BOLETIN LATINOAMERICANO Y DEL CARIBE DE PLANTAS MEDICINALES Y AROMÁTICAS
© / ISSN 0717 7917 / www.blacpma.ms-editions.cl

Revisión / Review

Accumulation of secondary metabolites in the family Lamiaceae as influenced by foliar micronutrients

[Acumulación de metabolitos secundarios en la familia Lamiaceae influenciada por micronutrientes foliares]

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Section: Review

Received: 9 February 2024
Accepted: 1 April 2024
Accepted corrected: 1 June 2024
Published: 30 November 2024

Citation:
Shahhat IMAM, Elsheikh SYS
Accumulation of secondary metabolites in the family Lamiaceae as influenced by foliar micronutrients
Bol Latinoam Caribe Plant Med Aromat
23 (6): 823 - 838 (2024)
https://doi.org/10.37360/blacpma.24.23.6.53

Abstract: The Lamiaceae family is rich in secondary metabolites, such as essential oils comprising flavonoids, phenolic compounds, and terpenoids. Micronutrients play a crucial role in plant metabolism and secondary metabolites production. This review summarizes and emphasizes the significance of foliar micronutrient nutrition in facilitating the accumulation of secondary metabolites in the Lamiaceae family, based on research literature from 2010 to 2023 using dependable databases like Scopus, Google Scholar, PubMed, and Science Direct. Spraying micronutrients notably enhanced the biosynthesis of various secondary metabolites in Lamiaceae species, especially for nutrients that do not move easily (Fe, Zn, Mn, Cu, B, and Si). Using nano-micronutrients as foliar application on Lamiaceae medicinal plants was more effective than traditional soil treatment. This review highlighted the importance of additional investigation on Cerium, Titanium, and Boron. Genera such as Lavandula, Satureja, Origanum, Lippia, and Hyssopus require more research in the future.

Keywords: Secondary metabolites; Lamiaceae; Foliar nutrition; Herbs; Plant stress

Resumen: La familia Lamiaceae es rica en metabolitos secundarios, como aceites esenciales que comprenden flavonoides, compuestos fenólicos y terpenoides. Los micronutrientes desempeñan un papel crucial en el metabolismo de las plantas y la producción de metabolitos secundarios. Esta revisión resume y enfatiza la importancia de la nutrición foliar de micronutrientes para facilitar la acumulación de metabolitos secundarios en la familia Lamiaceae, basándose en la literatura de investigación de 2010 a 2023 utilizando bases de datos confiables como Scopus, Google Scholar, PubMed y Science Direct. La pulverización de micronutrientes mejoró notablemente la biosíntesis de varios metabolitos secundarios en especies de Lamiaceae, especialmente para nutrientes que no se mueven fácilmente (Fe, Zn, Mn, Cu, B y Si). El uso de nano-micronutrientes como aplicación foliar en plantas medicinales de Lamiaceae fue más efectivo que el tratamiento tradicional del suelo. Esta revisión resaltó la importancia de investigaciones adicionales sobre Cerio, Titanio y Boro. Géneros como Lavandula, Satureja, Origanum, Lippia y Hyssopus requieren más investigación en el futuro.

Palabras clave: Metabolitos secundarios; Lamiaceae; Nutrición foliar; Hierbas; Estrés vegetal

INTRODUCTION

Secondary metabolites are natural compounds produced by plants, fungi, and bacteria, with low molecular weight and diverse chemical structures and biological functions (Zandavar & Babazad, 2023). Plant secondary metabolites, also known as phytochemicals, are produced in plants as a natural defense against microbes and environmental challenges. They have numerous medicinal applications, including as an ingredient in medications, therapeutics, and culinary goods, due to their biological activities (Kumar *et al*., 2022). On the other hand, they offer defense against harsh climatic conditions, pathogenic microorganisms, and insect pests, often possessing antibacterial properties against various foodborne microorganisms and their related toxins (Prakash, 2020). Generally, phytochemicals classified into major groups such as polyphenols, carotenoids, alkaloids, sulfur-containing groups, terpenes, and terpenoids (Barbieri *et al*., 2017; Prakash 2020). Secondary metabolites are utilized in various chemical reactions within enzymatically controlled metabolic pathways, which are a part of cell metabolism as depicted in Figure No. 1 (Twaij & Hasan, 2022).

