An overview of the medical utility of lavender

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Received: 22 January 2016; Accepted in revised form: 16 April 2016

Abstract

In recent years, several animal and human investigations have indeed evaluated traditional medical remedies of lavender using modern scientific methods. These studies raised the possibility of revival of lavender therapeutic efficacy in neurological disorders on the basis of evidence-based medicine. The oil is believed to have sedative, carminative, anti-depressive and anti-inflammatory properties, in addition to its recognized antimicrobial effects. The main constituents of lavender are linalool, linalyl acetate, 1,8-cineole B-ocimene, terpinen-4-ol, and camphor. Lavender was used predominantly in oral administration, aromatherapy or massage in several clinical studies. Many benefits are claimed for its use including relief of the symptoms of stress and depression, in improving 'mood' and relieving anxiety. Many human studies support its effectiveness in different neurological and psychological disorders.

Key words: lavender; Lavandula; aromatherapy

The genus *Lavandula* is native to the Mediterranean region and southern Europe through northern and eastern Africa and Middle Eastern countries to southwest Asia and southeast India. It includes more than 30 species, dozens of subspecies and hundreds of hybrids and cultivars. The different varieties range in height from 9 inches to 3 feet, although some may grow taller with age. The various lavenders have similar ethnobotanical properties and major chemical constituents (Cavanagh and Wilkinson 2002). Lavender essential oil is popular as a complementary medicine in its own right and as an additive to many over the counter complementary medicine and cosmetic products (Gattefosse 1937 and Cavanagh and Wilkinson 2002). Products derived from Lavender (*Lavandula* sp.) have been used for centuries as a therapeutic agent, with the more 'recent 'addition, the essential oils derived from these plants, being widely used as an antibacterial in World War I (Gattefosse 1937; Grieve 1931; Gorji 2003 and Denner 2009). The oil is believed to have sedative, carminative, anti-depressive and anti-inflammatory properties, in addition to its recognized antimicrobial effects (Cavanagh and Wilkinson 2005).

Many of the activities attributed to lavender oil have not, however, been substantiated in the scientific literature. This is further complicated by the fact that the majority of research into lavender essential oils has been based on oil derived from English lavender (*Lavandula angustifolia*), with little or no differentiation being made between this and other lavender essential oils. The therapeutic potential of essential oils produced from other varieties, such as *L. intermedia* (lavandin), *L. stoechas* (French lavender) and *L. allardii* have largely been ignored. Although the ethnobotanical uses and major chemical constituents are similar between various lavenders, some differences occur in both oil composition and in the reported therapeutic uses for different species (Cavanagh and Wilkinson 2002 and Agricultural Research Service 2000). The significant scientific interest in recent years into the validity/veracity of the traditional beliefs surrounding lavender oil and their scientific basis, if any, was recently reviewed by Cavanagh and Wilkinson (2002). In this review an overview of the use of lavender oil in infectious disease and an update on recent research on alternative uses of lavender oil was provided.

Constituents

The main constituents of lavender are linalool, linalyl acetate, 1,8-cineole B-ocimene, terpinen-4-ol, and

camphor. However, the relative level of each of these constituents varies in different species (Cavanagh and Wilkinson 2002 and Woronuk et al. 2011). Lavender oil, obtained from the flowers of *Lavandula angustifolia* (Family: Lamiaceae) by steam distillation, is chiefly composed of linalyl acetate (3,7-dimethyl-1,6-octadien-3yl acetate), linalool (3,7-dimethylocta-1,6-dien-3-ol), lavandulol, 1,8-cineole, lavandulyl acetate, and camphor. Whole lavender oil and its major components linalool and linalyl acetate are used in aromatherapy. The major components of lavender oil were identified as 51% linalyl acetate and 35% linalool measured by gas chromatography and gas chromatography-linked Fourier Transform Infrared analysis (Cavanagh and Wilkinson 2002 and Prashar et al. 2004).

Lavender as an anti-microbial agent

Similar studies have been carried out as comparative assessments of a range of essential oils and their efficacy as anti-microbial agents. Oils derived from a range of lavender species repeatedly rate highly in efficacy trials leading to the conclusion that many of the present usages that lavender has been advocated may have significant merit. Much of this research has been focussed on *L. angustifolia* with few trials using oil derived from other *Lavendula* species (Inouye et al. 2001).

