The therapeutic properties of Lemon balm (Melissa officinalis L.): Reviewing novel findings and medical indications

Article *in* Journal of Applied Botany and Food Quality · November 2019

DOI: 10.5073/JABFQ.2019.092.044

CITATIONS
24

READS
3,640

3 authors, including:

Katarzyna Świąder
Warsaw University of Life Sciences - SGGW
30 PUBLICATIONS **192** CITATIONS

SEE PROFILE

Christofora Hanny Wijaya
Bogor Agricultural University
108 PUBLICATIONS **1,616** CITATIONS

SEE PROFILE

Journal of Applied Botany and Food Quality 92, 327 - 335 (2019), DOI:10.5073/JABFQ.2019.092.044

[1]Institute of Human Nutrition Sciences, Warsaw University of Life Sciences-SGGW, Warsaw, Poland
[2]Department of Food Science and Technology, Bogor Agricultural University, IPB, Bogor, Indonesia

The therapeutic properties of Lemon balm (*Melissa officinalis* L.): Reviewing novel findings and medical indications

Katarzyna Świąder[1*], Katarzyna Startek, Christofora Hanny Wijaya[2]

(Submitted: September 11, 2019; Accepted: October 17, 2019)

Summary

Melissa officinalis, a perennial plant in the family *Lamiacae*, known as lemon balm, is a popular herb with multiple therapeutic properties. Significant content of active compounds (including rosmarinic acid) is reported to be responsible for the broad health effects of lemon balm. *Melissa officinalis* has antioxidant, anti-inflammatory, antimicrobial and antidepressant activities. It can be used in the treatment of sleep disorders, neurodegenerative diseases and obesity as well as in ophthalmology, gynaecology, oncology, gastroenterology and cardiology. This review includes literature on the chemical composition of *Melissa officinalis* and the possibilities of its use in medicine as well as functional food. Furthermore, the side effects and the contraindications to the usage of this herb were summarized.

Keywords: Lemon balm, *Melissa officinalis L.,* therapeutic, herb, health usage

Introduction

Melissa officinalis L. (Fig. 1) is a perennial plant in the family *Lamiacae*. It occurs naturally in the Mediterranean and West Asia. Moreover, it is cultivated widely in Europe and North America. *Melissa* is known for its characteristic lemon taste and aroma (Moradkhani et al., 2010). This herb is also known under other names as lemon balm, balm, common balm or balm mint. Notes about lemon balm come from the antiquity when it was described by among others -Hippocrates and Dioskurides. In the Middle Ages, Avicenna (980-1037) recommended it to strengthen the heart, and Paracelsus (1493-1541) prepared "the elixirs of life" containing the lemon balm. *Melissa officinalis* has been traditionally known for being able to restore youth, support weakened people and prevent baldness. In herbal medicine, leaf, herb and essential oil of lemon balm are used (Senderski, 2009). *Melissa officinalis* due to its numerous health-promoting properties, apart from medical use, is also increasingly used as an ingredient in supplements and functional foods. A compilation of the latest data on the therapeutic properties of lemon balm will facilitate its application also in food products.

The chemical composition

Fresh herbs contain phenolic compounds, L-ascorbic acid, carotenoids, flavonoids and terpenoids. Lemon balm leaves are rich in flavonoids (0.5 % dry weight) consist of quercitrin (a derivative of quercetin), ramnocitrin, luteolin and its derivatives (luteolin 7-*O*-*β*-D-glucuronopyranoside, luteolin 3'-*O*-*β*-D-glucuronopyranoside, apigenin 7-*O*-*β*-D-glucopyranoside, and luteolin 7-*O*-*β*-D-glucopyranoside-3'-*O*-*β*-D-glucuronopyranoside). The major components among terpenoids are neral. geranyl acetate, ursolic acid and tannins (Moradkhani et al., 2010; Miraj et al., 2017). 0.087 g/100 g of caffeic acid and 21.15 g/100 g of rosmarinic acid were detected in the hydroethanolic extract of lemon balm leaves and phenolic compounds constituted 33.97% (Ożarowski et al., 2016).

Fig. 1: *Melissa officinalis* L. https://commons.wikimedia.org/wiki/Melissa_officinalis#/media/File:Melissa_officinalis_001.JPG

The lemon balm essential oil, secreted by glandular trichomes, has a pale-yellow colour with lemony aroma (Moradkhani et al., 2010). Depending on the study, the amount of essential oil strongly varied, i.e. 0.02-0.30% of the plant weight (Moradkhani et al., 2010), 0.1% of herb (Sadraei et al., 2003), 0.34% of dry leaf mass (Abdellatif et al., 2014) or 0.01-0.35% (Kittler et al., 2018). The main components of lemon balm essential oil are listed in Tab. 1.

The therapeutic properties

On the basis of the literature review, the results indicating the health-promoting properties of lemon balm were collected. Individual studies were conducted *in vitro* and *in vivo*, including human studies (Tab. 2).

Antioxidant properties – mostly the therapeutic properties of lemon balm based on antioxidant activities

Due to the high content of flavonoids, *Melissa officinalis* has antioxidant properties. *In vitro* studies confirmed that 100-500 µg/ml of hydroethanolic extract from the herb had a cytoprotective activity against the toxic effects of hydrogen peroxide on human umbilical vein endothelial cells. The extract also reduced amount of hydrogen peroxide in intra- and extracellular fluids. This may be important in the prevention of cardiovascular diseases (Safaeian et al., 2016). Antioxidative activity was examined by three methods: the ABTS radical cation (ABTS·+), the DPPH free radical (DPPH) and the ferric reducing antioxidant power (FRAP). The activity of herb lemon

* Corresponding author

Tab. 1: The content of the main components of lemon balm essential oil (%) based on the results of various researches.

Components	Sadraei et al., 2003	Abdellatif et al., 2014	Meftahizade et al., 2010	Miraj et al., 2017	Kittler et al., 2018
(*Z*)-citral (neral)	24.5	30.2	43.8	-	0.8-45.7
(*E*)-citral (geranial)	35.3	44.2	5.2	-	0.5-34.3
citronellal	12.9	6.3	0.01	14.4	1.3-60
β-caryophyllene	4.9	1.3	13.5	8.1	1.2-18.6
β-caryophyllene oxide	2.7	1.3	0.3	11.0	0.4-54.1
linalool	0.9	0.3	-	-	-
citronellol	6.2		-	-	-
geraniol	0.7	0.6	5.3	-	-
isogeraniol	-	-	-	6.4	-
nerol acetate	-	-	-	5.1	-
geraniol acetate	7.1	-	2.3	10.2	-
germacrene D	-	-	-	-	0-13.6

balm was comparable to respectively 10.6, 36.1 and 61.8 µM trolox/100 g dry matter – trolox is a water-soluble derivative of vitamin E. Such antioxidant activity of lemon balm is average in comparison to other herbs that were analyzed (Wojdyło et al., 2007).
The antioxidant properties were also confirmed in the study involving radiology staff exposed to long-term low-dose ionizing radiation. They consumed lemon balm infusion (1.5 g dried leaves) twice a day for a period of 30 days. There was a significant improvement in the activity of catalase, superoxide dismutase and glutathione peroxidase in plasma as well as a reduction of DNA damage, lipid peroxidation and myeloperoxidase activity. Lemon balm supplementation may provide adequate protection against low-dose radiation (Zeraatpishe et al., 2011).

