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Review Article

Manuka Oil Vs. Oral Pathogens: An Overview

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Abstract

Manuka oil is obtained by steam distillation from the manuka tree (*Leptospermum scoparium*), a plant native to New Zealand and south-east Australia. The composition of manuka oil and the significance of its β-triketone content is briefly reviewed.

The potential application of manuka oil and to a lesser extent manuka honey, to treat dental caries and act as bactericidal agents against cariogenic bacteria is reviewed in detail. This activity against Gram-positive bacteria and dermatophytes was ascribed to the β-triketone content. The antibacterial activity of manuka oil against periodontopathic pathogens is also reviewed and discussed.

Keywords: *Manuka Oil; Oral Pathogens; Leptospermum scoparium; β-triketone*

Introduction

Although manuka oil and manuka honey have been recognized for their health-benefiting properties for centuries by the native Māori people of New Zealand and their importance in Rongoa Maori[1], manuka is a relatively new essential oil to the western world. Manuka is extracted from the flowering plant known as the manuka tree[2] (*Leptospermum scoparium*), which is native to New Zealand and south-east Australia and is part of the myrtle (*Myrtaceae)* family. Because the mānuka tree comes from the same family of trees as tea tree oil, eucalyptus and myrtle, manuka oil is often known as New Zealand's tea tree oil. In contrast, Australian tea tree oil is distilled from the *Melaleuca alternifolia* tree.

Manuka oil is obtained by comminution of young stems and leaves (and also the seeds) of the manuka plant harvested mostly in the spring, summer and autumn. The biomass is soaked and then steam-distilled to release the oil, with the oil yield ranging from 0.2 - 1%, depending on seasonal and geographical factors [1,2].

[1]*Rongoā Māori* is the traditional Māori healing system, encompassing herbal (plant-based) remedies, physical therapies and spiritual healing.

[2]*Leptospermum scoparium* is commonly called mānuka, mānuka myrtle, New Zealand tea tree, broom tea-tree, or just tea tree, is a species of flowering plant in the myrtle family *Myrtaceae*. It is native to New Zealand and south-east Australia. Its nectar produces Mānuka honey.

Composition of manuka oil

Mānuka grows abundantly throughout New Zealand but the constituents of mānuka oil vary depending on the source of the oil as well as the plant chemotype and season of collection [3-5]. About 100 individual components have been identified in mānuka oil, with 51 of these compounds comprising about 95% of the total content [2]. The major components of commercially available mānuka oils are indicated in table 1 [2-5].

Component	Content
Leptospermone	0.8 - 19.4%
Calamenene	2.5 - 18.5%
δ-Cadinene	0.9 - 6.9%
Cadina-1,4-Diene	0.1 - 5.9%
Flavesone	0.7 - 5.8%
Cadina-3,5-Diene	3.0 - 10.0%
α-Copaene	4.3 - 6.5%
α-Selinene	1.3 - 5.0%

Table 1: *Constituents of manuka oil.*

It should be noted that manuka oil sourced from plants growing on the East Coast of the North Island of New Zealand contains higher levels of β-triketones than that sourced from other regions [5]. It has been found that the age of the plant also affects the nature of the essential oil, with higher sesquiterpene content being found in young plants and a mixed levels of monoterpenes and sesquiterpenes in mature ones [3].

Because many factors influence the constituents of manuka oil, as with all essential oils, this can lead to some variability in medicinal properties [6]. Thus, for example, higher levels of triketones are found in manuka oil harvested from plants from the East Cape region of New Zealand and higher contents of the monoterpenes, α- and β-pinene, are found in plants from the Northland populations. Interestingly, oils from *L. scoparium* plants grown in Australia have higher monoterpene levels and almost no triketones compared to those from New Zealand *L. scoparium* plants [7].

Manuka oil, the essential oil derived from *Leptospermum scoparium*, has been used by the indigenous populations of New Zealand and Australia for centuries [8]. Both the extracted oil and its individual components have been associated with various medicinal properties, notably antibacterial activity [9,10].

Manuka oil vs. oral pathogens

Interest in the antibacterial activity of essential oils, especially against oral pathogens, started to gain traction in the early 1990s [11]. This interest resulted from the rise in resistance to conventional antibiotics and the potential for the development of antimicrobials with novel mechanisms of action from natural products.

In the case of manuka oil, early studies indicated that the *in vitro* antimicrobial activity against Gram-positive bacteria and dermatophytes[3] was ascribed to its β-triketone content [2,12].

[3]A dermatophyte is a pathogenic fungus that grows on skin, mucous membranes, hair, nails and other body surfaces, causing ringworm and related diseases.