The recent interest in the therapeutic use of hydrosols appears unlikely to have scientific merit as no antimicrobial activity has been found to be associated with any *Lavandula* hydrosols examined by this group to date (Moon et al. 2004). Hydrosols or distillate waters are a by-product of steam distillation and contain variable amounts of essential oil and other plant derived components. The variation found in the activity of the different oils suggests that different oils should be targeted for different therapeutic uses. Further work is required to determine whether the *in vitro* results are realised in a clinical environment, but it is clear that not all lavenders are equal in terms of their antimicrobial properties.

Antibacterial activity

There was considerable variability in the activity of the essential oils, with *L. angustifolia* and *L. intermedia* oils showing the highest activity against several bacteria. However, no one oil produced the highest level of antibacterial activity against all bacteria tested, suggesting that differences in chemical composition make some oils more effective against particular bacteria. No strong correlation has been observed between percentage of major chemical components and antibacterial activity and *P* aeruginosa was not susceptible to any *Lavandula* oil tested. These results support the anecdotal use of lavender oils as antibacterial agents and demonstrate that some oils which had previously not been investigated have good antibacterial activity. Despite the known antibacterial activity, questions remain about the clinical utility of lavender oil. The MIC (minimum inhibitory concentration) values of lavender oil (*L. angustifolia* and *L. latifolia*) have been reported as being comparable to that of tea tree oil (0.16% against *Haemophilus influenzae*, 0.32% against *S. pyogenes* and *S. aureus* and greater than 0.32% against *E. coli*) (Inouye et al. 2001). These figures would appear to support the use of lavender oils as a prophylactic or for use in topical application for surface infection rather than for use against deep-seated infections.

Antifungal activity

Lavender oil is an effective antifungal agent against fungi of both medical and agricultural importance, especially in inhibition of germ-tube growth (Daferera et al. 2000). It has been demonstrated that all *Lavandula* essential oils examined to date displayed some antifungal activity, with oils derived from *L. angustifolia* and *L. intermedia* demonstrating the greatest effect against *Aspergillus nidulans* and *Trichophyton mentagrophytes*. In contrast, oil derived from *L. stoechas* was particularly effective against the agricultural fungi *Leptosphaeria maculans* and *Sclerotinia sclerotiorum*, demonstrating that *Lavandula* oils have activity against fungi of both medical and agricultural importance, and suggesting that essential oils from various lavender varieties may be useful in the treatment of fungal infections (Moon et al. 2004). Interestingly, the volatile components of *Lavandula* essential oils have also been found to display potent antifungal activity; however, no significant differences in activity have been reported between different *Lauandula* oil volatiles (Moon et al. 2004 and Inouye et al. 2001). Vapour treatment would appear to have an advantage over solution treatment in that the microbial growth could be inhibited by a smaller amount of essential oil, while potentially also acting as a potent inhibitor of sporulation, assuming that suitable vapour concentration and treatment times can be determined. Initial studies suggest that the gaseous contact activity of the essential oils was determined mainly by the maximum vapour concentration at an early stage of incubation and that maintaining high vapour concentra-

tion for long periods of time was not necessary (Inouye et al. 2001). It is to be noted that the effective vapour concentrations in a clinical setting have not yet been directly related to the concentrations used routinely in aromatherapy.

Therapeutic use

The use of essential oil volatiles for therapeutic benefit is not new. Indeed, lavender oil today is used predominantly in aromatherapy or massage. Many benefits are claimed for its use in this way, including relief of the symptoms of stress and depression, in improving 'mood' and relieving anxiety (Cavanagh and Wilkinson 2002). Aromatherapy is thought to be therapeutically effective due to both the psychological effect of the odour and the physiological effects of the inhaled volatile compounds. The latter effects are believed to act via the limbic system, particularly the amygdala and hippocampus. However, although inhalation of lavender oil volatiles has been reported to be capable of altering patient mood and improving sleep patterns, the true therapeutic benefit of inhalation of lavender oil remains controversial (Cavanagh and Wilkinson 2002, Bumett et al. 2004 and Camped et al. 2004). This may be related to the fact that many studies combine both massage and lavender oil and are unable to determine whether the benefits seen are as a result of massage or of lavender oil inhalation/absorption.