Anti-inflammatory properties

The anti-inflammatory properties of the *Melissa officinalis* leaf oil were studied in rats with paw oedema. An oral dose of 200 or 400 mg/kg of essential oil or 10 mg/kg of indomethacin, a drug from the group of non-steroidal anti-inflammatory drugs, was used. It was observed that both doses of lemon balm oil significantly reduced swelling and the effect was similar to that of a standard medicine (Bounihi et al., 2013).

Antimicrobial properties

In *in vitro* tests, the essential oil of *Melissa officinalis* leaves had an inhibitory effect on the growth of Gram-positive (*Staphylococcus aureus, Bacillus subtilis, Listeria monocytogenes*) and Gram-negative (*Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Salmonella enterica*) bacteria, yeasts (*Candida albicans, Saccharomyces cerevisiae*) and fungi (*Fusarium oxysporum* spp., *Mucor ramannianus*) (Abdellatif et al., 2014). The water extract of lemon balm leaves and rosmarinic acid also have antiviral activity. In *in vitro* studies, it inhibited the binding of HSV-1 (herpes simplex virus 1) to host cells and virus penetration in cells (Astani et al., 2014). The inhibitory effect of concentrated methanolic lemon balm leaf extract on enterovirus 71 (EV71) has also been demonstrated (Chen et al., 2017).

Anxiolytic and anti-depressant properties

Lemon balm leaf is a frequently used herbal drug with anxiolytic and anti-depressant effect. It lowers the level of anxiety, facilitates falling asleep, prevents gastrointestinal disorders on the mental background and has sedative properties. It is usually recommended to consume infusions from 2-3 g of leaves 3 times a day (Nowak, 2009).
Mice subjected to chronic stress receiving aqueous extracts of *Melissa officinalis* and *Passiflora caerulea* (200 mg/kg) had lower levels of corticosterone and higher blood glucose (Feliú-Hemmelmann et al., 2013). In the rat study, however, it was shown that only chronic use of lemon balm (30, 100, 300 mg/kg of ethanolic extract) had an anxiolytic effect. The same doses did not give a satisfactory effect in a single portion (Taiwo et al., 2012). It was also found that the antidepressant effect of lemon balm can occur by regulating 5-HT turnover in brain regions associated with serotoninergic neurotransmission (Lin et al., 2015).
In the human study, it was shown that the best concentration was achieved after using a single dose of 600 mg lemon balm leaf extract, a feeling of calm after eating 300 mg, however, it was necessary to consume as much as 900 mg to reduce the sense of "vigilance" (Kennedy et al., 2003). On the other hand, 600 mg of a product containing lemon balm leaf extracts and valerian root weakened the negative symptoms of anxiety (Kennedy et al., 2006).
Lemon balm used in beverages or yoghurts can also have an effect that improves well-being and cognitive abilities. Consumption of a drink containing 0.3 g of lemon balm leaf extract (containing more than 6% of rosmarinic acid) and additionally a natural sweetener reduced the level of anxiety in the subjects and improved the memory up to 3 hours after consumption. However, this did not affect psychomotor skills. The intake of a higher dose (0.6 g) improved mathematical and psychomotor skills. Regardless of the dose, the drink with *Melissa officinalis* reduced the level of cortisol among the subjects. The results of lemon balm leaf extract in yogurt were partially different - lower doses of lemon balm improved alertness, remembering and mathematical abilities, but the use of a higher dose (0.6 g) was associated with a significant feeling of tiredness (Scholey et al., 2014).

Application in sleep disorders

Melissa officinalis is a frequently used sleeping remedy for the elderly (Lutomski, 2000). In a 30-day study in healthy subjects, 360 mg of *Valeriana officinalis* root extract and 240 mg of *Melissa officinalis* extract consumed 0.5 h before bedtime showed to improve its quality. However, this did not affect the general well-being of the subjects (Cerny and Schmid, 1999).
A 15-day pilot study showed that in the stressed group, 600 mg of lemon balm leaf extract (300 mg for breakfast and 300 mg for lunch) reduced anxiety (15-18%) and insomnia related to anxiety (42%). In

Tab. 2: Summary of human studies on using *Melissa officinalis*

TESTED PROPERTIES	APPLIED DOSE	TIME OF USE	OBSERVED EFFECT	TEST GROUP	STUDY
Antioxidant properties	2 × 1,5 g of leaf infusion	30 days	Increase in catalase, superoxide dismutase, glutathione peroxidase activity; Reduction of DNA damage, lipid peroxidation, myeloperoxidase activity	n=55	Zeraatpishe et al., 2011
Application in gynecology	1200 mg of extract	3 months	Reduction of PMS symptoms severity	n=50	Akbarzadeh et al., 2015
	1200 mg of essence	7 days/month for 3 months	Reduction of PMS psychosomatic symptoms, anxiety, depression, sleep problems and social problems	n=50	Heydari et al., 2018
	3 × 330 mg of herb extract	3 days/month for 2 months	Reduction of systemic symptoms (lethargy and fatigue) in dysmenorrhea	n=50	Mirabi et al., 2018
	2 × 1000 mg of aqueous extract of the dried leaves	4 weeks	Improvement in women with hypoactive sexual desire disorder	n=19	Darvish-Mofrad-Kashani et al., 2018
Anxiolytic and anti-depressant properties	300 mg of leaf extract	1 day	Feeling of calmness	n=20	Kennedy et al., 2003
	600 mg extract of *Melissa officinalis* leaves and *Valeriana officinalis root*	1 day	Reduction of anxiety symptoms	n=24	Kennedy et al., 2006
	0,3 g leaf extract (in a drink)	1 day	Reduction of anxiety symptoms	n=5	Scholey et al., 2014
	2 × 300 mg of leaf extract	15 days	Reduction of anxiety, aggression and hyperexcitation	n=20	Cases et al., 2011
	2 × 500 mg of leaf extract per day	14 days	Reduction of anxiety symptoms	n=28	Alijaniha, 2015
	60 drops of *Melissa officinalis* extract per day (1:1 in 45% alcohol; at least 500 μg citral/ml)	16 weeks	Reduction of agitation among patients with mild to moderate Alzheimer's disease	n=42	Akhondzadeh et al., 2003
Application in sleep disorders	240 mg of *Melissa officinalis* leaves extract and 360 mg of *Valeriana officinalis* root extract	30 days	Improvement of the sleep quality	n=66	Cerny and Schmid, 1999
	2 × 300 mg of leaf extract	15 days	Reduction in insomnia frequency	n=20	Cases et al., 2011
	2 × 160 mg of *Valeriana officinalis* extract and 80 mg of *Melissa officinalis extract*	1 day	Improvement of the sleep quality in women during menopause	n=50	Taavoni et al., 2013
Properties supporting the functioning of the nervous system and cognitive functions	600 mg of leaf extract	1 day	Improvement of the concentration	n=20	Kennedy et al., 2003
	0,3 g leaf extract (in drink)	1 day	Improvement of the cognitive abilities	n=5	Scholey et al., 2014
	0,6 g leaf extract (in drink)	1 day	Improvement of the mathematical and psychomotor skills	n=5	Scholey et al., 2014
	60 drops *of Melissa officinalis* extract per day (1:1 in 45% alcohol; at least 500 μg citral/ml)	16 weeks	Better outcome on cognitive function among patients with mild to moderate Alzheimer's disease	n=42	Akhondzadeh et al., 2003
Application in cardiology	3 × 1 g of herb extract	2 months	Increased ejection fraction, higher nitric oxide concentration, lower lactate dehydrogenase level and reduced systolic and diastolic blood pressure in patients with chronic stable angina	n=35	Javid et al., 2018
	2 × 500 mg of leaf extract	14 days	Reduction of heart rate palpitations by 36.8%	n=28	Alijaniha, 2015
	3 × 1000 mg of dried leaves	2 months	Reduction of aspartate transaminase activity	n=28	Jandaghi et al., 2016

