

## Mellisa Officinalis (lemon balm) - A Pharmacognostical Overview.

<sup>1</sup>C.Chandni, <sup>2</sup>V.Abarna, <sup>2</sup>A.Vedavani, <sup>2</sup>G.Gomathi, <sup>2</sup>D.Yasodha Lakshmi,

<sup>1,2</sup>Student, Vivekanandha Pharmacy College for Women,

Veerachipalayam, Sankari West, SankariTk

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### ABSTRACT:

Mellisa officinalis, commonly known as lemon balm, is a plant cultivated in certain regions of Iran. The leaves of this plant belonging to lamiaceae family have been utilized in Iranian traditional medicine for various purposes such as aiding digestion, relieving spasms, inducing relaxation, providing pain relief, acting as a tonic and promoting diuresis, this comprehensive review article not only introduces MO covering its growth requirements, chemical constituents and traditional application, but also provides an in-depth exploration of its properties by compiling and analysing available research, additionally, the study delves into a detailed examination of the anti-oxidant properties associated with mellisa officinalis. This review contributes to a comprehensive understanding of the plant's diverse attributes and potential health benefits.

**KEYWORDS:** Mellisa officinalis, badranjboya, lemon balm, depression, anti-cancer, anti-microbial effect, anti-oxidant, anti-spasmodic, alzheimer, anti-herpes.

### I. INTRODUCTION:

The active compounds present in medicinal plants can be derived from various plant parts, such as seeds, roots, leaves, fruits, skin, flowers or the entire plant itself. These extracted substances from medicinal plants often possess therapeutic effects either directly or indirectly. *Melissa officinalis* L is a widely used medicinal plant in traditional medicine across the globe. This aromatic perennial plant is predominantly found in the Mediterranean region and Western Asia with extensive cultivation in Europe. Due to its chemical composition and diverse pharmacological effects, it has been the subject of extensive research. Commonly known as lemon balm, honey balm, or balm mint, it belongs to the edible medicinal herb

category within the mint family Lamiaceae and the subfamily Nepetoideae. This plant typically has a lifespan of at least three years and grows in a bushy, upright manner reaching a height ranging from 60 to 100 cm. The leaves are soft, hairy, dark green and heart-shaped, measuring 2 to 8 cm in length. They have a coarse and deeply veined surface with a scalloped or toothed edge. The leaves are rich in biologically active components, which contribute to their specific properties. M.O possesses a hairy root system, enabling it to adapt to various environmental conditions. However, its upper parts die out in early winter and remerge in early spring. It is considered one of the easiest herbs to grow and has a tendency to spread rapidly, leading some gardeners to consider it a weed.

### DESCRIPTION:

*Melissa officinalis* L. is a hardy plant that can thrive in Zone 4 and is resistant to frost. It blooms from June to October, with its seeds maturing between August and October. The flowers of this plant are hermaphroditic, possessing both male and female reproductive organs and they rely on bees for pollination. *Melissa officinalis* is known for its ability to attract wildlife. When it comes to soil preferences, the plant does well in light (sandy) and medium (loamy) soil as long as the soil is well-drained. It can also tolerate a range of soil PH levels, including acidic, neutral and alkaline soils. In terms of sunlight requirements, it can grow in partially shaded areas, such as light woodlands, but it is also adaptable to no shade conditions. The plant can tolerate both dry and moist soil conditions, and it has a certain level of drought tolerance.

### TAXONOMICAL CLASSIFICATION:

**KINGDOM** - Plantae

**DIVISION** - Tracheophyta

**SUBDIVISION** - Spermatophyta  
**CLASS** - Magnoliopsida  
**SUPERORDER**- Asteranae  
**ORDER** - Lamiales  
**FAMILY** - Lamiaceae  
**GENUS** - Melissa  
**SPECIES** - Melissa officinalis L.