Manuka oil vs. cariogenic bacteria

Although thousands, if not millions, of hours and considerable resources have been devoted to the characterization, treatment and prevention of dental caries (dental decay), it is still the most prevalent disease known to mankind. Dental caries and periodontal disease are the primary causes of the loss of dental hard tissue and their treatment and, notably, their prevention are primary focuses of modern dentistry. It is now well-established that dental caries is primarily caused by Gram-positive facultative anaerobic bacteria belonging to a group of *mutans Streptococci* comprising *Streptococcus mutans*, *S. sobrinus* and several other species.

In the early years of the 21st century, a study compared the antibacterial efficacies of manuka, tea tree, eucalyptus, lavandula[4] and rosemary essential oils against oral pathogens [13]. The target oral pathogens were the cariogenic bacteria *Streptococcus mutans* and *Streptococcus sobrinus* and the periodontopathic bacteria *Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans* and *Fusobacterium nucleatum.* It was found that the essential oils inhibited the growth of the bacteria, with manuka oil being the most effective. It was also noted that, curiously, lavandula oil had a bacteriostatic action whereas the other essential oils were bactericidal in action.

Another study performed in 2005 [14] evaluated the 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. It was found that cinnamon exhibited the greatest antimicrobial potency (1.25 - 2.5 mg/ml) and whereas manuka, *L. morrisonii*, tea-tree oils and thymol did show antimicrobial potency, it was to a lesser extent. Interestingly, the combination effect of the essential oil-chlorhexidine mixture was greater against biofilm cultures of both *S. mutans* and *L. plantarum* than against planktonic cultures. It was also noted that 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®. These findings clearly support the suggestion that there is a role for essential oils in the development of novel anticaries treatments.

Since those early studies, there have been a few reports in the literature referring to the potential application of essential oils in the prevention and treatment of dental caries [15-17] but apparently very limited research work has been performed.

Manuka oil vs. periodontopathic pathogens

Traditionally, control of dental plaque-related diseases such as gingivitis and periodontitis has relied on non-specific plaque removal by mechanical means. This situation is changing with the knowledge that the primary pathogens involved in periodontal disease include the Gram-negative *Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, Prevotella intermedia* and *Fusobacterium nucleatum* [13] together with the greater use of antimicrobials to treat periodontal disease. It also has been suggested that targeted phototherapy with high-intensity monochromatic light can effect selective killing of *Porphyromonas gingivalis* and *Prevotella intermedia* in biofilms. Further, the use of protease inhibitors has been explored to control periodontitis [18] but again, there do not appear to be any follow-up studies available.

It is common in present day periodontal treatment to use antibiotics and antiseptics as locally-delivered antimicrobial adjuncts in conjunction with scaling and root planing (SRP), particularly to treat poorly- or non-responding and recurrent deep periodontal pockets. The underlying concept is that adjunctive therapy is necessary to support and optimize periodontal healing through the elimination (or at least suppression) of the Gram-negative bacteria associated with periodontal diseases.

[4]Lavender oil is extracted from both English Lavender and Lavandin. The key difference between lavender oil and lavandin oil is that the latter contains a much higher percentage of camphor, namely 6% - 10% camphor whereas English Lavender essential oil typically contains < 0.5% camphor.

However, the success of this treatment methodology may be becoming limited due to the increasing prevalence of bacterial antibiotic resistance. This situation has prompted a return to age-old remedies and traditional medicine, i.e. the use of alternative antimicrobials originating from plants, for the prevention and treatment of periodontal disease. In fact, a recent clinical report indicates that a mouth rinse based on essential oils can yield very successful responses in periodontal tissue health [19]. It should be mentioned, on the other hand, that a much earlier and limited study in 2005 [20] evaluated the effectiveness of a mouth rinse base on melaleuca, manuka, calendula and green tea against the periodontal pathogens *Actinobacillus actinomycetemcomitans* and *Tannerella forsythia.* The study data indicated no statistically significant differences between gingival index, plaque index or the relative abundance of either bacterial species when nine placebo subjects were compared with the eight test rinse subjects at baseline, 6 weeks and 12 weeks. This negative finding is in complete contrast to the findings of a near-contemporary study [13] that showed periodontopathic bacterial strains were killed completely by exposure for 30s to 0.2% manuka oil, tea tree oil and eucalyptus oil. It was also noted that manuka oil and tea tree oil in particular had strong antibacterial activity against periodontopathic and cariogenic bacteria.

Honey is an ancient natural remedy for the treatment of infected wounds and bacteriological/microbiological studies suggested that honey may have a broad-spectrum inhibitory effect against bacteria. In general, there appears to be limited data concerning antimicrobial activity of NZ manuka honey but there have been more recent reports of studies investigating the potential of manuka-derived products (manuka honey and manuka oil) as antimicrobials against oral pathogens.