	3 × 1 g of herb extract	2 months	Reduction of anxiety, stress, depression and sleep in patients with stable angina	n=35	Haybar et al., 2018
	3 × 500 mg of dried leaf powder	1 week	Improvement of the sleep quality and the anxiety in patients underwent coronary artery bypass surgery	n=80	Soltanpour et al., 2019
	700 mg/d of hydroalcoholic extract	12 weeks	Improvement of lipids, Apo A-I, Apo B/Apo A-I ratios in patients with type II diabetes	n=31	Asadi et al., 2018
	700 mg/d of hydroalcoholic extract	12 weeks	Improvement in glycemic control, lipid profile, inflammation and systolic blood pressure	n=31	Asadi et al., 2019
Application in obesity therapy	Infusion made of 2 g of lemon balm twice a day	1 month	Reduction in body mass, BMI, diastolic blood pressure	n=18	Jafari et al., 2018
Application in bruxism	20% tincture (2 × 15 drops/d)	30 days	No reduction in muscle activity	n=12	Bortoletto, 2016
	1 drop of homeopathic preparations per year of age	30 days	Reduction of tooth grinding in children with bruxism	n=39	Tavares-Silva et al., 2019

addition, aggression and hyperexcitation decreased. Reductions in other symptoms such as eating problems, guilt and tiredness, which were considered to be the cause of fear, were also observed (Cases et al., 2011).

Sleep disorders in women during menopause were also examined. It was shown that two doses of 160 mg of *Valeriana officinalis* extract and 80 mg of *Melissa officinalis* extract allows to reduce the symptoms of sleep disorders (Taavoni et al., 2013).

In the mouse study, it was found that lemon balm extract (400, 800 mg/kg) significantly reduced the time of falling asleep and extended sleep time. The effect correlated positively with the dose, and the dose of 800 mg/kg had almost identical effect to that of diazepam – a psychotropic drug. It was also shown that the mixture with lavender extract (*Lavandula angustifolia*) had a synergistic effect in terms of length of falling asleep and the sleep itself, which may be important in the treatment of insomnia (Hajhashemi and Safaei, 2015).

Effect on memory and neurodegenerative diseases

Numerous studies are directed to the action of *Melissa officinalis* in the prevention of memory disorders and neurodegenerative diseases. *Melissa officinalis* and rosmarinic acid can help patients with Alzheimer's disease via inflammatory and neuroprotective effects as well as inhibition of the acetylcholine esterase activity and β-amyloid plaque formation in brain (Mahboubi, 2019).

The rats received intraperitoneally 50-400 mg/kg lemon balm leaf extract. Some of them were additionally treated with scopolamine, which is toxic to the nervous system. The 200 mg/kg extract significantly improved the ability to learn and remember and diminished the effect of scopolamine. In addition, inhibition of acetylcholine esterase activity was observed (Soodi et al., 2014). In another study, in which rats were given a hydroethanolic extract of lemon balm leaves (200 mg/kg) for 28 days, an improvement in long-term memory was observed. At the same time, the level of acetylcholine esterase mRNA decreased in the cerebral cortex and the β-secretase mRNA transcription decreased, which may be important in the prevention of Alzheimer's disease (Ożarowski et al., 2016). In traditional Iranian medicine, a mixture of lemon balm herb and *Boswellia serrata* oleo gum resin extract is used to improve the ability to remember. The use of 200 or 400 mg extracts from both plants in adult rats for 4 weeks had a protective effect against the toxic action of scopolamine on neurons. A better effect in memory tests could be related to antioxidant and anti-inflammatory effects (Mahboubi et al., 2016).

In vitro tests have also shown that 15% aqueous leaf extract (10 μg/ml) protects hippocampal neurons against MDMA-induced apoptosis (3,4-methylenedioxymethamphetamine) and lowers caspase-3 activity (Hassanzadeh et al., 2010). The extract of the same concentration also had a protective effect on hypoxia in nerve cells. The level of caspase-3 and malondialdehyde decreased. In addition, lemon balm reduced the expression of the HIF-1α gene (hypoxia induced factor 1α). *Melissa officinalis* can thus be a neuroprotective factor in diseases related to oxidative stress (Bayat et al., 2012). It was found that the acid fraction of the ethanolic extract of lemon balm leaves (1:10) had a significant protective effect in the case of neurotoxicity caused by β-amyloid plaques and oxidative stress. Probably it was the action of polyphenols and triterpenoids through antioxidant mechanisms or stimulation of nicotinic receptors, and this fraction contains the highest concentration of rosmarinic acid. The use of 10 μg/ml extract or 1 μg/ml acid fraction reversed the effects of toxicity and increased cell viability to its original state (Sepand et al., 2013).

The efficacy of lemon balm has also been studied in people with mild to moderate Alzheimer's disease. Twenty patients received 60 drops of leaf extract a day (1:1 with 45% alcohol, 500 μg citral/ml) for 16 weeks and fifteen for placebo. Already from the fourth week of therapy, significantly better results in the cognitive assessment were observed, and from the 8th week also in the assessment of the severity of dementia. In addition, fewer patients experienced agitation (psychomotor anxiety) in the group using lemon balm than placebo (Akhondzadeh et al., 2003).

Application in ophthalmology

Macular degeneration is a common disease among older people. The main cause of this disease is the action of free oxygen radicals. The influence of hydroethanolic extract from lemon balm leaves ALS-L1023 (6.25-200 μg/ml) on oxidative stress in human cells of the retinal pigment layer was investigated *in vitro*. The extract significantly increased cell viability and decreased apoptosis caused by oxidative stress. This involved the inhibition of caspase-3/7 and PARP, which are the stimulators of apoptosis. The protective effect of lemon balm extract was mediated by the protein kinase B signal transduction pathway. It can be concluded that the lemon balm extract effectively protects against oxidative stress induced by hydrogen peroxide

through antiapoptotic and antioxidant effects (Jeung et al., 2016).
Diabetic retinopathy is another condition where medicinal plants are considered as a potential treatment. Due to capability to modulate blood sugar and lipid levels, *Melissa officinalis* can be used for preventing diabetes complications. Rosmarinic acid also shows beneficial suppressing retinal neovascularization by inhibition of retinal endothelial cells proliferation and angiogenic tube formation (Parveen et al., 2018).