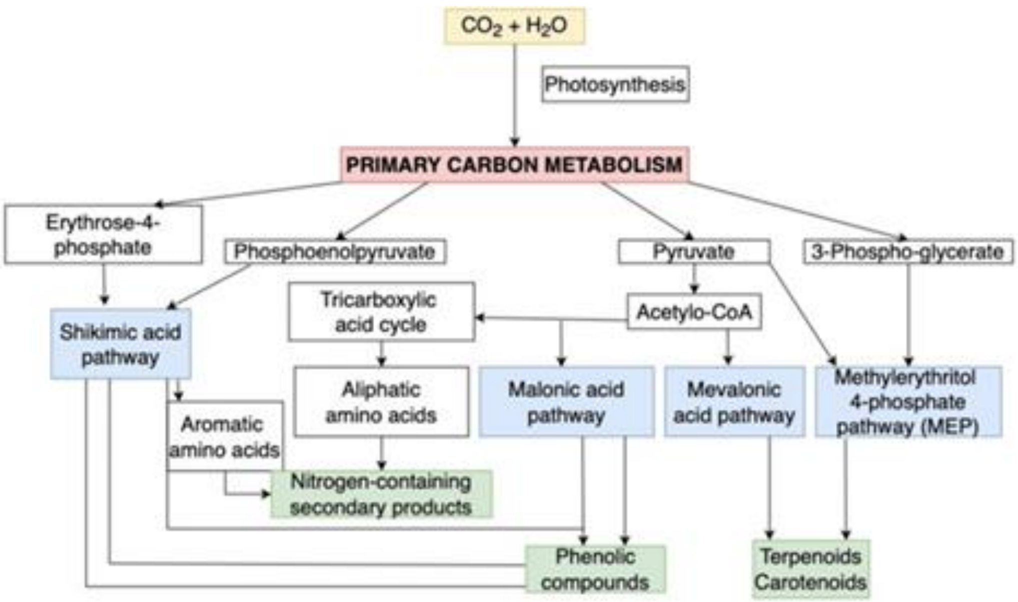


Figure No. 1
Main pathways for the synthesis of secondary metabolites in plants (Twaij & Hasan, 2022)

Recent scientific studies have linked the consumption of phytochemicals like polyphenols, carotenoids, and isoprenoids to health benefits like diabetes, obesity, cancer, and cardiovascular disease prevention, leading to their popularization. Plant secondary metabolites, including terpenoids, flavanols, and flavones, significantly influence plant-pathogen interactions and contribute to the development of plant immunity (Kumar *et al*., 2023).

