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MELISSA OFFICINALIS – AN OVERVIEW AND ITS PROPERTIES AS AN ANXIOLYTIC

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ABSTRACT: *Melissa officinalis* commonly known as Lemon balm belonging to mint family has been found to have an effective remedy as an anxiolytic. Anxiety is a prevalent psychological ailment spread worldwide and it impairs the normal functioning of an individual. Instead of numerous medications available, still it's not resolved completely and anxiolytic medications have its side effects as well. Therefore turning towards the herbal medications might provide a safe and effective way to treat this condition.

Keywords- *Melissa officinalis*, Lemon balm, Anxiety, Ayurveda, Traditional

1. INTRODUCTION

Melissa officinalis or the commonly called lemon balm plant is the perennial herbaceous species belonging to mint family (Lamiaceae). The taxonomical data of the plant revealed following details.

Kingdom - Plantae

Order - Lamiales

Family - Lamiaceae

Genus - Melissa

Species – Officinalis

More than a 2500 years, the aromatic leaves of the plant have been used widely in cooking for adding flavor (Osbaldeston; 2000). *Melissa officinalis* is enlisted in various pharmacopoeias e.g. Iranian Herbal Pharmacopoeia, the British Pharmacopoeia along with the European Pharmacopoeia. Novel pharmacology studies show that *Melissa officinalis* possesses many biological properties, including hypoglycemic, antioxidant, lipid-lowering, antibacterial, anticarcinogenic, for treatment of depression, anxiety, also as an antinociceptive, anti-inflammatory and an antispasmodic (Gabriela, et al; 2022). In addition,

phytochemical studies have showed the chemistry of volatile compounds, phenolic acid, phenolic acids as well as flavonoids as major active constituents of *Melissa officinalis*.



Fig.1. *Melissa officinalis* plant (Zarei, et al; 2015)

2. PLANT PROFILE

Melissa officinalis, also called lemon balm, melissa, sweet balsam, a lemon like smelling perennial plant. Family- Lamiaceae (Awad, et al; 2009). *Melissa officinalis* shows growth to 30 to 125 cm in height and is covered of short hairs or pale pink and consist of 4-12 small inflorescences in summer. There are 2 stamens and 4 lobed ovaries, forming 1-4 nuts. Small seeds, 1-1.5mm long, Ovate, brown and black in color. Lemon balm grows rapidly in a range of 35°C temperature, 500 to 600 mm of rainfall, and distributed well in the growing season. With irrigation required (Saeb, et al; 2012). *Melissa officinalis* shows haired root system alongside many lateral roots, allowing it to adapt better to different external environmental conditions.

2.1. Active constituents

Chemical screening of aerial parts of this plant such as leaf revealed few essential constituents such as Citral, Monoterpenes, Geranial along with Flavonoids such as luteolar7-o-Glucoside (0.0002%).

Dried leaves of this plant shows the presence of 0.134% Citral, 11.8% Polyphenolic constituent with 11.34% Cinnamic compounds. Chemical screening also revealed 2.2% Methyl heptenone, 14.4% Citronellal, 2.7% Linalool, 47.5% Geranial, 6-7% Isogeraniol, Geranyl acetate 10% and 11% Caryophyllene oxide along with alpha-pinene, Cispara-Meth-2-en-7-ol, Nerol acetate, IR-alpha-pinene, Carane, Verbenol, Verbenone, Menthol, Germanicol, Longifolene, Himachala 2, 4 -diene and Andropholide. This plant is known for exhibiting various medicinal importance in the conditions such as gastrointestinal



disturbance, oxidative stress and other neurological disorders (Abolfazl, et al; 2015). Pharmacological activities which has been performed over this plant include antiviral activity which was essentially done over HSV-1 (human herpes virus) and it was found that M1-M4 extracts of *Melissa officinalis* were showing antiviral or virucidal activities even in the small concentration of 1.5 µg/ml. The antioxidant and immune modulating activities are credited to its free radical scavenging property and was demonstrated in rats with acute oxidative stress. Novel pharmacological actions of *Melissa officinalis* is the inhibitory action against GABA transaminase in in-vitro studies by the methanolic extract of the plant is found to be effective against the neurological disorders such as anxiety, epilepsy and other disorders.

