A literature review of the medicinal properties of lemonbalm

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Introduction

This literature review aims to evaluate literature and research surrounding *Melissa officinalis* and its traditional and modern therapeutic uses, pharmacology and methods of preparation. The pharmacology, traditional and modern uses will be considered for each therapeutic action and current research will be critically reviewed to evaluate *Melissa’s* clinical potential.

*Melissa officinalis* L.

*Melissa officinalis*, otherwise known as lemon balm or balm, is a small perennial herb with a distinctive lemon smell and small white flowers (Mills, 1993). It is native to much of Europe and has been used traditionally since the time of the ancient Greeks where Dioscorides describes it used for dog bites and gout in the first century AD (Grieve, 1980). Traditionally it has been used in patients with fever, to apply to wounds, to treat melancholy and as an emmenagogue (Culpeper, 1977) (Gerard, 1994) (King and Fletcher, 1898).

Phytochemical Profile

*Melissa* contains essential oil which makes up between 0.02% and 0.3% of the dry weight and contains mostly citronellal and citral (Carnat *et al*, 1998). *Melissa* also contains polyphenolic compounds including caffeic acid and rosmarinic acid, several monoterpene glycosides and flavonoids (Carnat *et al*, 1998). The pharmacological properties of these chemicals will be considered in context alongside their therapeutic use.

Therapeutic Uses

Psychoneurological uses

*Melissa* has been used traditionally for many psychoneurological complaints and is

There is significant modern research in this field and a double blind, randomised controlled trial (RCT) showed that the group treated with *Melissa* had a very significant reduction of scores in both the Alzheimer’s disease assessment scale and the clinical dementia rating scale (Akhondzadeh *et al*, 2003). In this trial the control group showed an increase in scores, indicating that their condition had deteriorated while the treatment group’s condition had improved. Akhondzadeh *et al* (2003) suggest that Melissa is efficacious in managing mild to moderate Alzheimer’s and should be subject to further study. The conclusions drawn seem accurate since although the study only had 36 participants, the results were very statistically significant. The effect observed in this study is likely to be due to *Melissa’s* acetylcholine receptor agonist activity which has been shown *in vitro* (Wake *et al*, 2000). Furthermore, agitation was significantly statistically less common as a side effect in the *Melissa* group than placebo in Akhondzadeh *et al’s* (2003) study, supporting Bartram’s (1998) traditional indication for restlessness. A study by Lopez *et al* (2009) has shown that *Melissa* has a neuroprotective effect *in vitro* due to its protective antioxidant effect. This may explain why *Melissa* is effective in the treatment of Alzheimer’s as oxidative stress is a contributing factor to the progression of Alzheimer’s (Markesbery, 1997).

A double blind balanced crossover RCT by Kennedy *et al* (2002) investigated the effect of *Melissa* extract on cognitive performance and mood using a computerised test to take readings at intervals from 0-6 hours after administration of the *Melissa* extract. In this study there were 15 female and 5 male undergraduate participants between the ages of 18-22 with a mean age of 19.2 years. This is a very small sample size all with the same occupation, of a similar age and with an unbalanced proportion of female to male participants, which does not represent the general population accurately. The study reported an increase in the ‘accuracy of attention’ field at the middle dose (600mg), decreased memory performance at all doses, lower self-rated feelings
of alertness at a high dose (900mg) and calmness increased slightly at both high and low doses (Kennedy et al, 2002). Effects in this study were measured after acute administration, therefore the implications of this study on therapeutics, were Melissa is usually taken continuously, are unclear. These results do not support the role of Melissa in treating Alzheimer’s as memory performance was decreased, however it is notable that levels of nicotinic and muscarinic receptor binding were low in the Melissa batch tested, they attribute this to the lack of volatile oil content that was noticed in the batch used (Kennedy et al, 2002).

In a double blind cross over RCT a standardised extract of Melissa was shown to reduce induced stress at a doses of 600mg and increase self-rated feelings of calmness and alertness (Kennedy et al, 2004). At a dose of 300mg only slight differences were noticed in parameters, most of which were not statistically significant. This study had a sample size of 18 participants with each participant receiving 300mg and 600mg of extract and a placebo on separate days each set 7 days apart. The stress stimulator which was used was a computer running four simultaneous tasks which has shown to increase feelings and signs of stress. The computer task was automated removing experimenter bias and also used randomised stimuli in order to ensure that the test is effective when repeated on the same participant. This is a strong study design with the exception of the small sample size and the measurement of stress which was not in measurable biomarkers, but was measured by using self-rated scores of calmness, contentedness and alertness, which may not accurately reflect stress. This study supports Melissa’s traditional use as an anxiolytic, although how efficacy is unclear as the parameters used have weak clinical significance.

A study conducted by Cern and Schmid (1998) suggests that a combination of Melissa and Valariana is effective at improving quality of sleep in a double blind, parallel group RCT with 98 participants (Cerny and Schmid, 1998). It cannot however conclusively be said that Melissa improves quality of sleep as the study was conducted with Valariana which has been shown to be effective on its own and could have been responsible for the positive results seen (Bent et al, 2006).