One study [21] evaluated the antibacterial efficacy of different manuka honey products against *S. mutans*, *P. gingivalis* and *A. actinomycetemcomitans* with chlorhexidine and saline serving as positive and negative controls respectively. Chlorhexidine showed the highest inhibiting potential against all specimens tested whereas manuka honey preparations were more effective in inhibiting the growth of *P. gingivalis* and *A. actinomycetemcomitans* than *S. mutans*. These findings are interesting in that other research work suggests that manuka oil has selective antibacterial activity against many Gram-positive organisms but its activity against Gram-negative organisms is more limited [8,9,22].

A more recent study comprising the thesis for a PhD degree [23] investigated the potential of manuka-derived products (manuka honey and manuka oil) as antimicrobials for application within periodontal pockets as an adjunct to scaling and root planing. The underlying concept was to take advantage of the antibacterial properties and wound healing potential of manuka.

In vitro and *in vivo* investigations were performed. It was found that manuka honey exhibited broad-spectrum antimicrobial activity against a variety of plaque-associated bacteria, thereby confirming the findings of Schmidlin., *et al.* published in (2014). It was noted, as in the earlier study, that decreasing the concentration of honey not only reduced the antimicrobial activity but also promoted bacterial carbohydrate metabolism and consequent acid production by *Streptococcus mutans.* The latter effect is quite deleterious in that it will exacerbate enamel demineralization. It should also be noted that since the antibacterial action of manuka honey is slow-acting, any marked dilution would limit its efficacy in periodontal pockets.

An interesting finding within this detailed study was that a three-month follow-up did not show additional improvement in clinical parameters when periodontal pockets were treated with manuka honey following scaling and root planing compared to SRP alone. In contrast, manuka oil did show potential as a therapeutic substance in that the oil at an effective concentration of 0.1% w/v had greater potency than manuka honey at effective concentrations of 13 - 25% w/v. Clearly, manuka oil may be superior to manuka honey as an antimicrobial for intra-oral applications.

Despite the long-term application of chlorhexidine in periodontology, there are problems associated with its use [24,25]. One problem is that the IC_{50} of chlorhexidine was 100 times higher than its therapeutic concentration whereas manuka oil had a relatively rapid bactericidal effect and its toxicology profile determined at 96 hours and based on its IC_{50} was four times higher than the effective antimicrobial concentration [23]. These study findings also suggested that the mechanism of cell death induced by manuka oil under cell culture condi-

tions may be apoptosis rather than necrosis. This could be an important distinction since apoptosis is an active, programmed process of autonomous cellular dismantling which avoids stimulating inflammation. In contrast, necrosis is a passive, accidental cell death resulting from environmental perturbations accompanied by uncontrolled release of inflammatory cellular contents.

Another problem encountered with chlorhexidine is maintaining its presence within periodontal pockets and various approaches have been adopted to address this challenge [25]. It was noted [23] that manuka oil and manuka oil emulsion exhibited favorable rheological properties, notably pseudoplastic or shear thinning behavior, which might improve retention in periodontal pockets [23]. If this is the case, then when it is used in periodontology, manuka may exhibit increased effectiveness, duration of action and depth of antibacterial activity within biofilms.

Of late, there appears to be a growing trend of increased resistance being observed with opportunistic *Candida* infections [26]. *Candida* infections in the elderly are an important and expanding clinical problem since there is a significantly higher mortality in this group than in younger patients. The growing disease problem associated with invasive *Candida* infections may be related to the higher prevalence of immunocompromised older people and the increasing resistance to treatment. This situation has prompted studies evaluating the antimycotic activity of essential oils against different *Candida spp* [27]. The tested essential oils were cumin, fennel, manuka, sweet orange, cedar and juniper. Of these, cumin, fennel and manuka essential oils were found to be effective against *Candida spp*. and supported the findings of previous studies of manuka as a natural alternative treatment for diseases caused by infectious and inflammatory microorganisms [8,14,22,28]. In particular, it has been reported that manuka (and kanuka) essential oils are strong candidates for treating infections and immune-related disease because of their potent anti-microorganism and anti-inflammation properties [22,28].

Conclusion

It is clear from this review that despite the somewhat sporadic nature of research into the use of manuka oil to treat and prevent dental disease, this particular essential oil may hold great promise in dentistry. Manuka oil alone or in combination with chlorhexidine appears to be markedly beneficial with regard to periodontal disease and to be effective against cariogenic bacteria.

There is also a growing literature on the health benefits of manuka oil and manuka honey due to the unusually high content of vitamins and minerals as well as antioxidants, this making manuka honey one of the healthiest honeys available.

Bibliography

1. Broadsheet, C.F.R. Essential Oil Production from Manuka and Kanuka (2014).

2. Christoph F., et al. "The composition of commercial manuka oils from New Zealand". *Journal of Essential Oil Research* 11 (1999): 705-710.

3. Porter NG., *et al.* "Variability in essential oil chemistry and plant morphology within a *Leptospermum scoparium* population". *New Zealand Journal of Botany* 36.1 (1998): 125-133.