Lamiaceae family, a diverse plant group with 236 genera and over 7,000 species, is a significant source of essential oil (Hamed *et al*., 2021). Lamiaceae plants, known for their aromatic properties and essential oils, are commonly used in culinary and medicinal practices in various folk traditions (Napoli, *et al*., 2020). Lamiaceae can be categorized into two groups based on phytochemistry: species that produce volatile terpenoids in essential oils and those that biosynthesize polar fraction constituents. Examples of the first class include *Salvia* L., *Mentha* L., and *Rosmarinus* L., while the second class includes *Ajuga* L., *Teucrium* L., *Melittis* L., and *Stachys* L. Various phytochemicals, including α- and β-pinene, menthol, and limonene in essential oils, and di- and triterpenes, flavonoids, and iridoids in polar fractions (Frezza *et al*., 2019). Lamiaceae species contain hydroxycinnamic acids and phytochemical compounds with various biological properties, including antibacterial, antiviral, antioxidant, anti-inflammatory, antidepressive, anticancer, antiangiogenic, and antihepatotoxic effects (De *et al*., 2012). Lamiaceae species like *Origanum vulgare*, *Mentha piperita*, and *Rosmarinus officinalis* are used as medicinal and aromatic plants. *Ocimum is* a large genus in the Lamiaceae family, contains over 64 aromatic herbs, ranging from annual to perennial. These herbs have been used as flavoring agents and therapeutics, with flavonoids, phenolic acids, and terpenes being the main chemical classes (Zahran *et al*., 2020). Foliar fertilization is a more effective method than soil fertilization for meeting the needs of higher species (Abbas *et al*., 2019). It has a low exposure dose, can be applied repeatedly, and can be time-applied according to weather to avoid nutrient losses (Raliya *et al*., 2017). Foliar fertilizer spraying is the most effective practice in sustainable agriculture and horticulture production systems for increasing the quality and quantity of medicinal and aromatic plants. It has been shown to increase production, resistance to insects, pests, diseases, drought tolerance, and crop quality (Shahrajabian *et al*., 2022). Foliar fertilizer treatment is a highly effective method for ensuring plants meets their nutritional needs for essential elements (Alshaal & El-Ramady, 2017). This technique effectively fulfills plant needs for secondary nutrients like calcium, magnesium, sulfur, and micronutrients like zinc, manganese, iron, copper, boron, and molybdenum (Patil & Chetan, 2018). Plant growth and development require micronutrients in low doses (Yadegari, 2017). Foliar fertilizers provide secondary macro- and microelements, enabling optimal plant growth and stress resistance. They are a popular management tool for agricultural plant nutrition, often used alongside or as an alternative to root fertilization (Murtaza *et al*., 2022). Nano-fertilizers are superior to conventional fertilizers due to their stable physical properties, small particle size, increased surface area to volume ratio, high density, and high reactivity. They can also function as controlling agents for fertilizer release, overcoming technical limitations in gradual and regulated release of nutrients. (Tavallali *et al*., 2020). Plants require 14 essential mineral elements for their life cycle, with macronutrients like N, P, K, S, Ca, and Mg being more crucial than micronutrients like Fe, Mn, B, Zn, Cu, Mo, Ni, and Cl. Additionally, plants absorb beneficial elements like Na, Si, Co, I, Se, and Al (Kirkby, 2023). This review article explores the role of foliar application of micronutrients, including nanoparticles and bulk elements, in enhancing phytochemical accumulation in Lamiaceae plants from 2010 to 2023.

MATERIAL AND METHODS

In order to achieve the objective of this review article, relevant keywords such as micronutrients, secondary metabolites, foliar application, spraying, and essential oils were utilized in articles related to the research topic. The papers were obtained from reputable databases (Web of Science, Scopus, Google Scholar, PubMed, and Science Direct) and were published between 2010 and 2023. A total of 95 articles on the topic were reviewed. The findings from each study were summarized and documented in various sections of this review article. The results were analyzed to identify strengths and weaknesses, and to develop a future plan aimed at enhancing sustainability in cultivating plants from the Lamiaceae family and supporting environmental sustainable.

Effect of Foliar micronutrients on secondary metabolites accumulation in Family Lamiaceae