**Fig 1: Mellisaofficinalis**

#### **CULTIVATION DETAILS:**

Lemon balm is commonly cultivated in Europe and the United States, and it also grows wild along paths and roadsides. The plant thrives in sandy and loamy fertile soils with good drainage and a pH range of 5-7. While it prefers full sun, it can also grow in partial shade. Lemon balm shows larger leaves and habitat when grown in semi-shade compared to sunny conditions. It grows well at temperatures between 15 to 35°C and needs 500 to 600 mm of evenly distributed precipitation throughout the growing season. In case of insufficient rainfall, irrigation is necessary, especially during the establishment year when it is sensitive to drought. As the plant develops a deep root system, its water needs decrease additionally, our wild flora has three other naturally occurring subspecies: subsp. officinalis and subsp.

#### **CULTIVATION DIFFERENT BREED:**

The cultivars of *M. officinalis* include:

*M. officinalis* 'Citronella'  
*M. officinalis* 'Lemonella'  
*M. officinalis* 'Quedlinburger'  
*M. officinalis* 'Lime'  
*M. officinalis* 'Mandarina'  
*M. officinalis* 'Variegata'  
*M. officinalis* 'Aurea'

Each cultivar may exhibit different characteristics in terms of leaf color, scent or growth habit providing options for various preferences and garden design

#### **CHEMICAL COMPOSITION:**

The essential oil content in lemon balm, a member of the labiatae family, varies between 0.02% and 0.30%, which is relatively low compared to other family members. Consequently, the production cost and market price of the essential oil are notably high. The essential oil's primary constituents are Citral (geranial and neral), citronellal, geraniol, beta-pinene and beta-caryophyllene, constituting around 96% of the oil. Citral constitutes 48% of the essential oil, with citronellal accounting for 39.47%, and caryophyllene contributing

2.37%. In a separate investigation, Sarer and Kokdil identified key components like alpha-pinene (2.86%), beta-pinene(11.37%), linalool (2.74%), citronellal (5.86%), borneol (0.62%), neral (12.22%), and geraniol (38.13%) in lemon balm. Moreover, fresh lemon balm is abundant in significant quantities of total phenolic compounds (2253 /100 mg), L-ascorbic acid (53.2 /100 mg), and carotenoids (46.3 /100 mg). It's worth noting that various subspecies of *Melissa* exhibit distinct chemical profiles. Subspecies *altissima*'s oil consists mainly of beta-cubebene, terpinolene, gamma-3-carene, terpinene, beta-caryophyllene, and muurolol. Subspecies *inodora*, used in Turkish folk medicine, contains beta-cubebene, beta-caryophyllene, alpha-cadinol, geranial, and neral (7% and 6% respectively). While the quantitative composition of lemon balm's essential oil may vary, its qualitative components remain relatively constant.

Citral isomers geranial and neral are consistently identified as the main components of *M. officinalis*. In the chemical analysis of essential oils from *M. officinalis* L., neral and beta-caryophyllene emerged as the primary components.

Fresh herbs contain a range of beneficial compounds, including phenolic compounds, l-ascorbic acid, carotenoids, flavonoids, and terpenoids. Lemon balm leaves, for instance, are notably abundant in flavonoids, comprising 0.5% of their dry weight. These flavonoids consist of quercitrin (a derivative of quercetin), rannocitrin, luteolin, and its various derivatives (like 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 glucuronopyranoside). Among the prominent terpenoids found are neral, geranyl acetate, ursolic acid, and tannins. Notably,

the hydroethanolic extract of lemon balm leaves reveals the presence of 0.087 g/100 g of caffeic acid and 21.15 g/100 g of rosmarinic acid



Fig 2: Various health properties of the Melissa officinalis.

**PLANT EXTRACT PREPARATION:**

The dried leaves of *M.Officinalis* were provide d by centoflora group (Botucatu ,Brazil) along with a plant identity and quality certification. To extract, 1900g of powdered plant material was macerated at room temperature (24±3°C) using ethanol as the solvent. The solvent was then

removed under vacuum condition below 40°C using a Helidolph system (Helidolph system ® Instruments, Germany) consisting of a rota vapour ,vacuum pump D-91126 and chiller MX07R-20HD2E. The resulting crude ethanolic extract (EE) with a yield 13%, was stored at -18°C.