Lastly, a study by Guginski et al (2009) demonstrated that systemic administration of an alcoholic Melissa extract reduced neurogenic and inflammatory pain in mice significantly and in a dose dependant manner. The results also suggest that the antinociception effect of Melissa is due, at least partly, to its effect on nicotinic and muscarinic acetylcholine receptors (Guginski et al, 2009). The observed reduction in inflammato-
Gastrointestinal pain could be in part attributed to rosmarinic acid which has been found to inhibit complement activated inflammation (Peake et al, 1991).

These studies mostly support the traditional and modern indications for Melissa with the exception of its anti-depressive effect which remains un-investigated. Regarding its effect on Alzheimer’s and memory, it is likely that Melissa is an effective agent in treating Alzheimer’s due to its acetylcholine receptor agonist activity and although these results were not supported by Kennedy et al’s (2002) experiment it is very plausible that this was because of the low acetylcholine receptor binding properties of the Melissa extract used. A study on memory and Alzheimer’s using an extract with a higher essential oil content and proven receptor binding properties would clarify this conclusion.

**GIT**

Melissa has been used traditionally for GIT disorders and was used by Culpeper (1977) to promote digestion and for griping pains of the belly. The German commission E monograph indicates Melissa in functional gastrointestinal complaints (American Botanical Council, 1998). Hoffmann (2003) is more specific about the indications for Melissa and indicates it for spasm in the digestive tract and flatulent dyspepsia. Grieve (1980) also attributes it with carminative properties.

Both Melissa essential oil and citral (a component of the essential oil) have been shown to have an antispasmodic effect on ileum muscle in a study on rats (Sadraei et al, 2003). This spasmyloytic action could also be due to a flavonoid in Melissa called apigenin which has a phosphodiesterase inhibitory action (Savino et al, 2005).

Colic is thought to be due to GIT disturbances and unknown causes disturbing the temperament of child and it is the antispasmodic, anti-inflammatory, anxiolytic and sedative actions in Melissa that may have a role to play in treating colic. A double blind RCT showed that a standardised extract of Melissa officinalis, Matricariae recutita and Foeniculum vulgare reduced crying time by 85.4% in infants over one week compared to a 48.9% reduction in the control group (Savino et al, 2005). The fact that a combination of plants is used means that it is unclear whether the reduction of crying time can be attributed to Melissa. Crying time was measured in this study by the parents, possibly introducing inaccuracies. However the results are sufficiently statistically significant to suggest that this combination of herbs is effective despite any minor inaccuracies perhaps present in the study.
These studies suggest that *Melissa* may be beneficial in digestive complaints particularly where there is a spasmodic or functional element. Furthermore it’s antibacterial (Mimica-Dukic *et al*, 2004) and anti-inflammatory (Peake *et al*, 1991) properties may increase its therapeutic effect, especially in gastritis and peptic ulcers where there are usually bacterial and inflammatory elements. There is not extensive research into these uses and its antispasmodic effect is only supported by studies on rats or infants with colic, in which spasm are only partially implicated.

**Antioxidant**

*Melissa* essential oil has been shown to have antioxidant properties that increase with dose and it is the mono and sesquiterpenes components that have the strongest antioxidant properties (Mimica-Dukic *et al*, 2004) (Dastmalchi *et al*, 2008). Also *Melissa* contains caffeic acid and flavonoids which have antioxidant properties (Pietta, 2000). A study on mice has shown rosmarinic acid, contained in *Melissa*, to protect the liver from damage with its antioxidant action (Osakabe *et al*, 2002). These studies indicate that *Melissa* has a strong antioxidant property. This may give it therapeutic potential in treating Alzheimer’s (Lopez *et al*, 2009) and protecting the liver, although research into its liver protective qualities has so far only been in mice and the same effect may not be applicable to humans.

**Antiviral and Immunity**

*Melissa* has been shown *in vitro* to have an antiviral effect against many different viruses and both the polyphenolic and tannin portions have been found to possess an antiviral action (Herrmann and Kucera, 1967a) (Herrmann and Kucera, 1967b). A double blind RCT with 66 participants showed an extract of the hydrophilic portion of *Melissa* to be somewhat effective at treating herpes simplex labialis (Koytchev *et al*, 1999). The study monitored the progression of the size and symptoms of the herpes lesions every day for five days and patient compliance was monitored. The outcomes measured showed that *Melissa* cream reduced symptoms significantly by day 2, however over the whole 5 days, although there was a trend for the *Melissa* cream to be more effective, a statistically significant result was not shown (Koytchev *et al*, 1999). Koytchev *et als* (1999) study still suggests that the *Melissa* cream is effective as it was the results measured on day 2 that were the primary target parameter of the study as herpes simplex is increasingly likely to spontaneously heal over time. A double blind RCT with 116 participants by Wölbling and Leonhardt (1994) showed
highly statistically significant results treating herpes simplex after two days using a cream made from an extract of dried leaves. The results also indicated that treatment was most effective when the interval between the onset of the condition and treatment was smallest (Wölbling and Leonhardt, 1994). A study on monkey kidney cells in vitro has shown Melissa essential oil to have a direct antiviral effect on HSV1 and HSV2 viruses before cell adsorption, suggesting that it interferes with either viral proteins involved in penetrating the host cell or it directly damages the virus itself (Schnitzler et al, 2008).