Genetic and environmental factors influence biosynthesis and secondary metabolite quantity in plants, while environmental variables like water, light, temperature, pH, and insect invasion can also impact plant formation (Kumar *et al*., 2022). According to earlier research, the production of secondary metabolites is heavily influenced by the environment in addition to genetic regulation (Badi *et al*., 2004). Micronutrients like copper, manganese, iron, and zinc are essential for living organisms' growth and reproduction, and are utilized by plants for various cellular and molecular functions, including chlorophyll synthesis, photosynthesis, respiration, and DNA stabilization (Bashir *et al*., 2019). Foliar application of nutrients, specifically micronutrients, is an age-old method for treating deficient symptoms (Shahrajabian *et al*., 2022). Foliar sprayed nano-fertilizers offer quick plant absorption, lower cost, and minimal soil health impact compared to traditional soil-applied fertilizers (Meier *et al*., 2020). Nanoparticles (NPs) can protect plants from environmental stresses like salt or drought, reduce heavy metal accumulation, and act as micronutrient sources, boosting fitness and stress management. Some NPs can also activate enzymes involved in metabolism and nutrition acquisition (Landa, 2021). Lamiaceae species produce numerous secondary metabolites, including chemicals found in plant essential oils, which possess biological and medicinal properties (Harley, 2012). Volatile oils have two or three primary components. For example, *Mentha arvensis* L. showed as major compounds menthol, menthone, and isomenthone (Chagas *et al*., 2020); *Ocimum gratissimum* L. showed as major constituents 1,8-cineole, eugenol, and terpineol-4 (Rodrigues *et al*., 2020); *Origanum vulgare* L. showed terpinen-4-ol and trans-sabinene hydrate (Ramos *et al*., 2011); and in the species *Plectranthus ornatus* Codd, the major compounds identified were α-thujene, α-pinene, sabinene, β-pinene, 1-octen3-ol, 3-carene, (E)-β-ocimene, α-terpinyl acetate, β-caryophyllene, and germacrene D (Passinho-Soares *et al*., 2017). Essential oil composition can vary due to factors like growth conditions, plant origin, maturity stage, physiological changes, harvesting time, drying methods, isolation methods, and GC/MS analysis solvents (Arranz *et al*., 2015; Moghaddam & Mehdizadeh, 2017). Stressors can influence plant phenolic content development, affecting plant type and sensitivity, and flavonoids act as antioxidants in plant cells (Agati *et al*., 2012). The synthesis and accumulation of nutrients in plants are influenced by various factors such as soil type, abiotic stressors, environmental conditions, and nutritional status (Ballizany *et al*., 2012). Researchers studied various micronutrients, including Zn, Fe, Mn, Cu, Se, Ti, and B, in traditional, Nano-particles, and EDTA forms, and examined Lamiaceae plants like *Melissa officinalis* L., *Lallemantia iberica* (M. Bieb.) Fisch., *Majorana hortensis* M., *Origanum majorana* syn., *Rosmarinus officinalis* L., and *Ocimum basilicum* L., to examine the effects of micronutrient foliar application on secondary metabolite accumulation.

Iron (Fe)

Fe is a micronutrient that serves multiple purposes in living beings, including growth, development, physiological, and cellular processes (Pasricha *et al*., 2021). It carries oxygen and promotes chlorophyll synthesis (Zewide & Sherefu, 2021). Fe is necessary for many important processes, including DNA synthesis, respiration, photosynthesis, and nitrogen reduction (Rout & Sahoo, 2015).

Essential oil %, caryophyllene β, citronellal, linalool, neral, thymol, carvacrol, geranial, geraniol and geranyl acetate in *Melissa officinalis* L. were significantly affected by the Fe^{2+} (Yadegari & Shakerian, 2014), also Nano-Fe had a considerable effect on essential oil production and composition. On the other hand, iron nanoparticle treatments reduced the detrimental effects of reduced watering by increasing proline accumulation and decreasing certain antioxidant activities, increasing lemon balm's drought tolerance (Mohasseli *et al*., 2020).