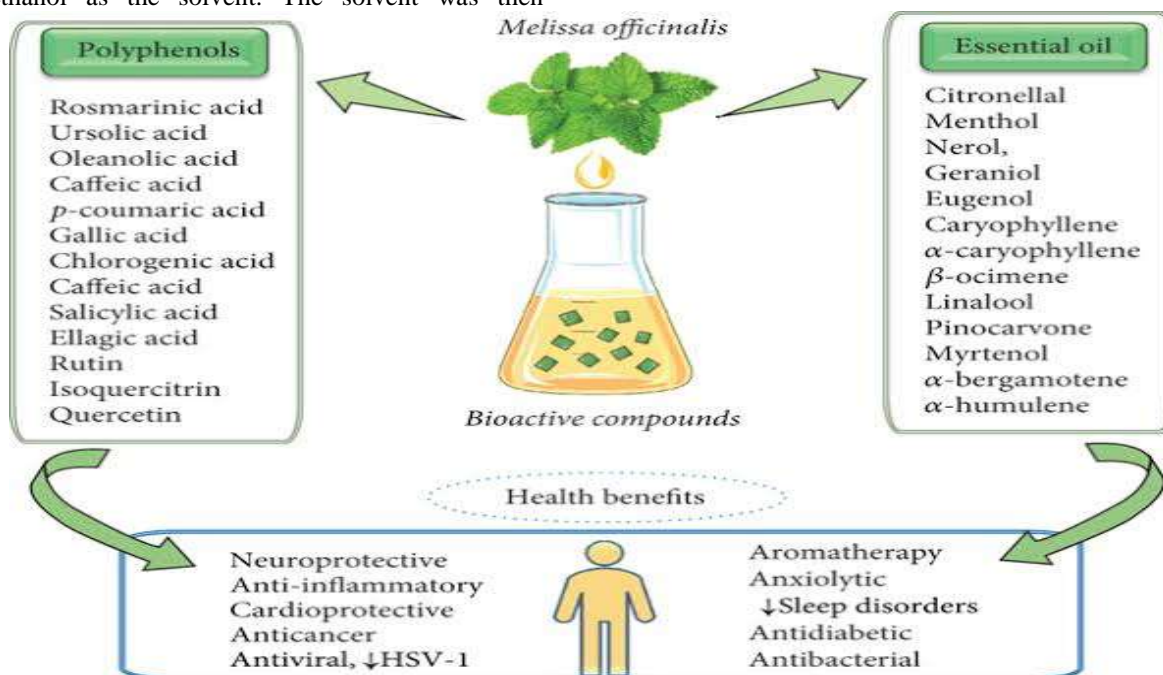


Fig 3:

Bioactive compounds from *M officinalis* and their correlation with biological activities.

### PHARMACOLOGICAL ACTION:

The essential oils extracted from Sefrou lemon balm contains six main components, including citronellal (14.40%), isogeraniol (6.40%), geraniol acetate (10.20%), nerol acetate (5.10%), caryophyllene (8.10%) and caryophyllene oxide (11.00%), which together made up 55.20% of the total oil. The leaf components consist of citral, monoterpenes geranial and neral, along with flavonoid luteolin-7-o-glucoside (0.0002%). The oil extracted contained geranial, neral, 6-methyl-5-hepten-2-one, citronellal, geranyl-Acetate,

$\beta$ -caryophyllene, and  $\beta$ -caryophyllene oxide. The dried leaves of lemon balm contained 0.13% citral (composed of neral and geranial) and a total of 11.8% polyphenol compounds. Among these, the lemon balm leaves had 11.3% total hydroxycinnamic compounds, with rosmarinic acid contributing to 4.1% of this amount and total flavonoid compounds at 0.5%. Known compounds were identified from dried stems and leaves of *Melissa officinalis*, including quadranoside III, salvianic acid A, rosmarinic acid and luteolin. The extracts' free radical scavenging and antimicrobial activities, as well as those of rosmarinic acid, the major component, were evaluated.

### ANTI-MICROBIAL EFFECT:

The essential oil demonstrated strong antimicrobial effects against various microorganisms, notably five bacteria harmful to humans, one yeast known as *Candida albicans*, and two plant-damaging fungi.

The essential oil displayed antifungal properties against *Trichophyton* species. Additionally, the antimicrobial capabilities of the essential oil extracted from Romanian *Melissa officinalis* were tested, revealing significant activity against *Candida albicans*. Lemon balm oil did not impact gram-negative bacteria.