2.2.Traditional uses-

The medical use of *Melissa officinalis* began more than 200 decades back. In traditional European writings, *Melissa officinalis* was addressed as melissafillon, baulme, lemon balm. Dioscorides (40-90 AD), mentioned this plant in the book De Materia Medica. He also recommended this plant for amenorrhea, dysentery, asphyxia due to mushroom poisoning, intestinal ulcers, abdominal pain, dyspnea, swollen tumors and other tumors, toothache and joint pain(Osbaldeston, 2000).

Lemon balm was used in stopping bleeding , relieving toothache, morning sickness, baldness and neck pain in the middle age (Saad, et al; 2011). *Melissa officinalis* can increase longevity and restore memory .Thomas Cogan (1545-1607) claimed that drinking *Melissa officinalis* tea daily in his students improved their comprehension and improving memory. Also he suggested the use of distilled water made with blended berglos and borage with melissa to soothe melancholy. Evelyn (1620–1706), through his Acetaria Discourse on Salad , the first recorded book on lettuce, referred to lettuce as “Melissa and Baum” with descriptive qualities such as “burnt and spicy”. Dry”, “hearty an Invigorating”, improving memory and antidepressive.

Melissa officinalis can be used in treating insomnia by depression and sadness (Haybar et al; 2018). *Melissa officinalis* being an important medicine plant in ITM i.e. Iranian Traditional Medicine. Avicenna (981- 1037AD), an outstanding Iranian physician and philosopher, described the plant in his “Medicine Canon” as remedy for all ailments caused due to phlegm , black bile, including depression, anxiety, obsessive-compulsive disorder with psychosis. He believed that due to the plant’s scent there was a powerful invigorating effect (Scholey, et al; 2014).

Aromatherapy inhalation using the plant has been suggested for treating nightmares and other sleep disorder (Aghili Khorasani, 1992). *Melissa officinalis* is used for certain eye related



disorders like severe conjunctivitis and vision impairment due to aqueous humor opacity. According to the main pharmacopeia of ITM, in a simple preparation, 40 gm dry leaves, 80 gm fresh leaves and 9 gm dried plant seeds used. However, *Melissa officinalis* has been used as multi-component preparations to enhance efficacy due to synergistic effects of herbal medication. *Melissa officinalis* in dosage of these formulations varies sufficiently.

In Ayurvedic system, *Melissa officinalis* is believed to improve memory-related issues and thus have a nootropic action (Soodi, et ; 2014). Interestingly, there are similarities in the traditional uses of the plant in various cultures like the treatment of mental conditions, particularly anxiety as well as depression, Recovery from cardiac related diseases with nootropic action.

As described above, *Melissa officinalis* has been commonly used as complex herb formulas to enhance efficacy. It's worth noting traditionally that the aerial parts of the plant were utilized with less attention being paid to roots. Also it should be noted, the *Melissa officinalis* preparations had been mainly available as infusions and teas to prevent degradation and preserve active ingredients, especially essential oil of *Melissa officinalis* of countries around the world.

3. PHARMACOLOGICAL POTENTIALS

Various pharmacological potentials of *Melissa officinalis* plant are as follows-

3.1 Antidepressants activity

Traditionally, *Melissa officinalis* has been used as invigorating medicine which is documented ancient texts. With an in-vitro study, methanolic and aq. extracts of *Melissa officinalis* were able to slightly suppress monoamine oxidase (MAO-A), with latter extraction showing more inhibitory effect. (Lopez, et al; 2009).

3.2 Neuroprotective activity

Usage of *Melissa officinalis* for the treating of several CNS related diseases in several countries has been supported by in vitro and in vivo research of neuro-protective activities. Treatment of cells (PC12) with *Melissa officinalis* methanolic extract protected these cells from hydrogen peroxide toxicity in MTT as well as LDH assays (a cell viability assays which are often used in determining cytotoxicity after being exposed to toxic substances). However, both of the aqueous extract as well as methanolic extract significantly reduced intra-cellular "ROS" production, indicating an essential neuroprotective activity(Lopez, et al; 2009).