Application in gynecology

Lemon balm is used in menstrual disorders, such as lack of or irregular menstruation, in menstrual pain and during excessive bleeding (Kapczyński, 2000). The use of 1,200 mg of lemon balm extract among high school students significantly reduced the severity of premenstrual syndrome symptoms during the 3-month treatment. The observed positive effect concerned psychological, physiological and social symptoms. The regulation of the GABA-ergic system may be a likely mechanism for the action of *Melissa officinalis* (Akbarzadeh et al., 2015). These results were confirmed by similar research in which female adolescents were treated with 1,200 mg of lemon balm essence during first 7 days of menstruation for three cycles. There was observed an improvement in psychosomatic symptoms, anxiety, sleep disturbances, depression and social dysfunction (Heydari et al., 2018).
Lemon balm seems to be helpful in reduction of systemic symptoms that are associated with dysmenorrhea. Fifty students with dysmenorrhea received 330 mg of lemon balm herb extract three times for three days during two menstrual cycles. Trial showed a significant decrease in severity of lethargy and fatigue (Mirabi et al., 2018). Another indication of lemon balm is hypoactive sexual desire disorder – the most common sexual dysfunction in women. In a randomized, double-blind placebo-controlled study a group of 19 women (18 to 50 years old) consumed twice a day two capsules of *Melissa officinalis* (containing 500 mg of aqueous extract of the dried leaves) for four weeks. The treatment led to the increase in frequency of sexual intercourse and had beneficial effects in every domain of this sexual dysfunction (arousal, orgasm, satisfaction, pain, lubrication, desire). Improvement can be connected with anti-depressive and anti-anxiety effects, as well as a role of increased norepinephrine and cholinergic activity in sexual desire and arousal (Darvish-Mofrad-Kashani et al., 2018).

Application in oncology

Glioblastoma multiforme is one of the most common and most fatal cancers of the central nervous system. The *in vitro* effects of aqueous and ethanolic extracts of lemon balm and rosmarinic acid on C6 cell lines of this tumour were investigated in rats. In each case, cytotoxic effects and suppression of proliferation were observed, however, rosmarinic acid showed the weakest effect, and its higher doses (≥ 200 μM) had pro-oxidative properties and initiated cell death through necrosis. In various ways, lemon balm can be a neuroprotective factor in the treatment of glioma (Ramanauskiene et al., 2016). An ethanol lemon balm leaf extract of 5 μg/ml significantly reduces the proliferation of HCT-116 cells (human colon cancer cells), and at a concentration of 1,000 μg/ml significantly reduces their viability (Encalada et al., 2011). The effect of hydroethanolic extract of lemon balm leaf extract (5-1,000 μg/ml) on several different tumour cell lines: A549 (lung cancer cells), MCF-7 (breast cancer), SKOV3 (ovarian cancer cells) and PC-3 (prostatic adenocarcinoma). Even the lowest concentrations of the extract significantly reduced cell viability and inhibited their growth (Jahanban-Esfahlan et al., 2015; Jahanban-Esfahlan et al., 2017). *Melissa officinalis* extract was also examined as a potential treatment against human pancreatic cancer cells. However, this plant extracts did not show efficient as antitumoral agent (Mouhid et al., 2018).
Doxorubicin (DOX) is a cytostatic drug with high activity in various types of cancer, however, it also has a cardiotoxic effect. It was found that lemon balm herb extract reduced the oxidative stress caused by DOX – decreased lipid peroxidation, protein oxidation and increased antioxidant capacity. It also inhibited inflammatory reactions by lowering the expression of the nuclear factor $\varkappa\beta$ (NF-$\varkappa\beta$), tumour necrosis factor-α (TNF-α) and cyclooxygenase-2 and myeloperoxidase activity. Incorporation of lemon balm herb extract into doxorubicin may provide a safer cancer treatment protocol (Hamza et al., 2016).

Effect on muscle activity

Bruxism is a disorder that occurs in 13.5-33% of children, and is characterized by repetitive muscle activity, e.g. clenching and rubbing of teeth during sleep. The effect of 20% tincture from lemon balm (2 × 15 drops/d, 30 days) on muscle activity was studied in 12 children aged 6-10 years. However, no reduction in muscle activity was observed in children (Bortoletto, 2016). Another research with outcomes measured by a visual analogue scale of children's teeth showed beneficial effects on bruxism. 39 children (3-12 years old) were treated with homeopathic preparations of *M. officinalis, Phytolacca decandra,* a combination of both or placebo (1 drop per year of age for 30 days). The study showed that the use of lemon balm can reduce tooth grinding in children with bruxism (Tavares-Silva et al., 2019).

Application in gastroenterology

Lemon balm can be used in the irritable bowel syndrome. In an *in vitro* study, it was demonstrated that essential oil and citral (one of the main components of the oil) have the effect of relieving intestinal spasms caused by potassium chloride, serotonin and acetylcholine (Sadraei et al., 2003). The possibility of modulating the visceral hypersensitivity by the hydroalcoholic lemon balm extract in the irritable bowel syndrome in rats is also indicated (Dolatabadi et al., 2018).
It has also been shown that the methanolic leaf extract (150, 300 and 450 mg/kg) in single dose may have a protective effect on stomach ulcers in rats. The potential mechanism was to increase the activity of superoxide dismutase and glutathione peroxidase and inhibition of lipid peroxidation in cell membranes – reduction of malondialdehyde production (Saberi et al., 2016).
In the study involving patients with infantile colic there was a positive effect of the supply of chamomile (*M. chamomilla* L.), lemon balm and *L. acidophilus* (HA122). The group, that was administered 2 ml of solution (18 mg chamomile, 130 mg lemon balm and 2 × 109 lactic bacteria) in two doses over 28 days, showed a significantly lower incidence of crying in comparison to infants who received simethicone (Martinelli et al., 2017).

Application in cardiology

Melissa officinalis is considered as safe alternative to pharmacotherapy in mild palpitations. The use of a dry leaf extract (2 × 500 mg/d, 14 days) among 28 people resulted in a reduction in the rate of palpitations by 36.8%. In addition, a decrease in anxiety symptoms was observed (Alijaniha, 2015). In a rat study, it was found that the supply of lemon balm herb extract for one week (50, 100, 200 mg/kg) was associated with changes in electrocardiographic results. The effects were similar to anti-arrhythmic drugs (Joukar and Asadipour, 2015).
In addition, lemon balm may support hyperlipidaemia therapy.

In the study, various doses of ethanolic extract (25, 50 and 75 mg/kg) were given to hypercholesterolemic rats. It was found that irrespective of the dose, lemon balm reduced the activity of hepatic enzymes: alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase, as well as decreased the level of cholesterol in the blood. The effect of lemon balm was the same as atorvastatin – a drug commonly used to treat hyperlipidaemia (Zarei et al., 2014). A similar result was obtained in a study involving people with hyperlipidaemia. A two-month treatment with powdered lemon balm leaves (3 × 1,000 mg/d) resulted in a decrease in the mean LDL level and aspartate aminotransferase (Jandaghi et al., 2016). *Melissa officinalis* was also found to improve lipids and Apo A-I, Apo B/Apo A-I ratio in patients with type II diabetes who received 700 mg/d hydroalcoholic extract of lemon balm for 12 weeks. These effects can be useful in preventing cardiovascular diseases in this group of patients (Asadi et al., 2018). This treatment resulted also in a positive changes in glycemic control (HbA_{1c}, activity of β-cells, fasting blood sugar), lipid profile (triglycerides, HDL-c), inflammation (high-sensitivity C-reactive protein) and systolic blood pressure (Asadi et al., 2019).