4. Porter NG and Wilkins AL. "Chemical, physical and antimicrobial properties of essential oils of *Leptospermum scoparium* and *Kunzea ericoides*". *Phytochemistry* 50.3 (1999): 407-415.

5. Douglas MH., *et al.* "Essential oils from New Zealand manuka: Triketone and other chemotypes of *Leptospermum scoparium*". *Phytochemistry* 65.9 (2004): 1255-1264.

6. Bent S. "Herbal medicine in the United States: Review of efficacy, safety, and regulation: Grand rounds at University of California, San Francisco Medical Center". *Journal of General Internal Medicine* 23.6 (2008): 854-859.

7. Perry NB., *et al.* "Essential oils from New Zealand manuka and kanuka: Chemotaxonomy of *Leptospermum*". *Phytochemistry* 44.8 (1997): 1485-1494.

8. Mathew C., *et al.* "Mānuka oil-A review of antimicrobial and other medicinal properties". Pharmaceuticals 13.11 (2020): 343-366.

9. Lis-Balchin M., et al. "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". *Phytotherapy Research* 14.8 (2000): 623-629.

10. Williams LR., *et al.* "Essential oils with high antimicrobial activity for therapeutic use". *International Journal of Aromatherapy* 8.4 (1998): 30-40.

11. Shapiro S., et al. "The antimicrobial activity of essential oils and essential oil components towards oral bacteria". *Oral Microbiology and Immunology* 9.4 (1994): 202-208.

12. Christoph F., et al. "A comparative study of the *in vitro* antimicrobial activity of tea tree oils s.l. with special reference to the activity of β-triketones". *Planta Medica* 66.6 (2000): 556-560.

13. Takarada K., *et al.* "A comparison of the antibacterial efficacies of essential oils against oral pathogens". *Oral Microbiology and Immunology* 19.1 (2004): 61-64.

14. Filoche SK., et al. "Antimicrobial effects of essential oils in combination with chlorhexidine digluconate". *Oral Microbiology and Immunology* 20.4 (2005): 221-225.

15. Islam B., et al. "Dental caries: From infection to prevention". *Medical Science Monitor* 13.11 (2007): RA196-RA203.

16. Besra M and Kumar V. "Antimicrobial activity of essential oils and herbal extracts against etiological agent of dental caries". *Journal of Essential Oil Bearing Plants* 19.7 (2016): 1807-1815.

17. Lenetha GG and Dzogbewu TC. "Use of essential oils in dentistry against dental caries-A review". *Natural Volatiles and Essential Oils* 9.1 (2022): 1633-1644.

18. Allaker RP and Douglas CWI. "Novel anti-microbial therapies for dental plaque-related diseases". *International Journal of Antimicrobial Agents* 33.1 (2009): 8-13.

19. von Fraunhofer JA and Massa L. „Essential oils and periodoontal disease". *EC Dental Science* 18.8 (2019): 1939-1943.

20. Lauten JD., *et al.* "A clinical study: melaleuca, manuka, calendula and green tea mouth rinse". *Phytotherapy Research* 19.11 (2005): 951-957.

21. Schmidlin PR., *et al.* "Antibacterial potential of manuka honey against three oral bacteria *in vitro*". Swiss Dental Journal 124.9 (2014): 922-924.

22. Chen C-C., *et al.* "Investigations of kanuka and manuka essential oils for *in vitro* treatment of disease and cellular inflammation caused by infectious microorganisms". *Journal of Microbiology, Immunology and Infection* 49.1 (2016): 104-111.

23. Safii SH. "Manuka-derived products as an adjunct to scaling and root planing in the treatment of chronic periodontitis". Thesis, Doctor of Philosophy. University of Otago (2018).

24. Vinholis AH., *et al.* "Subgingival utilization of a 1% chlorhexidine collagen gel for the treatment of periodontal pockets. A clinical and microbiological study". *Brazilian Dental Journal* 12.3 (2001): 209-213.

25. Deus FP and Ouanounou A. "Chlorhexidine in Dentistry: Pharmacology, uses, and adverse effects". *International Dental Journal* 72.3 (2022): 269-277.

26. Dekkers BGJ., *et al*. "Invasive candidiasis in the elderly: Considerations for drug therapy". *Drugs and Aging* 35.9 (2018): 781-789.

27. Elisa B., *et al*. "Chemical composition and antimycotic activity of six essential oils (cumin, fennel, manuka, sweet orange, cedar and juniper) against different *Candida* spp". *Natural Product Research* 35.22 (2021): 4600-14605.

28. Reichling J., *et al.* "Essential oils of aromatic plants with antibacterial, antifungal, antiviral, and cytotoxic properties-an overview". *Complementary Medicine Research* 16.2 (2009): 79-90.

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