Melissa

Species (Family)

Melissa officinalis L. (Labiatae)

Synonym(s)

Balm, Honeyplant, Lemon Balm, Sweet Balm

Part(s) Used

Dried leaves and flowering tops

Pharmacopoeial and Other Monographs

BHP 1996[G9]
BP 2001[G15]
Complete German Commission E (Lemon Balm)[G3]
ESCOP 1996[G52]
Martindale 32nd edition (Lemon Balm)[G43]
Mills and Bone (Lemon Balm)[G50]
PDR for Herbal Medicines 2nd edition[G36]
Ph Eur 2002[G28]

Legal Category (Licensed Products)

GSL[G37]

Constituents[G2,G52,G64]

Volatile oil 0.06–0.375% v/m (volume in mass).[1,G52] Contains at least 70 components,[G2] including: *Monoterpenes* >60%. Mainly aldehydes, including citronellal, geranial, neral; also citronellol, geraniol, nerol, β-ocimene.[2,3] *Sesquiterpenes* >35%. β-Caryophyllene, germacrene D.

Flavonoids 0.5%. Including glycosides of luteolin (e.g. luteolin 3′-*O*-β-D-glucuronide[4]), quercetin, apigenin and kaempferol.

Polyphenols Protocatechuic acid, hydroxycinnamic acid derivatives,[2] caffeic acid, chlorogenic acid, rosmarinic acid,[2] 2-(3′,4′-dihydroxyphenyl)-1,3-benzodioxole-5-aldehyde.[5]

Food Use

Lemon balm is used to give fragrance to wine, tea and beer. Lemon balm (herb, flowers, flower tips) is listed by the Council of Europe as a natural source of food flavouring (category N2). This category indicates that lemon balm can be added to foodstuffs in small quantities, with a possible limitation of an active principle (as yet unspecified) in the final product.[G16] In the USA, lemon balm is listed as GRAS (Generally Recognised As Safe).[G65]

Herbal Use

Lemon balm has been used traditionally for its sedative, spasmolytic and antibacterial properties.[G54] It is also stated to be a carminative, diaphoretic and a febrifuge,[G64] and has been used for headaches, gastrointestinal disorders, nervousness and rheumatism.[5] Current interest is focused on its use as a sedative, and topically in herpes simplex labialis as a result of infection with herpes simplex virus type 1 (HSV-1). The German Commission E monographs state that lemon balm can be used for nervous sleeping disorders and functional gastrointestinal complaints.[G4]

Dosage

Dried herb 1.5–4.5 g as an infusion in 150 mL water several times daily.[G4]

Topical application Cream containing 1% of a lyophilised aqueous extract of dried leaves of *Melissa officinalis* (70 : 1) two to four times daily.[G52]

Pharmacological Actions

In vitro and animal studies

Antiviral activity Aqueous extracts of *Melissa officinalis* have been reported to inhibit the development of several viruses.[6–8,G52] The virucidal effect of several aqueous extracts of *M. officinalis* against HSV-1 has been demonstrated in a rabbit kidney cell line.[9] However, the extracts appeared to have no activity against experimental HSV-1 infection in the eyes of rabbits.[9]

Anti-human immunodeficiency virus type 1 (HIV-1) activity has been reported for an aqueous extract of *M. officinalis* in *in vitro* studies using MT-4 cells; the ED_{50} (50% effective dose for inhibition of HIV-1-induced cytopathogenicity) was found to be 16 μg/mL.[10] Furthermore, the aqueous extract demon-

strated potent inhibitory activity ($ED_{50} = 62\ \mu g/mL$) against HIV-1 replication (KK-1 strain, freshly isolated from a patient with acquired immune deficiency syndrome (AIDS). In other *in vitro* studies, an aqueous extract of *M. officinalis* inhibited giant cell formation in co-cultures of MOLT-4 cells with and without HIV-1 infection, and showed inhibitory activity against HIV-1 reverse transcriptase ($ED_{50} = 1.6\ \mu g/mL$).[10]

Aqueous extracts of *M. officinalis* have been reported to inhibit protein biosynthesis in a cell-free system from rat liver cells, and it has been suggested that this effect may be due to caffeic acid and a component isolated from the glycoside fraction of the extract.[11] The latter component appears to block the binding of the elongation factor EF-2 to ribosomes, thus terminating peptide elongation.[11]