Medical lemon balm was also tested for the use in stable angina. In a double-blind study, 80 patients with this disorder were given 3 g of lemon balm herb extract per day or placebo. The study lasted three months. After this time, a higher cardiac ejection fraction, higher nitric oxide concentration, lower lactate dehydrogenase concentration and reduced systolic and diastolic blood pressure were found in the study group compared to control (Javid et al., 2018). There was also a significant reduction of anxiety, stress, depression and sleep problems that are common in patients with stable angina (Haybar et al., 2018).

It has been shown that lemon balm can be administered to patients who underwent coronary artery bypass surgery due to its beneficial effects on anxiety and sleep disorders that are common in this group of patients. For a week, eighty people three times a day took 500 mg of lemon balm dried leaf powder or placebo. The treatment improved the sleep quality and reduced the anxiety in patients after coronary artery bypass surgery (Soltanpour et al., 2019).

Application in obesity therapy

The effectiveness of lemon balm in the treatment of obesity was also examined. It was used in genetically obese mice of the Ob-X mix (0.5 mg per day for 5 days), which consisted of *Morus alba*, *Melissa officinalis* and *Artemisia capillaris*. It was observed that weight gains slowed down and visceral fat content decreased without affecting other organs. Probably these components act specifically on adipose tissue (Yoon and Kim, 2011). ALS-L1023 (made from lemon balm leaves by extraction with ethyl acetate) was administered to obese rats at 0.4 or 0.8% of the diet mass. The preparation inhibited the growth of body fat, significantly reduced its mass and protected against weight gain. Inhibition of angiogenesis and MMP activity was also found. ALS may be a potential method in the prevention and treatment of obesity (Park et al., 2015). ALS-L1023 was also administered to rats on a high-fat diet. It was observed that in comparison with the group on a high-fat diet without supplementation there was a decrease in body weight (without affecting the calorie intake of food), alanine aminotransferase and aspartate aminotransferase as well as suppression of steatosis, inflammatory cell infiltration and collagen accumulation in the liver. Medical lemon balm may have a potentially positive effect in the prevention and treatment of obesity-induced human NAFLD (Kim et al., 2017).

In the study involving twenty welders, two monthly interventions were used with the use of green tea or lemon balm infusions (2 × 2 g/d). In both cases, a similar decrease in body weight, BMI index and diastolic blood pressure was observed (Jafari et al., 2018).

Safety of use

There was no negative effect of a single dose of lemon balm extract (containing 100, 250 or 500 mg of rosmarinic acid) on the overall health and morphological and biochemical results of blood (Noguchi-Shinohara et al., 2015). In one study, the only side-effect of using lemon balm (1,000 mg dry extract/day) was increased appetite (Alijaniha, 2015). One of the cases described in the literature indicates the risk of withdrawal syndrome with such symptoms as anxiety, irritability, decreased appetite, concentration and sleep. However, the described patient consumed up to 4 cups of lemon balm infusion per day for about 2 months, and symptoms appeared two days after cessation (Demirci et al., 2015).

No adverse reactions are observed in healthy adults after a recommended intake of up to 30 days or in amounts contained in food. *Melissa officinalis* has the GRAS (Generally Regarded as Safe) status with a maximum level of 0.5% in baked products. There are, however, risk statements when consumed by pregnant women, nursing women and paediatric patients, since genotoxic properties have been demonstrated in *in vitro* studies. Lemon balm should also not be used in people with thyroid disorders or those who use tranquilizers (Abudayyak et al., 2015; Miraj et al., 2017).

The Panel on Food Additives and Nutrient Sources added to Food (ANS) concludes that due to the lack of an appropriate dossier supporting the use of oregano and lemon balm extracts as additives, the safety of lemon balm extracts at the proposed uses in eight food categories and use levels respectively 2.0 mg/kg bw/day for women and 2.3 mg/kg bw/day for men cannot be assessed (EFSA, 2010).

Conclusions

Lemon balm can be used for both prevention and treatment. *Melissa officinalis* indicates antioxidant, anti-inflammatory, antimicrobial and antidepressant properties, as well as a wide range of applications in the treatment of sleep disorders, neurodegenerative diseases and obesity as well as in ophthalmology, gynaecology, oncology, gastroenterology and cardiology. Most of the therapeutic properties of lemon balm are based on antioxidant activities. This plant as quite safe and can be widely used in many fields of medicine, as well as a component of supplements and functional food.

References

Abdellatif, F., Boudjella, H., Zitouni, A., Hassani, A., 2014: Chemical composition and antimicrobial activity of the essential oil from leaves of Algerian *Melissa officinalis* L. EXCLI J. 13, 772-781. DOI: 10.17877/DE290R-6927

Abudayyak, M., Özdemir Nath, E., Özhan, G., 2015; Toxic potentials of ten herbs commonly used for aphrodisiac effect in Turkey. Turkish J. Med. Sci. 45, 496-506. DOI: 10.3906/sag-1401-153

Akbarzadeh, M., Dehghani, M., Moshfeghy, Z., Emamghoreishi, M., Tavakoli, P., Zare, N., 2015: Effect of *Melissa officinalis* capsule on the intensity of premenstrual syndrome symptoms in high school girl students. Nurs. Midwifery Stud. 4, e27001. DOI: 10.17795/nmsjournal27001

Akhondzadeh, S., Noroozian, M., Mohammadi, M., Ohadinia, S., Jamshidi, A.H., Khani, M., 2003: *Melissa officinalis* extract in the treatment of patients with mild to moderate Alzheimer's disease: a double blind, randomised, placebo controlled trial. J. Neurol. Neurosurg. Psychiatry 74, 863-866. DOI: 10.1136/JNNP.74.7.863

Alijaniha, F., Naseri, M., Afsharypuor, S., Fallahi, F., Noorbala, A., Mosaddegh, M., Faghihzadeh, S., Sadrai, S., 2015: Heart palpitation relief with *Melissa officinalis* leaf extract: double blind, randomized, placebo controlled trial of efficacy and safety. J. Ethnopharmacol. 164, 378-384. DOI: 10.1016/j.jep.2015.02.007

Asadi, A., Shidfar, F., Safari, M., Malek, M., Hosseini, A.F., Rezazadeh, S., Rajab, A., Shidfar, S., Hosseini, S., 2018: Safety and efficacy of *Melissa officinalis* (lemon balm) on ApoA-I, Apo B, lipid ratio and ICAM-1 in type 2 diabetes patients: A randomized, double-blinded clinical trial. Complement. Ther. Med. 40, 83-88. DOI: 10.1016/j.ctim.2018.07.015