### ANTI-OXIDANT:

Research revealed that lemon balm extract possesses the capability to neutralize both artificial

and natural free radicals. This finding holds significance as it suggests the extract might have the potential to counteract oxidative damage in living organisms by mitigating oxidative stress caused by free radicals. The extract's antioxidant potential was further enhanced due to its ability to chelate iron (II).

Lemon balm underwent analysis to assess its antioxidant properties, total phenolic content, L-ascorbic acid and carotenoid levels. The extract demonstrated a notably high capacity to neutralize the DPPH free radical (2,2-diphenyl-1-picrylhydrazyl).

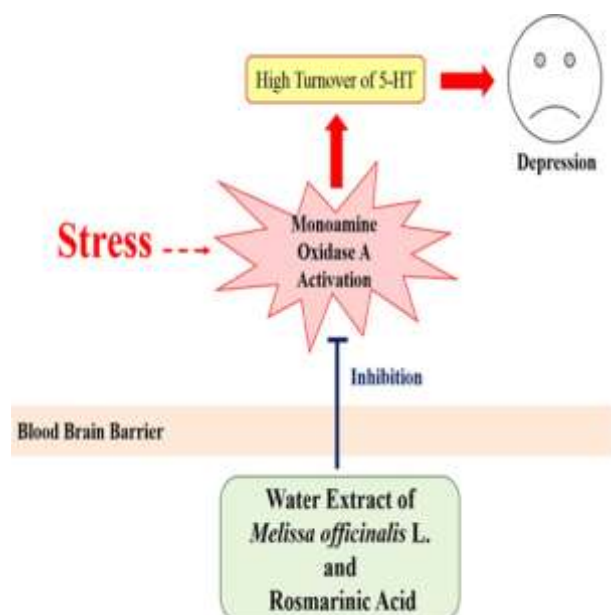
### ANTI-DEPRESSANT:

Investigation into the water extract of this plant focused on its potential antidepressant-like effects. This was assessed through an examination of its impact on rat behavior and relevant neurotransmitters during a forced swimming test.

The behavioral outcomes resulting from the acute or subacute oral administration of *M. officinalis* ethanol extract were also studied in relation to anti-depression effects.

The study aimed to explore the potential neuroprotective properties of the complete ethanolic extract as well as the acidic and nonacidic fractions derived from *Melissa officinalis*. The focus was on their ability to counteract cytotoxicity and oxidative stress in PC12 cells, alongside an assessment of their anticholinesterase activity in vitro.

The observed neuroprotective effects of both the total extract and the acidic fraction of *Melissa officinalis* were found to be independent of their anticholinesterase activity. Notably, the acidic fraction exhibited a stronger protective effect compared to the total extract. This suggests that the neuroprotective potential could be attributed to the presence of polyphenolic compounds and terpenoid acids, which are concentrated within this specific fraction of the extract.



#### ANTI-HERPES & ANTI-HIV EFFECT:

The study delved into investigating the virucidal and antiviral properties inherent in extracts derived from *Melissa officinalis* L. (referred to as M1, M2, M3, and M4) in relation to their impact on Herpes simplex Virus type 1. The results indicated that M1, M2, and M3 did not yield significant inhibitory effects on the Virus, both in vitro and in vivo. The antiviral potency of *Melissa officinalis* L. was ascribed to the presence of specific compounds, namely Caffeic, rosmarinic, and ferulic acids. These compounds were found to play a contributory role in the Observed antiviral activity against Herpes simplex virus type.

#### ALZHEIMER'S DISEASE:

The study aimed to explore how the cholinergic system influences the memory-enhancing effects of *M. Officinalis* extract. The findings suggest that *M. officinalis* has the capacity to enhance memory, with the cholinergic characteristics of the extract potentially playing a role in the Observed. Memory-improving effects. Consequently, the extract from *M. officinalis* holds promise as a Potential therapeutic option for ameliorating specific memory impairments often observed in Alzheimer's disease (AD).