Human Studies

Although there is considerable debate about whether lavender species have a significant clinical potential either alone or as additives to other substances, many human studies support its effectiveness in different neurological and psychological disorders. Lavender was used predominantly in oral administration, aromatherapy, or massage in several clinical studies, and many benefits were claimed for use in such a manner. In addition to psychological effects, aromatherapy is thought to be therapeutically effective due to physiological effects of the inhaled volatile compounds. It is believed that inhaled lavender act via the limbic system, particularly the amygdala and hippocampus (Cavanagh and Wilkinson 2002). Linalool and linalyl acetate are rapidly absorbed through the skin after topical application with massage and are thought to be able to cause central nervous system depression (Morris 2002). For example, a recent study investigating the use of lavender oil aromatherapy in dementia patients found no evidence that a purely olfactory form of aromatherapy led to decreased agitation in severely demented patients and suggested that cutaneous application of the essential oil may be necessary to achieve the optimum effect (Snow et al. 2004).

Similarly, although percutaneous administration of one of the main ingredients of lavender oil, (-)-linalool, led to a decrease in systolic blood pressure and skin temperature, compared to a corresponding control group receiving a placebo, no effect on subjective evaluation of well-being was noted (Heuberger et al. 2004).

NEUROLOGICAL EFFECTS OF LAVENDER

Aromatherapy is believed to be therapeutically effective due to both the psychological effect of the odour and the physiological effects of the inhaled volatile compounds. The latter effects are thought to act via the limbic system, particularly the amygdala and hippocampus. The exact cellular mechanism of action is unknown. It has suggested that lavender (*L. angustifolia*) may have a similar action to the benzodiazepines and to enhance the effects of gamma- aminobutyric acid in the amygdala (Tisserand 1988). It is also found that linalool inhibits acetylcholine release and alters ion channel function at the neuromuscular junction (Re et al. 2000). Linalool and linalylacetate are rapidly absorbed through the skin after topical application with massage, reaching peak plasma levels after approximately 19 min (Jager et al. 1992) and are thought to be able to cause central nervous system depression. Linalyl acetate has narcotic actions and linalool acts as a sedative (Tisserand and Balacs, 1999; Re et al. 2000). These calming actions of lavender may be the origin of the traditional use of a lavender herb pillow to help induce sleep. The high camphor content in some lavenders (*L. stoechas*) is believed to precipitate convulsions when used at high concentrations (Tisserand and Balacs 1999).

Lavender oil is used predominantly in aromatherapy or massage. In 1993, mixture of essential oils (basil, juniper, lavender and sweet marjoram) was used in improving sleep in older patients at the General Hospital, Tullamore (Ireland) (Graham 1995). The aim was to reduce sleep disturbance. Following a combination of oil vaporization, with or without a 5 min hand-massage, over a 2 week period there was a significant increase in the number of patients reporting having had a good sleep at nights' and a reduction in those requiring additional night sedation. Dunn et al. (1995) demonstrated anxiety alleviation in patients in the intensive care unit

received at least one session of lavender (1% *L. angustifolia*) aromatherapy treatment. Each patient had a 24 h break between treatments and a number of physical, behavioural and psychological measures were recorded. No significant differences in the indicators of physiological stress (blood pressure, heart rate and rhythm, respiratory rate) or behavioural responses (e.g. motor activity, facial expressions or Glasgow coma rating for unconscious patients) were observed between individuals treated with massage, aromatherapy or rest. There was a significant improvement in the anxiety levels in the aromatherapy group during the first session of treatment. Although there was no statistically significant improvement during the second or third session this appears to be due to an increased effectiveness of the other therapies rather than a loss of effectiveness of the aromatherapy.

Long-stay neurology in-patients, in a pilot study by Walsh and Wilson (1999) also showed increased mood scores and reduced psychological distress following aromatherapy (tea tree, rosemary and *L. Angustifolia* oils). The above studies suggest that lavender aromatherapy can improve patients' experiences in intensive care with no detrimental physical or behavioural outcomes.