Asadi, A., Shidfar, F., Safari, M., Hosseini, A.F., Huseini, H.F., Heidari, I., Rajab, A., 2019: Efficacy of *Melissa officinalis* L. (lemon balm) extract on glycemic control and cardiovascular risk factors in individuals with type 2 diabetes: A randomized, double-blind, clinical trial. Phytother. Res. 33, 651-659. DOI: 10.1002/ptr.6254

Astani, A., Navid, M. H., Schnitzler, P., 2014: Attachment and penetration of acyclovir-resistant *Herpes Simplex Virus* are inhibited by *Melissa officinalis* extract. Phytother. Res. 28, 1547-1552. DOI: 10.1002/ptr.5166

Bayat, M., Azami Tameh, A., Hossein Ghahremani, M., Akbari, M., Mehr, S.E., Khanavi, M., Hassanzadeh, G., 2012: Neuroprotective properties of *Melissa officinalis* after hypoxic-ischemic injury both *in vitro* and *in vivo*. DARU J. Pharm. Sci. 20, 42. DOI: 10.1186/2008-2231-20-42

Bortoletto, C.C., Cordeiro da Silva, F., Salgueiro, M. da C.C., Motta, L.J., Curiki, L.M., Mesquita-Ferarri, R.A., Fernandes, K.P.S., Bussadori, S.K., 2016: Evaluation of electromyographic signals in children with bruxism before and after therapy with *Melissa officinalis* L. – a randomized controlled clinical trial. J. Phys. Ther. Sci. 28, 738-742. DOI: 10.1589/jpts.28.738

Bounihi, A., Hajjaj, G., Alnamer, R., Cherrah, Y., Zellou, A., 2013: *In vivo* potential anti-inflammatory activity of *Melissa officinalis* L. essential oil. Adv. Pharmacol. Sci. 2013, 1-7. DOI: 10.1155/2013/101759

Cases, J., Ibarra, A., Feuillère, N., Roller, M., Sukkar, S.G., 2011: Pilot trial of *Melissa officinalis* L. leaf extract in the treatment of volunteers suffering from mild-to-moderate anxiety disorders and sleep disturbances. Med. J. Nutrition Metab. 4, 211-218. DOI: 10.1007/s12349-010-0045-4

Cerny, A., Schmid, K., 1999: Tolerability and efficacy of valerian/lemon balm in healthy volunteers (a double-blind, placebo-controlled, multicentre study). Fitoterapia 70, 221-228. DOI: 10.1016/S0367-326X(99)00018-0

Chen, S.-G., Leu, Y.-L., Cheng, M.-L., Ting, S.C., Liu, C.-C., Wang, S.-D., Yang, C.-H., Hung, C.-Y., Sakurai, H., Chen, K.-H., Ho, H.-Y., 2017: Anti-enterovirus 71 activities of *Melissa officinalis* extract and its biologically active constituent rosmarinic acid. Sci. Rep. 7, 12264. DOI: 10.1038/s41598-017-12388-2

Darvish-Mofrad-Kashani, Z., Emaratkar, E., Hashem-Dabaghian, F., Emadi, F., Raisi, F., Aliasl, J., Kamalinejad, M., Hasheminejad, S.A., Eftekhar, T., Zafarghandi, N., 2018: Effect of *Melissa offcinalis* (Lemon balm) on sexual dysfunction in women: A double-blind, randomized, placebo-controlled study. Iran J. Pharm. Res. 17 (Special Issue), 89-100. PMID: 29796033.

Demirci, K., Akgönül, M., Demirdaş, A., Akpinar, A., 2015: Does *Melissa officinalis* cause withdrawal or dependence? Med. Arch. (Sarajevo, Bosnia Herzegovina) 69, 60-61. DOI: 10.5455/medarh.2015.69.60-61

Dolatabadi, F., Abdolghaffari, A.H., Farzaei, M.H., Baeeri, M., Ziarani, F.S., Eslami, M., Abdollahi, M., Rahimi, R., 2018: The protective effect of *Melissa officinalis* L. in visceral hypersensitivity in rat using 2 models of acid-induced colitis and stress-induced irritable bowel syndrome: a possible role of nitric oxide pathway. J. Neurogastroenterol. Motil. 24, 490-501. DOI: 10.5056/jnm17035

EFSA, 2010: Scientific opinion on the use of oregano and lemon balm extracts as a food additive. EFSA J. 8 (2), 1514. DOI: 10.2903/j.efsa.2010.1514

Encalada, M.A., Hoyos, K.M., Rehecho, S., Berasategi, I., de Ciriano, M.G.-Í., Ansorena, D., Astiasarán, I., Navarro-Blasco, Í., Cavero, R.Y., Calvo, M.I., 2011: Anti-proliferative effect of *Melissa officinalis* on human colon cancer cell line. Plant Foods Hum. Nutr. 66, 328-334. DOI: 10.1007/s11130-011-0256-y

Feliú-Hemmelmann, K., Monsalve, F., Rivera, C., 2013: *Melissa officinalis* and *Passiflora caerulea* infusion as physiological stress decreaser. Int. J. Clin. Exp. Med. 6, 444-451. PMID: 23844268.

Hajhashemi, V., Safaei, A., 2015: Hypnotic effect of *Coriandrum sativum, Ziziphus jujuba, Lavandula angustifolia* and *Melissa officinalis* extracts in mice. Res. Pharm. Sci. 10, 477-484. PMID: 26779267.

Hamza, A.A., Ahmed, M.M., Elwey, H.M., Amin, A., 2016: *Melissa officinalis* protects against doxorubicin-induced cardiotoxicity in rats and potentiates its anticancer activity on MCF-7 cells. PLoS One 11, e0167049. DOI: 10.1371/journal.pone.0167049

Hassanzadeh, G., Pasbakhsh, P., Akbari, M., Shokri, S., Ghahremani, M., Amin, G., Kashani, I., Azami Tameh, A., 2011: Neuroprotective properties of *Melissa officinalis* L. Extract against ecstasy-induced neurotoxicity. Cell J. 13, 25-30. PMID: 23671824.

Haybar, H., Javid, A.Z., Haghighizadeh, M.H., Valizadeh, E., Mohaghegh, S.M., Mohammadzadeh, A., 2018: The effects of *Melissa officinalis* supplementation on depression, anxiety, stress, and sleep disorder in patients with chronic stable angina. Clin. Nutr. ESPEN. 26, 47-52. DOI: 10.1016/j.clnesp.2018.04.015

Heydari, N., Dehghani, M., Emamghoreishi, M., Akbarzadeh, M., 2018: Effect of *Melissa officinalis* capsule on the mental health of female adolescents with premenstrual syndrome: a clinical trial study. Int. J. Adolesc. Med. Health. DOI: 10.1515/ijamh-2017-0015

Jafari, F., Salehi-Abargouei, A., Zare Sakhvidi, M.J., Ranjbar, A.M., Zavar Reza, J., Fallahzadeh, H., Nadjazadeh, A., 2018: Comparison of the effects of green tea and *Melissa officinalis* on weight and blood pressure in welders: a single-blind, crossover clinical trial. J. Nutr. Food Secur. 3, 130-138. http://jnfs.ssu.ac.ir/article-1-194-en.html