Pretreatment in PC12 cells with acidic *Melissa officinalis* ethanolic extract contains polyphenols, terpenoids and flavones has a protective effect in A β -induced toxic effects and



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oxidation related stress, which could explain the antioxidant property of the plant(Sepand, et al; 2013).

3.3 Nootropic activity

Melissa officinalis has traditionally been used to treat dementia with amnesia, which are closely related to Alzheimer's (AD). The plant is also registered as an antipsychotic. Acetylcholinesterase inhibitors (AChE) enhance and prolongs the action of acetylcholine on brain synapse. The cholinergic effect can aggravate AD along with its cognitive symptoms like mainly memory and learning disability (Soodi, et al; 2014).

3.4 Cardiovascular activity

Melissa officinalis being a traditional remedy for palpitations and has been considered as powerful cardiac tonic and cardio protective herb. Studies have focused on the anti-arrhythmic profile of *Melissa officinalis*. In vivo studies demonstrated the ethanol extract of plant reducing the ventricular extra systole (PV) along with ventricular fibrillation (VF) and tachycardia (VT) after Calcium chloride stimulated arrhythmias in rat models (Akhondali, et al; 2015).

3.5 Hypoglycemic activity

Melissa officinalis shows obvious sugar lowering effects both in vivo and vitro with treating diabetic conditions. *Melissa officinalis* ethanolic extract in concentration of (0.6 mg/mL) to primary human adipose cells induced expression of "PPAR" genes in metabolic-related cells. Further studies at doses less likely to be administered to humans are needed to reproduce the same effects in a clinical setting. Treatment in insulin-resistant mice for 6 weeks by an ethanolic extract of dosage (200 mg/kg) of lemon balm significantly decreased the hypoglycemic and insulin resistant conditions (Weidner, et al; 2014).

3.6 Hypolipidemic activity

Melissa officinalis can remove harmful substances present in blood. Also, it is widespread used as a cardio-protective agent second to its lipid-lowering activity. Intraperitoneal administration of an ethanolic extract of *Melissa officinalis* in rats with hypercholesterolemia (25- 75 mg/kg) results in uptaking liver enzymes such as Alanine aminotransferase (ALT), Alkaline Phosphatase (AP) and Aspartate amino Transferase (AST) decreased levels. Serum homologous to atorvastatin in effect (Zarei, et al; 2014). Additionally, treating obese rats resistant to insulin by ethanolic extract of dosage (200 mg/kg/day) effectively reduces the plasma triacylglycerols levels (TAGs), Low density lipoprotein (LDL) /Very low density lipoprotein (VLDL) cholesterol and fatty acids which are non esterified (Weidner, et al; 2014).



3.7 Anti-inflammatory & anti-nociceptive activity

Referring to traditional literature, *Melissa officinalis* was used to treating several inflammatory diseases along with asthma and inflammation in joints. Also been used as pain relieving medicine. Numerous pharmacology studies has shown activity against inflammation and nociceptive effects by lemon balm. *Melissa officinalis* significantly reduces induced inflammation in rat's paw model(Birdane, et al; 2007). In addition, the ethanolic extract of MO exhibited a dosage-dependent anti-nociceptive effect in mice through inhibitory effect on the L-arginine-nitric oxide path and activates the cholinergic mechanism and it was due the presence of rosaminic acid in plant(Guginski, et al; 2009).

3.8 Anxiolytic activity

Anxiety can be defined as the psychological condition associated with the feeling of dread and nervousness which is the major cause of the decrement in the individual's quality of life. Physiological effects of the anxiety or anxiousness effects the cerebral cortex, hippocampus and the thalamus as those reach lateral amygdala which in turn relay the basolateral amygdala and then to central amygdala and thus initiates the anxiety responses which includes nervousness , feeling of worry and sense of danger. (Elizabeth, et al; 2009). Anxiety can be differentiated into two types i.e. state and trait . State anxiety is an acute condition caused due to hypervigilance of a situation and it seem to facilitate memory consolidation . Trait anxiety is a chronic condition which is caused due to long term exposure of stress like conditions (Naval, et al; 2018).