Aqueous extracts from Melissa have been shown to increase aspects of cellular immunity in mice in a study by Drozd and Anuszewska (2003). In Drozd and Anuszewskas (2003) paper the conclusions drawn are not phrased correctly and some of the meaning and coherence of the paper appears to have been lost in translation. Also, how these results may relate to the immune stimulating properties of Melissa in humans is unclear as the study was conducted in mice.

Koytchev et als (1999) and Wölbling and Leonhardt’s (1994) trials strongly suggests that Melissa is effective at treating herpes topically if applied early enough. There is not enough research to support any other therapeutic use in this area. However research does suggest Melissa stimulates the immune system and has an antiviral effect, which does support Melissa’s traditional use in fevers (Culpeper, 1977) (Gerard, 1994) (King and Fletcher, 1898).

**Endocrine effects**

There is some research to indicate Melissa may be useful in treating hyperthyroidism and Graves’ disease. Firstly, a freeze dried extract of Melissa has shown to inhibit bovine TSH from binding to human thyroid plasma membranes in vitro (Auf’molk et al, 1984). Auf’molk et al (1985) have shown Melissa inhibits the binding of Graves’ disease immunoglobulins to the thyroid in a dose dependent manner. These studies suggest that Melissa is potentially useful in treating Graves’ disease and hyperthyroidism. Conducting clinical trials in vivo may clarify whether Melissa is effective and has sufficient bioavailability in humans. Melissa has been used therapeutically for indications such as insomnia, anxiety, depression and palpitations all of which can be symptoms of hyperthyroidism (Porter et al, 2006). Furthermore some research suggests that anxiety and depression are reported more frequently as a result of symptoms produced by hyperthyroidism (Kathol and Delahunt, 1986) and so per-
haps this is one of the mechanisms by which *Melissa* displays anxiolytic and anti-depressive actions.

**Methods of preparation**

*Melissa* is normally taken at a dose of 2 to 6ml of tincture three times a day (1:5 in 40%) or 1.5g to 4.5g of dried herb in infusion three times a day (Hoffmann, 2003) (American Botanical Council, 1998). Preparations vary in their phytochemical content and considerable variation in nicotinic and muscarinic activity between various samples of *Melissa* have been observed in studies (Wake *et al*, 2000) (Kennedy *et al*, 2002). This variation is likely to be a combination of factors including natural variation between plants, growing conditions and harvesting and preparation technique.

A study on harvesting patterns on the essential oil content of *Melissa* has shown the most effective methods of preserving essential oil content are to harvest before or after flowering in the morning or evening and to dry the plant in the shade (Ayanoglu *et al*, 2005). This study supports traditional harvesting patterns, which is to harvest *Melissa* before flowering (King and Fletcher, 1898).

Studies have shown that the essential oil accounts for many of Melissa’s therapeutic attributes (Mimica-Dukic *et al*, 2004) (Sadraei *et al*, 2003) and a study has shown low essential oil content may reduce its nicotinic and muscarinic activity (Kennedy *et al*, 2002). It is therefore important that correct harvesting and preparation techniques are used to maximise essential oil content. Carnat *et al* (1998) showed that tea only extracted 31% of essential oil content. Alcohol may be a more effective solvent as it avoids high temperatures which result in the loss of volatile oils. To maximise essential oil content further, fresh plant tincture could be used to stop essential oil lost in the drying process. Brewing *Melissa* infusion in a closed or covered container may also decrease loss of volatile oils and hence increase efficacy (Mills, 1993).

**Safety**

*Melissa* is recognised as safe and side effects are very rare and generally mild when they do occur (Ulbricht and Seamon, 2010). Care should be taken when combining *Melissa* with other sedatives as it may cause tiredness (Gyllenhaal *et al*, 2000). Also since *Melissa* may inhibit TSH binding, it should be used with caution in patients with hypothyroidism (Auf’molk *et al*, 1984).

**Evaluation**
Melissa officinalis is a generally safe herb and could be effective in treating Alzheimer’s, herpes, Graves’ disease, hyperthyroidism, colic, insomnia and functional dyspepsia. It has demonstrated muscarinic and nicotinic receptor agonist, anti-inflammatory, antioxidant, TSH inhibiting, antiviral, antimicrobial, antispasmodic and anxiolytic actions. Current research supports many of the traditional uses for this plant and is also finding new therapeutic uses. However, there is no current research into Melissa as an antidepressant, emmenagogue or febrifuge. Research in this area would be particularly enlightening as these are the actions consistently mentioned in traditional sources.

References


http://www.earthmedicines.co.uk/articles/lemonbalm-literature-review/
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