Jahanban-Esfahlan, A., Modaeinama, S., Abasi, M., Abbasi, M.M., Jahanban-Esfahlan, R., 2015: Anti proliferative properties of *Melissa officinalis* in different human cancer cells. Asian Pac. J. Cancer Prev. 16, 5703-5707. DOI: 10.7314/apjcp.2015.16.14.5703

Jahanban-Esfahlan, R., Seidi, K., Monfaredan, A., Shafie-Irannejad, V., Abbasi, M.M., Karimian, A., Yousefi, B., 2017: The herbal medicine *Melissa officinalis* extract effects on gene expression of p53, Bcl-2, Her2, VEGF-A and hTERT in human lung, breast and prostate cancer cell lines. Gene 613, 14-19. DOI: 10.1016/j.gene.2017.02.034

Jandaghi, P., Noroozi, M., Ardalani, H., Alipour, M., 2016: Lemon balm: A promising herbal therapy for patients with borderline hyperlipidemia – A randomized double-blind placebo-controlled clinical trial. Complement. Ther. Med. 26, 136-140. DOI: 10.1016/j.ctim.2016.03.012

Javid, A.Z., Haybar, H., Dehghan, P., Haghighizadeh, M.H., Mohaghegh, S.M., Ravanbakhsh, M., Mohammadzadeh, A., Bahrololumi, S.S., 2018: The effects of *Melissa officinalis* on echocardiography, exercise test, serum biomarkers, and blood pressure in patients with chronic stable angina. J. Herb. Med. 11, 24-29. DOI: 10.1016/J.HERMED.2017.10.002

Jeung, I.C., Jee, D., Rho, C.-R., Kang, S., 2016: *Melissa officinalis* L. extracts protect human retinal pigment epithelial cells against oxidative stress-induced apoptosis. Int. J. Med. Sci. 13, 139-146. DOI: 10.7150/ijms.13861

Joukar, S., Asadipour, H., 2015: Evaluation of *Melissa officinalis* (Lemon Balm) effects on heart electrical system. Res. Cardiovasc. Med. 4, e27013. DOI: 10.5812/cardiovascmed.4(2)2015.27013

Kapczyński, W., 2000: Phytotherapy in contemporary medical treatment in gynaecology and obstetrics. Postępy Fitoter. 2, 10-16. PMID: 11355224.

Kennedy, D.O., Wake, G., Savelev, S., Tildesley, N.T.J., Perry, E.K., Wesnes, K.A., Scholey, A.B., 2003: Modulation of mood and cognitive performance following acute administration of single doses of Melissa. Neuropsychopharmacology 28, 1871-1881. DOI: 10.1038/sj.npp.1300230

Kennedy, D.O., Little, W., Haskell, C.F., Scholey, A.B., 2006: Anxiolytic effects of a combination of *Melissa officinalis* and *Valeriana officinalis* during laboratory induced stress. Phyther. Res. 20, 96-102. DOI: 10.1002/ptr.1787

Kim, J., Lee, H., Lim, J., Oh, J., Shin, S., Yoon, M., 2017: The angiogenesis inhibitor ALS-L1023 from lemon-balm leaves attenuates high-fat diet-induced nonalcoholic fatty liver disease through regulating the visceral

adipose-tissue function. Int. J. Mol. Sci. 18, E846. DOI: 10.3390/ijms18040846

Kittler, J., Krüger, H., Ulrich, D., Zeiger, B., Schütze, W., Böttcher, Ch., Krähmer, A., Gudi, G., Kästner, U., Heuberger, H., Marthe, F., 2018: Content and composition of essential oil and content of rosmarinic acid in lemon balm and balm genotypes (*Melissa officinalis*). Genet. Resour. Crop Evol. 65, 1517-1527. DOI: 10.1007/s10722-018-0635-4

Lin, S.-H., Chou, M.-L., Chen, W.-C., Lai, Y.-S., Lu, K.-H., Hao, C.-W., Sheen, L.-Y., 2015: A medicinal herb, *Melissa officinalis* L. ameliorates depressive-like behavior of rats in the forced swimming test via regulating the serotonergic neurotransmitter. J. Ethnopharmacol. 175, 266-272. DOI: 10.1016/j.jep.2015.09.018

Lutomski, J., 2000: Phytotherapy of geriatric diseases. PostępyFitoter. 3, 24-32.

Mahboubi, M., Taghizadeh, M., Talaei, S.A., Takht Firozeh, S.M., Rashidi, A.A., Tamtaji, O.R., 2016: Combined administration of *Melissa officinalis* and *Boswellia serrata* extracts in an animal model of memory. Iran. J. Psychiatry Behav. Sci. 10, e681. DOI: 10.17795/ijpbs-681

Mahboubi, M., 2019: *Melissa officinalis* and rosmarinic acid in management of memory functions and Alzheimer disease. Asian Pac. J. Trop. Biomed. 9 (2), 47-52. DOI: 10.4103/2221-1691.250849

Martinelli, M., Ummarino, D., Giugliano, F.P., Sciorio, E., Tortora, C., Bruzzese, D., De Giovanni, D., Rutigliano, I., Valenti, S., Romano, C., Campanozzi, A., Miele, E., Staiano, A., 2017: Efficacy of a standardized extract of *Matricaria chamomilla* L., *Melissa officinalis* L. and tyndallized *Lactobacillus acidophilus* (HA122) in infantile colic: An open randomized controlled trial. Neurogastroenterol. Motil. 29, e13145. DOI: 10.1111/nmo.13145

Meftahizade, H., Sargsyan, E., Moradkhani, H., 2010: Investigation of antioxidant capacity of *Melissa officinalis* L. essential oils. J. Med. Plant Res. 4, 1391-1395. DOI: 10.5897/JMPR10.148

Mirabi, P., Alamolhoda, S.H., Yazdkhasti, M., Mojab, F., 2018: The effects of lemon balm on menstrual bleeding and the systemic manifestation of dysmenorrhea. Iran. J. Pharm. Res. 17 (2), 214-223. PMID: 31011354.

Miraj, S., Rafieian-Kopaei, M., Kiani, S., 2017: *Melissa officinalis* L: A review study with an antioxidant prospective. J. Evid. Based. Complementary Altern. Med. 22, 385-394. DOI: 10.1177/2156587216663433

Moradkhani, H., Sargsyan, E., Bibak, H., Naseri, B., Sadat-Hosseini, M., Fayazi-Barjin, A., Meftahizade, H., 2010: *Melissa officinalis* L., a valuable medicine plant: A review. J. Med. Plants Res. 4, 2753-2759.

Mouhid, L., Gómez de Cedrón, M., Vargas, T., García-Carrascosa, E., Herranz, N., García-Risco, M., Reglero, G., Fornari, T., Ramírez de Molina, A., 2018: Identification of antitumoral agents against human pancreatic cancer cells from Asteraceae and Lamiaceae plant extracts. BMC Complement. Altern. Med. 18 (1), 254. DOI: 10.1186/s12906-018-2322-6

Noguchi-Shinohara, M., Ono, K., Hamaguchi, T., Iwasa, K., Nagai, T., Kobayashi, S., Nakamura, H., Yamada, M., 2015: Pharmacokinetics, safety and tolerability of *Melissa officinalis* extract which contained rosmarinic acid in healthy individuals: A randomized controlled trial. PLoS One 10, e0126422. DOI: 10.1371/journal.pone.0126422

Nowak, G., 2009: Surowce roślinne o działaniu przeciwlękowym i antydepresyjnym. Herba Pol. 55, 84-97.