Anxiety can be caused due to the exposure of certain chemicals and such chemicals can be used for the induction of anxiety in various animal models for the purpose of pharmacological evaluation of anxiolytics. Such activity is found to be due to the active principles such as Oleanolic acid and Rosaminic acid. Studies revealed cognitive and mood regulating activity of *Melissa officinalis* performed on human subjects during double blind trial (Do, et al; 2003).

The dosage regimen of 300 mg of the plant extract was identified as producing 'Calmness' in human subjects and dosage of 600mg was reported to have increased the attentiveness in the subjects. Anti-acetylcholinesterase activity of the *Melissa officinalis* is demonstrated in a dosage depending manner in previous studies (Ferreira, et al ; 2006).It was found that in pregnant females 600 mg capsules was administered and statistics showed a decrease in the pregnancy related anxiety (Naval, et al; 2017).



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Aqueous extraction of the *Melissa officinalis* has shown decrease in corticosterone levels in the dosage of 60 mg/kg. *Melissa officinalis* has also plant is branched, erect and glabrous. Leaves being petiolate with ovate shape upto 6 cm in length and 3 cm wide along with toothed crenate with punctuate glands underneath. In June and August the crop is grown in Northern hemisphere. Predominantly it is marketed along with 49 products out of which the combination with *Valeriana officinalis* is widely used for the sleep disorders (Do, et al; 2003).

The tumourocidal activity was studied in mouse melanoma cell lines in ratio of 1:50000 to 1:2000 inhibition. Antioxidant activity is due to 1,1 diphenyl-2-picrylhydrazyl radical was studied at absorbance of 575 nm by hydroalcoholic extract of lemon balm (Joner, et al; 2019). Anxiety is a neuropsychological disorder which has been crippling millions of people and even though there are various anxiolytic medication available, still the condition is not controlled effectively and research is ongoing regarding its prevention. Most population is on prescription medications of benzodiazepines and barbiturates. For the research of anxiolytic medication rats are often chose as a test species due to their resemblance with humans in anxiety response as increased vigilance and freezing.

In brain the bed nucleus of Stria Terminalis produces anxiety like symptoms (Kimberly, et al; 2017). GABA being an inhibitory neurotransmitter in CNS which reduce the nerve impulse transmission among neurons by hyperpolarization of post-synaptic membranes and reducing the neurotransmitter release in synapse through pre-synaptic GPCR (G-protein coupled receptors) inhibiting calcium ion-gated voltage mechanism (Elizabeth, et al; 2009).

Therefore this system is responsible for the cognitive behavior in rats as well as humans.(Eivan, et al; 2020). Melissa also displaces the (3H) (N)-escopolaminica, (3-H-N) nicotinic and M receptors by increasing the acetylcholine (Ach) following nerve stimulation which might improve cognitive function (Barbara, et al; 2015).There is a dependency risk too which is associated with lemon balm which is due to its tolerance build up in longer administration (Barbara, et al; 2015).There has been several recordings of the usage of *Melissa officinalis* in sedation. Several recent studies have confirmed the anxiolytic profile of *Melissa officinalis*. With an in-vitro study of rats' brains, *Melissa officinalis* with its main compound i.e. RA, shows inhibitory activity in GABA-T pathway(Awad, et al; 2009).



4. CONCLUSION

Melissa officinalis has been an essential plant from ancient times for the variety of traditional and medicinal uses. The chemistry of the plant has been reported for effectivity against various physiological and psychological ailments and various clinical studies have been conducted so far. The activity includes anti-depressant to nootropic and anxiolytic effect including hypoglycemic, hypolipidemic and anti-inflammatory as well. Still there is a room for further research and learning about its other pharmacological activities which can be used further into treating diseases.

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