Several studies have also shown an association between lavender odour and positive emotional states. Alaoui-Ismaili et al. (1997) found that the odour of lavender oil is rated as a pleasant one and is correlated with changes in the autonomic nervous system. Subsequently Tysoe (2000), while investigating the effects of oil burners and lavender oil on those working in or visiting an extended care ward, found that 88% of respondents thought that lavender oil had a positive effect on the ward and suggest that lavender oil vapour may help combat the unpleasant odours that can sometimes be present in hospitals. Millot and Brand (2001) found that lavender odour increased the pitch of both male and female voices, with greater increases in female voices. Vocal changes can be used to gauge emotion with increases in pitch associated with socio-positive emotions (e.g. happiness and joy). Diego et al. (1998) found that individuals receiving lavender oil (10%) odour for 3 min were significantly more relaxed, had decreased anxiety scores, better moods and showed increased alpha power in their EEGs (an indication of increased drowsiness). Masago et al. (2000) have also found that inhalation of lavender produces EEG patterns characteristic of subjects 'feeling comfortable'.

Diego et al. (1998) also found that lavender oil aromatherapy increased the speed and accuracy of mathematical calculations—perhaps the origin of the sixteenth century belief that lavender skullcaps could enhance intelligence! Study by Degel and Koster (1999) further support these findings. Subjects performed a number of tests in rooms which were only weakly scented with an essential oil. Although the subjects did not identify that the room was scented, those in the lavender-scented rooms had superior performances to those in the jasmine or unscented rooms. In addition, a study in NSW, Australia found that when patients in a dementia day-care facility received a 10 to 15 min hand-massage with a mix of three oils, including lavender, they had a significant improvement in all areas measured. These included the patients' feelings of well-being, increased alertness, decreased aggression and anxiety and improved sleeping patterns (Kilstoff and Chenoweth, 1998).

A crossover study by Lindsay et al. (1997), however, implied that lavender oil used in hand massage did not seem to improve concentration in subjects with profound learning disabilities. This study was, however, limited by small sample size (8 participants), and the lack of a control group. From these data it appears that lavender oil used alone, or in combination with other oils, is of considerable benefit in a number of situations and is safe, effective and easily administered to both conscious and uncon- scious patients. Further it is likely that a room scented with lavender oil will be perceived to be a pleasant environment and this may be particularly beneficial in some health care settings. The only caveat to this statement is that several difficulties arise in the interpretation of these results as often combinations of oils and therapies are used, details of lavender oil species and volumes used are often absent, massage effects are often not separated from those as a result of odour alone and the sample sizes are generally very small. Nevertheless, it does appear that lavender oil, particularly when combined with massage has the potential to be of significant benefit to patients, visitors and workers in many health care settings.

Aromatherapy has also been advocated as useful in the treatment of chronic or intractable pain (Buckle, 1999) with oils high in 1,8-cineole, for example *L. latifolia*, appearing to be particularly good analgesics. Buckle (1999) reports several studies those demonstrate

that aromatherapy, with or without massage, can reduce the perception of pain and the need for conventional analgesics in both adults and children. However, almost all studies cited by this author were small, uncontrolled or lacking in the normal scientific rigour associated with clinical trials. There seems to be, however, considerable anecdotal and case report data for a beneficial effect of lavender in pain. Using a quasi- experimental cross-over study Brownfield (1998) showed that massage with lavender oil (L. angustifolia) reduced the patients' perception of pain and improved the perception of sleep quality and well-being in those suffering the effects of chronic rheumatoid arthritis. It is worth noting that the effects reported in this study are related to the patient's own perception of pain, sleep or well-being as the quantitative data from a visual analogue scale did not reveal any reduction in pain levels or sleep improvement. Ghelardini et al. (1999) have further demonstrated that L. angustifolia oil, as well as linalyl acetate and linalool, possess local anaesthetic activity both in vitro and in vivo. These authors suggest that the mechanism of action is related to antimuscarinic activity and/or ion (Na‡ or Ca2‡) channel blockade.

It is suggested that, as there appears to be a high uptake of aromatherapy as a therapeutic modality by nurses (Trevelyan 1996), settings with extended nursing care, for example palliative care facilities, are more likely to adopt complementary therapies in a bid to ease the discomfort of the patients. Lavender, along with other essential oils, has a role in reducing the side effects such as aches and pains, hair loss and anxiety associated with either the cancer itself or with the effects of chemotherapy (Nelson 1997b). Aromatherapy use in palliative care settings has also been reported to be of benefit to the patients (Kite et al. 1998).