#### ANTI-CANCER:

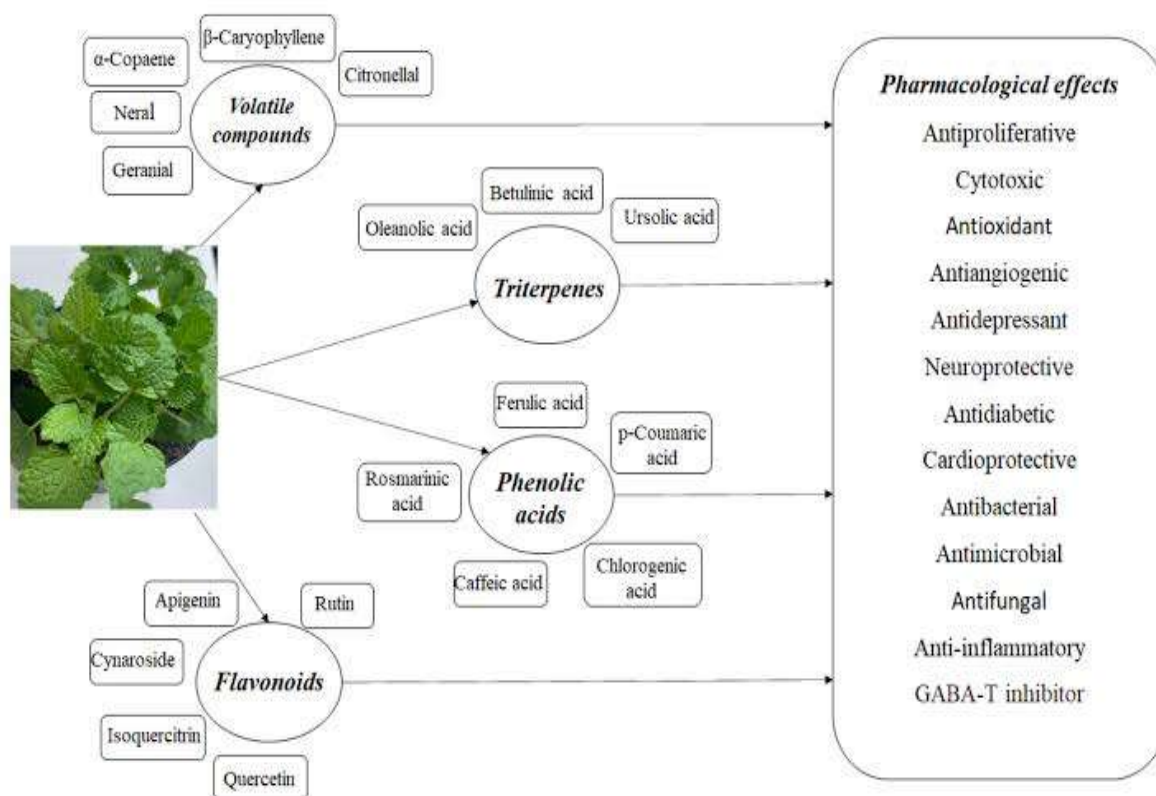
The study focused on exploring the impact of the ethanolic leaves extract of *Melissa Officinalis* on human colon carcinoma cells, aiming to uncover its antiproliferative and proapoptotic effects. The findings revealed that the

extract effectively hindered the proliferation of colon carcinoma cells and Triggered apoptosis by generating reactive oxygen species (ROS). In an independent study, researchers evaluated the impact of both *Melissa officinalis* essential oil (EO) And its primary constituent, citral, on GBM cell lines. These results suggest that the essential oil, particularly through its primary component citral, could hold potential as a therapeutic approach for Treating GBM. Furthermore, it was suggested that *Melissa officinalis* extract (MOE) contributes to increased cell Proliferation, differentiation of neuroblasts, and integration into granule cells.

#### ANTI-SPASMODIC ACTIVITY:

The study delved into investigating the anti-inflammatory properties present in *Melissa officinalis* L leaves. The essential oil derived from *Melissa officinalis* L demonstrated noteworthy anti-inflammatory effects, Lending support to the plant's traditional use in addressing various conditions associated with inflammation And pain. Moreover, the study investigated the potential antinociceptive properties of the ethanolic extract derived From *Melissa officinalis* L, along with the influence of rosmarinic acid using chemical behavioral models to Assess nociception. The outcomes of the study indicated that the extract exhibited dose-dependent Antinociception across several chemical pain models, involving muscarinic and nicotinic acetylcholine Receptors, as well as the L-arginine-nitric oxide pathway. Additionally, it was observed that the presence of Rosmarinic

acid within the plant contributed to the antinociceptive attributes of the extract.



