil of Leptospermum scoparium which is an essential oil component of the Leptospermum scoparium which is a plant naturally growing in New Zealand.

Manuka Oil Oral Hygiene Studies.

Lauten J.D., Boyd L., Hanson M.B., Lille D., Gullion C. & Madden T.E. (2005) "A clinical Study: Melaleuca, Manuka, Calendula & Green Tea Mouth Rinse." **Phytotherapy Research19(11), 951-957. Abstract. A novel mouthrinse (IND 61,164) containing essential oils and extracts from four plant species (Melaleuca alternifolia, Leptospermum scoparium, Calendula officinalis & Camellia sinensis) were tested. This study aimed to evaluate safety, palatability, & preliminary efficiency of the rinse. Fifteen subjects completed the Phase 1 safety study. Seventeen subjects completed the Phase II randomised placebo-controlled study. Plaque was collected, gingival & plaque indices were recorded (baseline, 6 weeks & 12 weeks). The relative abundance of two periodontal pathogens (Actinobacillus actinomycetemcomitans, Tanerella forsythensis) was determined using digoxigen-labelled DNA-probes. ANCOVA was used at the p=0.05 level of significance. Two subjects reported a minor adverse event. One subject withdrew from the study. Several subjects objected to the taste of the test rinse but continued treatment. Differences between gingival index, plaque index, or relative abundance of either bacterial species did not reach statistical significance when comparing nine placebo subjects with eight test rinse subjects. Subjects exposed to the test rinse experienced no abnormal oral lesions, altered vital signs, changes in liver, kidney or bone marrow functions. Larger scale studies would be necessary to determine the efficacy & oral health benefits of the test rinse.**

Manuka Oil Pharmacological/Microbiological Effects.

Lis-Balchin M., Hart S.L & Deans S.G. (2000) "Pharmacological and antimicrobial studies on different tea-tree oils (Melaleuca alternifolia, Leptospermum scoparium or Manuka and Kunzea ericoides or Kanuka), originating in Australia and New Zealand." Phytother. Res. 14(8), 623-629. Abstract. Three different species of Myrtaceae growing in Australia and New Zealand are known as 'Tea-tree': the Australian Tea tree (Melaleuca alternifolia), the New Zealand Manuka (Leptospermum scoparium) and Kanuka (Kunzea ericoides). All three essential oils are used by aromatherapists, although only Melaleuca has been tested for toxicity, and its antimicrobial effects studied. The pharmacology and antimicrobial activity of the three 'tea-tree' oils was determined using guinea-pig ileum, skeletal muscle (chick biventer muscle and the rat phrenic nerve diaphragm) and also rat uterus in vitro. Differences were shown between the three essential oils in their action on smooth muscle: Manuka had a spasmolytic action, while Kanuka and Melaleuca had an initial spasmogenic action. Using the diaphragm, Manuka and Melaleuca decreased the tension and caused a delayed contracture; Kanuka had no activity at the same concentration. The action on chick biventer muscle was, however, similar for all three oils, as was the action on the uterus, where they caused a decrease in the force of the spontaneous contractions. The latter action suggests caution in the use of these essential oils during childbirth, as cessation of contractions could put the baby, and mother, at risk. The comparative antimicrobial activity showed greater differences between different samples of Manuka and Kanuka than Melaleuca samples. The antifungal activity of Kanuka was inversely proportional to its strong antibacterial activity, whilst Manuka displayed a stronger antifungal effect, though not as potent as Melaleuca. The antioxidant activity of Manuka samples was more consistent than that of Kanuka, while Melaleuca showed no activity. The variability in the Manuka and Kanuka essential oils suggests caution in their usage, as does the fact that the oils have not been tested for toxicity.