Lavender oil has uses in midwifery where it can be added to bath water to relieve pain and discomfort following labour. In a clinical trial it was shown that the mothers using lavender oil consistently reported lower discomfort scores 3 to 5 days post-natally (Dale and Cornwell 1994; Cornwell and Dale 1995). Lavender oil is also currently used in many delivery rooms for its general calming action. In the past, lavender poultices were applied to the small of the back during labour, to relieve muscle tension, or to the abdomen, to assist placental expulsion. There does not appear to be any scientific evidence for the latter two uses, however, the inhalation of the oil may have an anti-anxiety and relaxing action which is beneficial to the mother.

Mechanism of action of lavender in the nervous system: Several investigations were performed to clarify the mechanism of action of lavender in neuronal tissues. Lavender inhibited lipopolysaccharide-induced inflammatory reaction in human monocyte THP -1 cells effect, which might be associated with the expression of HSP70 (Huang et al. 2012). Antioxidant and relatively weak cholinergic inhibition was reported for lavender (Wang et al. 2012 and Salah and Jäger 2005) and linalool (Perry et al. 2000 and Perry et al. 2003). Linalool inhibited acetylcholine release and alters ion channel function at the neuromuscular junction (Savelev et al. 2003). These findings indicate that several targets relevant to treatment of Alzheimer's disease; anticholinergic, neuroprotective and antioxidant activities could be found in lavender. The neuroprotective effect of lavender oil against cerebral ischemia/reperfusion injury is suggested to be attributed to its antioxidant effects (Wang et al. 2012). Intraperitoneal application of lavender significantly increased rotarod activity and enhanced dopamine receptors subtype $_{D3}$ in the olfactory bulbs of mice (Re et al. 2000). Lavender oil is also suggested to modulate GABAergic neurotransmission, especially on GAB_{AA} receptors and enhance inhibitory tone of the nervous system (Kashani et al. 2011; Sousa de et al. 2010 and Kim et al. 2009). Cholinergic system is suggested to play a role in lavender analgesic, antianxiety, antidepression, and anticonvulsant effects of lavender (Umezu 2000; Barocelli et al. 2004 and Yamada et al. 1994). Fos is a nuclear transcription factor protein encoded by an immediate early gene c-fos, and it is an early marker of neuronal activation. It serves as a transcriptional factor controlling the expression of genes expected to be involved in effective adaptation to certain situations. Lavender oil reduced c-fos expression in paraventricular nucleus of the hypothalamus and dorsomedial hypothalamic nucleus (Shaw et al. 2007).

Lavender oil inhibited dose-dependently the histamine release and anti-DNP IgE-induced tumor necrosis factor -alpha secretion from peritoneal mast cells in mice (Aoshima and Hamamoto 1999). It has been shown that lavender oil inhibited the sympathetic nerves innervating the white and brown adipose tissues and adrenal gland and excites the parasympathetic gastric nerve (Shen et al. 2005 and Tanida et al. 2007). Odour of lavender oil and especially its component linalool, affects autonomic nerves probably through a histaminergic

response, decreases lipolysis and heat production (energy consumption), and increases appetite and body weight in rats (Tanida et al. 2007). Lavender may inhibit the sympathetic nerve activity and lipolysis through activation of H_3-receptors. The hypothalamic suprachiasmatic nucleus and histamine neurons are involved in the lipolytic responses to the lavender oil, and tyrosine phosphorylation of BIT (a brain immunoglobulin-like molecule with tyrosine-based activation motifs, a member of the signal-regulator protein family) is implicated in the relevant signalling pathways (Tanida et al. 2007).

Conclusion

A recent increase in the popularity of alternative medicine and natural products has renewed interest in lavender and their essential oils as potential natural remedies (Woronuk et al. 2011). This review may be useful to increase our knowledge of lavender pharmacological effects and improve our future experimental and clinical research plans. Although some studies defined the contents of lavender, it is essential that all future clinical studies specify the exact derivation of the oils used in the study and, preferably, include a profile of the liquid or the percentage composition of the major constituents (Woronuk et al. 2011). Despite this lack of evidence for many claims, lavender continues to be used by the general public and clinical staff, perhaps because any potential therapeutic benefit is seen as a possible 'bonus' to the simple love of lavender.

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