**Fig 4: The composition of *Melissa officinalis* and its pharmacological effects**

**SAFETY CONSIDERATIONS:**

A single dose of lemon balm extract (containing 100, 250 or 500 mg of rosmarinic acid) didn't show adverse effects on health, blood morphology or biochemistry. Another study found increased appetite as the only side effect of using lemon balm (1,000 mg dry extract/day). However, withdrawal symptoms, including anxiety, irritability, decreased appetite, concentration and sleep disruption, were observed in a case where a person consumed up to 4 cups of lemon balm infusion daily for around 2 months.

**SAFETY PROFILE:**

In healthy adults, no adverse reactions were reported after up to 30 days of recommended intake or amounts found in food. Lemon balm (*Melissa officinalis*) is categorized as generally regarded as Safe. However, caution is advised for pregnant women, nursing mothers and paediatric patients due to demonstrated genotoxic properties in *In Vitro* studies. Lemon balm is also not recommended for those with thyroid disorders or using tranquilizers

**CASES STUDIES:**

*M. officinalis* extract reduced liver cholesterol, total lipid, lipid peroxidation and liver enzymes while increasing glutathione levels in Hyper-Lipidemic rats. Liver showed that *M. officinalis* extract positively affected the pituitary-thyroid axis in rats with hypercholesterolemia, leading to increased thyroid hormone levels and decreased thyroid stimulating hormone (TSH) levels through a feedback mechanism.

**RECIPROCITY:**

When using this substance during pregnancy or lactation, in paediatric patients, and in individuals with thyroid disorders or when combined with sedatives, as it may pose potential risks

**MEMORY ENHANCEMENT:**

In a separate study, BS and MO tablet supplementation improved memory scores in participants, particularly in older adults who often

experience age-associated memory impairment. The combined effects of BS and MO supplementation on memory haven't been extensively studied before.

#### **FUTURE PERSPECTIVE:**

These plants possess a wealth of bioactive substances and can serve as valuable resources for the development of novel semi-synthetic drugs. Additional research is necessary to conduct clinical trials on cancer and develop new anticancer drugs. Future investigations should focus on exploring through correlation between the overall antioxidant capacity and the content, as well as the composition of antioxidants. Further studies are also required to delve into the mechanism underlying the antioxidant activity of phenolic compounds. These studies would enhance our understanding of how these compounds scavenge reactive oxygen species (ROS) and bind to metals, providing oxidative protection and facilitating the design of improved antioxidants for disease treatment and prevention. Moreover, it is essential to examine the interrelationship between phenolic compounds and their antioxidant and anticancer activities to elucidate potential mechanisms for cancer prevention and treatment. By conducting such research, we can gain valuable insights into the possible therapeutic effects of these compounds in combating cancer. In the context of future prospects, the interplay between *Melissa officinalis*' phytochemical profile and its pharmacological benefits stands poised to catalyse novel controlled release systems, presenting exciting possibilities for targeted delivery solutions. Additional research is required to conduct clinical trials focusing on the development of new anticancer drugs. Subsequent investigations should emphasize understanding the relationship between total antioxidant capacity, antioxidant content and composition. Further more, there is a need for further studies to delve into the mechanism responsible for the antioxidant activity of phenolic compounds. Such endeavours would advance our

knowledge of how the scavenging of reactive oxygen species and the metal-binding antioxidant mechanisms contribute to oxidative protection, ultimately leading to improved design of antioxidants for disease prevention and treatment. Additionally, exploring the interplay between phenolic compounds and antioxidant/anticancer activity will provide insights into potential mechanisms for both preventing and treating cancer.