Ożarowski, M., Mikolajczak, P.L., Piasecka, A., Kachlicki, P., Kujawski, R., Bogacz, A., Bartkowiak-Wieczorek, J., Szulc, M., Kaminska, E., Kujawska, M., Jodynis-Liebert, J., Gryszczynska, A., Opala, B., Lowicki, Z., Seremak-Mrozikiewicz, A., Czerny, B., 2016: Influence of the *Melissa officinalis* leaf extract on long-term memory in scopolamine animal model with assessment of mechanism of action. Evidence-Based Complement. Altern. Med. 2016, 1-17. DOI: 10.1155/2016/9729818

Park, B.Y., Lee, H., Woo, S., Yoon, M., Kim, J., Hong, Y., Lee, H.S., Park, E.K., Hahm, J.C., Kim, J.W., Shin, S.S., Kim, M.-Y., Yoon, M., 2015: Reduction of adipose tissue mass by the angiogenesis inhibitor ALS-L1023 from *Melissa officinalis*. PLoS One 10, e0141612. DOI: 10.1371/journal.pone.0141612

Parveen, A., Kim, J.H., Oh, B.G., Subedi, L., Khan, Z., Kim, S.Y., 2018: Phytochemicals: Target-based therapeutic strategies for diabetic retinopathy. Molecules. 23 (7), 1519. DOI: 10.3390/molecules23071519

Ramanauskiene, K., Raudonis, R., Majiene, D., 2016: Rosmarinic acid and *Melissa officinalis* extracts differently affect glioblastoma cells. Oxid. Med. Cell. Longev. 2016, 1-9. DOI: 10.1155/2016/1564257

Saberi, A., Abbasloo, E., Sepehri, G., Yazdanpanah, M., Mirkamandari, E., Sheibani, V., Safi, Z., 2016: The effects of methanolic extract of *Melissa officinalis* on experimental gastric ulcers in rats. Iran. Red Crescent Med. J. 18, e24271. DOI: 10.5812/ircmj.24271

Sadraei, H., Ghannadi, A., Malekshahi, K., 2003: Relaxant effect of essential oil of *Melissa officinalis* and citral on rat ileum contractions. Fitoterapia 74, 445-452. DOI: 10.1016/S0367-326X(03)00109-6

Safaeian, L., Sajjadi, S., Javanmard, S., Montazeri, H., Samani, F., 2016: Protective effect of *Melissa officinalis* extract against H_2O_2-induced oxidative stress in human vascular endothelial cells. Res. Pharm. Sci. 11, 383-389. DOI: 10.4103/1735-5362.192488

Scholey, A., Gibbs, A., Neale, C., Perry, N., Ossoukhova, A., Bilog, V., Kras, M., Scholz, C., Sass, M., Buchwald-Werner, S., 2014: Anti-stress effects of lemon balm-containing foods. Nutrients 6, 4805-4821. DOI: 10.3390/nu6114805

Senderski, M.E., 2009: Melisa lekarska, in: Zioła. Praktyczny poradnik o ziołach i ziołolecznictwie. Wydawnictwo K.E. Liber. Warszawa, 422-426.

Sepand, M.R., Soodi, M., Hajimehdipoor, H., Soleimani, M., Sahraei, E., 2013: Comparison of neuroprotective effects of *Melissa officinalis* total extract and its acidic and non-acidic fractions against a β-induced toxicity. Iran. J. Pharm. Res. IJPR 12, 415-423. PMID: 24250617.

Soltanpour, A., Alijaniha, F., Naseri, M., Kazemnejad, A., Heidari, M.R., 2019: Effects of *Melissa officinalis* on anxiety and sleep quali-ty in patients undergoing coronary artery bypass surgery: A double-blind randomized placebo controlled trial. Eur. J. Integr. Med. 28, 27-32. DOI: 10.1016/j.eujim.2019.01.010

Soodi, M., Naghdi, N., Hajimehdipoor, H., Choopani, S., Sahraei, E., 2014: Memory-improving activity of *Melissa officinalis* extract in naïve and scopolamine-treated rats. Res. Pharm. Sci. 9, 107-114. PMID: 25657779.

Taavoni, S., Nazem Ekbatani, N., Haghani, H., 2013: Valerian/lemon balm use for sleep disorders during menopause. Complement. Ther. Clin. Pract. 19, 193-196. DOI: 10.1016/j.ctcp.2013.07.002

Taiwo, A., Leite, F., Lucena, G., Barros, M., Silveira, D., Silva, M., Ferreira, V., 2012: Anxiolytic and antidepressant-like effects of *Melissa officinalis* (lemon balm) extract in rats: Influence of administration and gender. Indian J. Pharmacol. 44, 189-192. DOI: 10.4103/0253-7613.93846

Tavares-Silva, C., Holandino, C., Homsani, F., Luiz, R.R., Prodestino, J., Farah, A., Lima, J.P., Simas, R.C., Castilho, C.V.V., Leitão, S.G., Maia, L.C., Fonseca-Gonçalves, A., 2019: Homeopathic medicine of *Melissa officinalis* combined or not with *Phytolacca decandra* in the treatment of possible sleep bruxism in children: A crossover randomized triple-blinded controlled clinical trial. Phytomedicine. 58, 152869. DOI: 10.1016/j.phymed.2019.152869

Wojdyło, A., Oszmiański, J., Czemerys, R., 2007: Antioxidant activity and phenolic compounds in 32 selected herbs. Food Chem. 105, 940-949. DOI: 10.1016/J.FOODCHEM.2007.04.038

Yoon, M., Kim, M.-Y., 2011: The anti-angiogenic herbal composition Ob-X from Morusalba, *Melissa officinalis*, and *Artemisia capillaris* regulates obesity in genetically obese ob/ob mice. Pharm. Biol. 49, 614-619. DOI: 10.3109/13880209.2010.539617

Zarei, A., Changizi Ashtiyani, S., Taheri, S., Rasekh, F., 2014: Comparison between effects of different doses of *Melissa officinalis* and atorvastatin on the activity of liver enzymes in hypercholesterolemia rats. Avicenna J. Phytomed. 4, 15-23. PMID: 25050297.

ZERAATPISHE, A., ORYAN, S., MOHAMMAD HADI BAGHERI, M.H., ALI ASGHAR PILEVARIAN, A.A., ALI AKBAR MALEKIRAD, A.A., BAEERI, M., ABDOLLAHI, M., 2011: Effects of *Melissa officinalis* L. on oxidative status and DNA damage in subjects exposed to long-term low-dose ionizing radiation. Toxicol. Ind. Health 27, 205-212. DOI: 10.1177/0748233710383889

ORCID
Katarzyna Świąder https://orcid.org/0000-0003-2706-2327
Christofora Hanny Wijaya https://orcid.org/0000-0002-2938-7662

Address of the corresponding author:
Katarzyna Świąder, Institute of Human Nutrition Sciences, Warsaw University of Life Sciences-SGGW, Warsaw, Poland