Antimicrobial activity Antimicrobial activity of essential oil extracted from *M. officinalis* by steam distillation, determined using a micro-atmospheric technique, has been reported against the yeasts *Candida albicans* and *Saccharomyces cerevisiae*, and against *Pseudomonas putida*, *Staphylococcus aureus*, *Micrococcus luteus*, *Mycobacterium smegmatis*, *Proteus vulgaris*, *Shigella sonnei* and *Escherichia coli*.[12]

Other activity In studies in mice, a hydroalcoholic extract of *M. officinalis* leaves administered intraperitoneally significantly reduced behavioural activity in two tests, compared with control, suggesting that the extract has sedative effects.[13] In both tests, the effect was maximum at 25 mg/kg. The same extract demonstrated peripheral analgesic activity by reducing acetic acid-induced writhing and stretching in mice when administered intraperitoneally at doses of 25–1600 mg/kg 30 minutes after intraperitoneal administration of 1.2% acetic acid solution.[13] However, no analgesic effects were observed on heat-induced pain (hotplate test) which suggests a lack of central analgesic activity. In other tests, low doses (3 and 6 mg/kg) of a hydroalcoholic extract of *M. officinalis* leaves administered intraperitoneally induced sleep in mice given an infrahypnotic dose of pentobarbital.[13] By contrast, in the same battery of tests, essential oil obtained from *M. officinalis* by distillation did not demonstrate sedative or sleep-inducing effects.[13]

A 30% alcoholic extract of *M. officinalis* demonstrated an antispasmodic effect on rat duodenum *in vitro*.[14]

Aqueous methanolic extracts of the aerial parts of *M. officinalis* demonstrated inhibition of lipid peroxidation *in vitro* in both enzyme-dependent and enzyme-independent systems.[15] The same tests carried out on the main known phenolic components of *M. officinalis* revealed that rosmarinic acid, caffeic acid, luteolin and luteolin-7-O-glucoside were more potent inhibitors of enzyme-dependent lipid peroxidation than enzyme-independent lipid peroxidation.

Clinical studies

Antiviral effects The effects of a topical preparation of a standardised aqueous extract of *M. officinalis* leaves (drug/extract 70 : 1) have been investigated in herpes simplex virus (HSV) infection. In an open, multicentre study, 115 patients with HSV infection of the skin or transitional mucosa applied lemon balm leaf extract five times daily for a maximum of 14 days; complete healing of lesions was achieved after eight days of treatment in 96% of participants.[16,17] Subsequently, a randomised, double-blind, placebo-controlled trial involving 116 patients with HSV infection of the skin or transitional mucosa reported statistically significant differences between the treatment (applied locally two to four times daily over 5–10 days) and placebo groups for some (including redness, physician's assessment, patient's assessment), but not all, outcome measures (e.g. extent of scabbing, vesication, pain).[17] Another randomised, double-blind trial involved 66 patients with an acute episode of recurrent (at least four episodes per year) herpes simplex labialis compared verum cream (applied on the affected area four times daily over five days) with placebo.[18] There was a significant difference in the primary outcome measure – symptom score after two days' treatment – between the two groups ($p = 0.042$). However, further investigation is required to determine if time to recurrence is prolonged.

Sedative effects The acute sedative effects of several plant extracts, including a preparation of *M. officinalis* leaves, were explored in a randomised, double-blind, placebo-controlled, crossover study involving 12 healthy volunteers.[19] *M. officinalis* extract 1200 mg was administered orally as a single dose about 2 hours before administration of caffeine 100 mg. Melissa extract was one of the extracts tested that showed least effects on increasing tiredness (i.e. it was no different than placebo) as measured using a visual analogue scale score for alertness.

Several other studies have investigated the sedative effects of combination preparations containing extracts of lemon balm and valerian (*Valeriana officinalis*). A randomised, double-blind trial involving healthy volunteers who received Songha Night (*V. officinalis* root extract 120 mg and *M. officinalis*

leaf extract 80 mg) three tablets daily taken as one dose 30 minutes before bedtime for 30 days ($n = 66$), or placebo ($n = 32$), found that the proportion of participants reporting an improvement in sleep quality was significantly greater for the treatment group, compared with the placebo group (33.3% versus 9.4%, respectively; $p = 0.04$).[20] However, analysis of visual analogue scale scores revealed only a slight but statistically non-significant improvement in sleep quality in both groups over the treatment period. Another double-blind, placebo-controlled trial involving patients with insomnia who received Euvegal forte (valerian extract 160 mg and lemon balm extract 80 mg) two tablets daily for 2 weeks reported significant improvements in sleep quality in recipients of the herbal preparation, compared with placebo recipients.[21] A placebo-controlled study involving 'poor sleepers' who received Euvegal forte reported significant improvements in sleep efficiency and in sleep stages 3 and 4 in the treatment group, compared with placebo recipients.[22]