#### **II. CONCLUSION:**

This comprehensive review has succinctly outlined the phytochemical makeup and therapeutic impacts of *Melissa officinalis*, alongside an exploration of the researched controlled release methodologies. Diverse studies have delved into the essential oil's chemical composition and an array of extracts, revealing distinct concentrations of bioactive compounds influenced by geographical factors, harvesting methods and time frames. Predominantly, the pharmacological effects of these extracts have been ascribed to their rich poly phenolic content, yielding an array of benefits such as antioxidant, antimicrobial, anti-proliferative and cytotoxic attributes.

A promising avenue for advancing our understanding lies in a deeper analysis of the extracts' mechanisms of action and pharmacokinetics, which could yield novel biologically active systems for both human well-being and environmental sustainability. The evolving realm of controlled release systems offers an optimistic outlook for future developments. These systems may encompass alternative delivery mediums or refined iterations of existing approaches. The treasure trove of essentials oils, natural plant extract and myriad substances opens doors to functionalized controlled release systems. Potential encapsulation carriers span materials like silica, polysaccharides, polymers and lipids, while augmentation with diverse agents can tailor these systems to specific domains.

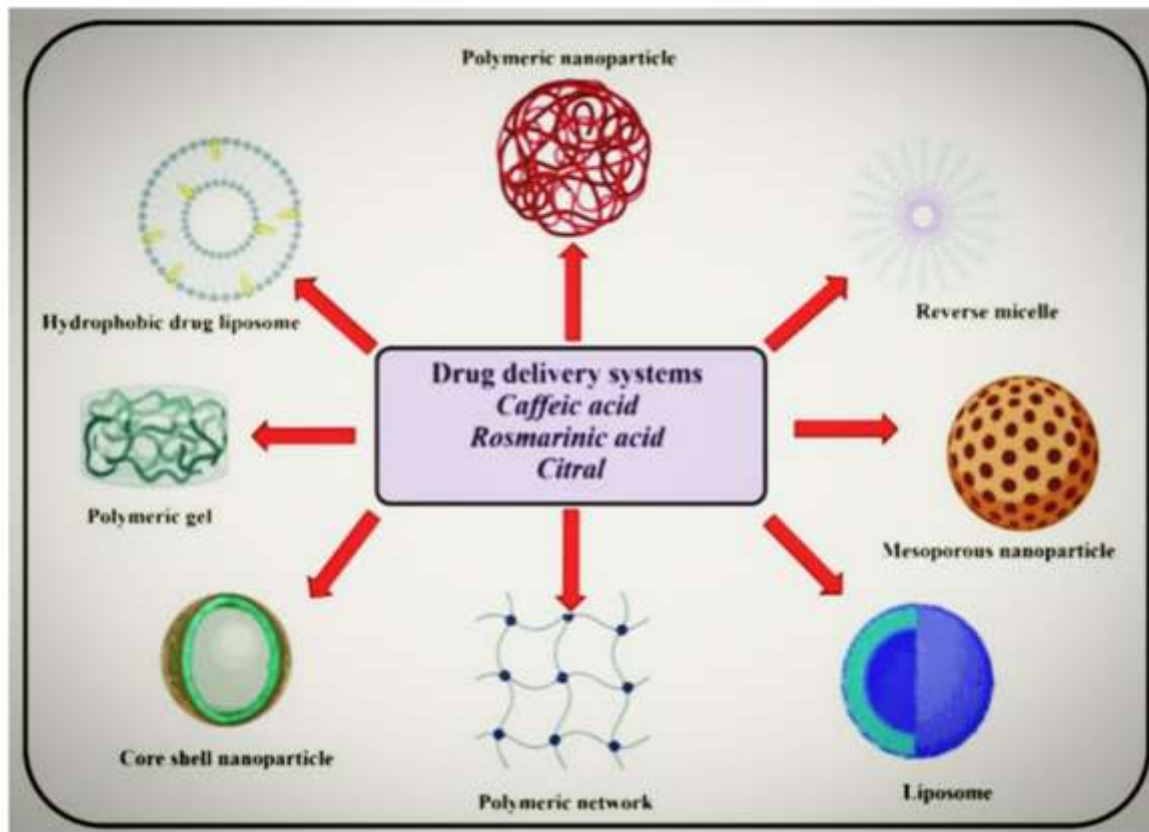


Fig 5: Drug delivery systems for *Melissa officinalis* components

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