Related Articles on Manuka Oil

Filoche S.K., Soma K. & Sissons S.H. (2005) "Anti-microbial effects of essential oils in combination with chlorhexidine digluconate." Oral Microbiol Immunol 20(4), 221-225. Abstract.The aim of the present study was to compare antimicrobial effects of essential oils alone and in combination with chlorhexidine digluconate against planktonic and biofilm cultures of Streptococcus mutans and Lactobacillus plantarum. The essential oils included cinnamon, tea-tree (Melaleuca alternifola), manuka (Leptospermum scoparium), Leptospermum morrisonii, arnica, eucalyptus, grapefruit, the essential oil mouthrinse Cool Mint Listerine and two of its components, menthol and thymol. Cinnamon exhibited the greatest antimicrobial potency (1.25-2.5 mg/ml). Manuka, L. morrisonii, tea-tree oils, and thymol also showed antimicrobial potency but to a lesser extent. The combination effect of the essential oil-chlorhexidine was greater against biofilm cultures of both S. mutans and L. plantarum than against planktonic cultures. The amount of chlorhexidine required to achieve an equivalent growth inhibition against the biofilm cultures was reduced 4-10-fold in combination with cinnamon, manuka, L. morrisonii, thymol, and Listerine. We conclude that there may be a role for essential oils in the development of novel anticaries treatments.

van Klink J.W., Larsen L., Perry N.B., Weavers R.T., Cook G.M., Bremer P.J., MacdKenzie A.D. & Kirikae T. (2005) "Triketones active against antibiotic-resistant bacteria: Synthesis, structure–activity relationships, and mode of action." Bioorganic & Medicinal Chemistry 13(24), 6651-6662. Abstract. A series of acylated phloroglucinols and triketones was synthesized and tested for activity against methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus faecalis (VRE) and multi-drug-resistant Mycobacterium tuberculosis (MDR-TB). A tetra-methylated triketone with a C_{12} side chain was the most active compound (MIC of around 1.0 μg/ml against MRSA) and was shown to stimulate oxygen consumption by **resting cell suspensions, suggesting that the primary target was the cytoplasmic membrane.**

Rammussen P.L. (1997) "Phytotherapy in the treatment of benzodiapine withdrawal." Eur. J. Herb. Med. 3(1), 11-21.

Manuka Oil Spasmolytic Activity.

Lis-Balchin M. & Hart S.L. (1998). "An investigation of the actions of the essential oils of Manuka (**Leptospermum scoparium) and Kanuka (Kunzea ericoides), Myrtaceae on guinea-**pig smooth muscle." **Journal of Pharmacy and Pharmacology 50(7), 809-811. Abstract. Three different species of Myrtaceae growing in Australia and New Zealand are known as 'Tea-tree': the Australian Tea tree (Melaleuca alternifolia), the New Zealand Manuka (Leptospermum scoparium) and Kanuka (Kunzea ericoides). All three essential oils are used by aromatherapists, although only Melaleuca has been tested for toxicity, and its antimicrobial effects studied. The pharmacology and antimicrobial activity of the three 'tea-tree' oils was determined using guinea-pig ileum, skeletal muscle (chick biventer muscle and the rat phrenic nerve diaphragm) and also rat uterus in vitro. Differences were shown between the three essential oils in their action on smooth muscle: Manuka had a spasmolytic action, while Kanuka and Melaleuca had an initial spasmogenic action. Using the diaphragm, Manuka and Melaleuca decreased the tension and caused a delayed contracture; Kanuka had no activity at the same concentration. The action on chick biventer muscle was, however, similar for all three oils, as was the action on the uterus, where they caused a decrease in the force of the spontaneous contractions. The latter action suggests caution in the use of these essential oils during childbirth, as cessation of contractions could put the baby, and mother, at risk. The comparative antimicrobial activity showed greater differences between different samples of Manuka and Kanuka than Melaleuca samples. The antifungal activity of Kanuka was inversely proportional to its strong antibacterial activity, whilst Manuka displayed a stronger antifungal effect, though not as potent as Melaleuca. The antioxidant activity of Manuka samples was more consistent than that of Kanuka, while Melaleuca showed no activity. The variability in the Manuka and Kanuka essential oils suggests caution in their usage, as does the fact that the oils have not been tested for toxicity.**