Other studies have investigated the sedative effects of combination preparations of extracts of lemon balm, valerian and hops (*Humulus lupulus*). In an open, uncontrolled, multicentre study, 225 individuals who were experiencing nervous agitation and/or difficulties falling asleep and achieving uninterrupted sleep were treated for two weeks with a combination preparation containing extracts of valerian root, hop grains and lemon balm leaves.[23] Significant improvements in the severity and frequency of symptoms were reported, compared with the pretreatment period. Difficulties falling asleep, difficulties sleeping through the night, and nervous agitation were improved in 89%, 80% and 82% of participants, respectively.

Side-effects, Toxicity

Small-scale, short-term (two weeks' duration) studies investigating the sedative effects of oral combination preparations containing lemon balm extract indicate that these preparations are well-tolerated and do not appear to induce a 'hangover effect'. In an open, uncontrolled, multicentre study, 225 individuals who were experiencing nervous agitation and/or difficulties falling asleep and achieving uninterrupted sleep were treated for two weeks with a combination preparation containing extracts of valerian root, hop grains and lemon balm leaves.[23] The tolerability of the preparation was rated as 'good' or 'very good' by 97% of physicians and 96% of patients. In a randomised, double-blind, placebo-controlled trial involving healthy volunteers who received Songha Night (*V. officinalis* root 120 mg and *M. officinalis* leaf extract 80 mg) three tablets daily for 30 days ($n = 66$), or placebo ($n = 32$), the proportion of volunteers reporting adverse events was similar in both groups (around 28%).[20] Sleep disturbances and tiredness were the most common adverse events reported during the study. (N.B. the study was designed to assess the effects of the preparation on sleep quality.) No severe adverse events were reported. A randomised, double-blind, placebo-controlled study involving 48 adults assessed the adverse effects of 2 weeks' treatment with a combination preparation (valerian root extract 95 mg, hops extract 15 mg and lemon balm leaf extract 85 mg) taken alone or with alcohol.[24] Compared with placebo, the herbal combination preparation did not have adverse effects on performance (e.g. concentration, vigilance). Furthermore, co-administration of the combination preparation with alcohol did not have potentiating effects on performance parameters.[24] No serious adverse events were observed during the study.

A randomised, double-blind, placebo-controlled trial of a topical preparation containing 1% dried extract of *M. officinalis* leaves (drug/extract 70 : 1) involving 116 patients with HSV infection of the skin or transitional mucosa reported that there were no statistically significant differences between the treatment and placebo groups with regard to the frequency of adverse effects.[17] Adverse events reported were minor (irritation, burning sensation); there were no reports of allergic contact reactions. However, skin sensitisation may occur with melissa.[G58]

Contra-indications, Warnings

None documented.

Pregnancy and lactation In view of the lack of toxicity data, oral administration of lemon balm during pregnancy and lactation should be avoided. Topical use of lemon balm during pregnancy and lactation is unlikely to be problematic.

Pharmaceutical Comment

Randomised clinical trials have suggested that topical lemon balm extract may have some effects on healing cutaneous lesions resulting from HSV-1 virus infection,[17,18] although further rigorous studies are required to determine whether there is any effect on recurrence of infection.

In the German Commission E monograph, lemon balm is indicated for nervous disturbance of sleep and functional gastrointestinal complaints.[G4] While there is some evidence from randomised controlled

trials of combination preparations containing lemon balm leaf extract to support the efficacy of such products in individuals with minor sleep disorders, there has been little investigation of the effects of lemon balm extract alone on sleep quality. Further studies are required to determine the effects of preparations of lemon balm leaf extract in individuals with sleep disorders. Supporting evidence for the use of lemon balm for gastrointestinal complaints is limited to *in vitro* work and requires clinical investigation.

Small-scale, short-term studies indicate that oral combination preparations containing lemon balm extract and topical preparations of lemon balm extract are well tolerated.[17,20] However, there is a lack of research investigating the safety of long-term administration of lemon balm.

References

See also General References G2, G4, G9, G15, G16, G28, G36, G43, G50, G52, G54, G58 and G64.

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