Nano Fe^{2+} considerably boosted the essential oil percentage, menthone, menthol, and menthofuran in *Mentha piperita* L. (Nemati Lafmejani *et al*., 2018). Positive effect of nano-Fe chelate on phenol content, essential oil and main component; methyl chavicol, neral, nerol, geranial, octanol acetate, α-humulene in *Ocimum basilicum* L. (Danaee & Abdossi, 2021). Using micro element Fe increased the percentage of essential oil, camphor, α-pinene, and 1.8-cineole in *Rosmarinus officinalis* L. as compared to the control (Massoud *et al*., 2016). In *Mentha piperita* L. foliar application containing Fe enhanced the essential oil, menthofuran, menthol, menthone, menthyl acetate, pulegone, and limonene (Asle-Mohammadi *et al*., 2023). Essential oil % of *Marjorana hortensis* M. was significantly affected by the foliar application of Nano-Fe at two levels 50 and 100 ppm compared to the non-sprayed plants. Sabinene % and P-cymene significantly increased with all Nano-Fe, while trans sabinene hydrate increased with only Nano-Fe 100 ppm treatments. There is no significant effect on 1-4-terpineol (El-Khateeb *et al*., 2020). In *Melissa officinalis* L., the micronutrient Fe favorably increases the concentration of anthocyanins and rosmarinic acid (Kiani *et al*., 2014). Nano-Fe foliar spray improved total phenolic and total flavonoid content. On the other hand, Nano-Fe improved salinity stress tolerance of rosemary (*Rosmarinus officinalis* L.) by decreasing both H_2O_2 and MDA (Hassanpouraghdam *et al*., 2020). Yadegari (2015), showed that the flavonoids, phenols, carotenoids, carvacrol and thymol % in *Thymus vulgaris* L. was significantly affected by foliar application of micronutrient Fe at four concentrations 0, 200, 400 and 600 ppm, and the highest amount of these secondary metabolites were obtained from 400 ppm of micronutrients foliar application.

Zinc (Zn)

Zinc (Zn) is the second most prevalent transition metal in living things after iron (Marschner, 2012); its structural, catalytic, and activating properties are critical in plant development, reproduction, and signaling (Lehmann *et al*., 2014). Zinc supports plant growth hormones and the enzyme system (Zewide & Sherefu, 2021). Many enzymes, including carbonic anhydrase, carboxypeptidase, and Zn-superoxide dismutase, require Zn as a cofactor (Balafrej *et al*., 2020). It is an enzyme cofactor that is involved in plant metabolism, auxin production, and membrane integrity in ion transport systems (Sakya *et al*., 2023). Zn's mobility in plants is limited, therefore foliar treatments must include Zn sources. The small gap between Zn essentiality and toxicity in plants has caught the scientific community's attention to its impacts on plants and critical role in agricultural sustainability (Kaur & Garg, 2021). Zn nano-Particles (NPs) increased essential oil yield by 42% in sage (*Salvia officinalis* L.) treated with foliar spray under lead (Pb) and cadmium (Cd) stress (Bakhtiari *et al*., 2023). Using micro element Zn increased the percentage of essential oil, camphor, α-pinene, and 1.8-cineole in *Rosmarinus officinalis* L. as compared to the control (Massoud *et al*., 2016). Foliar Zn spraying in *Mentha piperita* L. increased the essential oil, menthofuran, menthol, menthone, menthyl acetate, pulegone, and limonene levels (Asle-Mohammadi *et al*., 2023). The foliar spraying of nano-Zn at 50 and 100 ppm had a substantial effect on the essential oil percentage of *Marjorana hortensis* M. as compared to non-sprayed plants. Sabinene % and P-cymene levels increased significantly with all Fe treatments, but there was no influence on 1-4-terpineol (El-Khateeb *et al*., 2020). Flavonoids, phenols, carotenoids, carvacrol, and thymol % in *Thymus vulgaris* L. were significantly affected by foliar application of micronutrients Zn at four concentrations (0, 200, 400, and 600 ppm), with 400 ppm producing the highest amounts of these secondary metabolites (Yadegari, 2015). All Zn resources, including EDTA-chelated Zn, Zn sulfate, nano-zinc, and citrate-chelated Zn, increased the chemical composition of essential oil in *Melissa officinalis* L., such as geranial, caryophyllene oxide, and phthalic acid (Najafian *et al*., 2022). Zinc produced higher levels of essential oil and total flavonoids during the vegetative stage than control treatments in three plants: *Dracocephalum moldavica*, *Hyssopus officinalis*, and *Salvia officinalis* (Hegazy *et al*., 2016). The essential oil contains caryophyllene β and citronellal. Zn^{2+} had a substantial effect on linalool, neral, thymol, carvacrol, geranial, geraniol, and geranyl acetate in *Melissa officinalis* L. (Yadegari & Shakerian, 2014). Zinc had a considerable effect on essential oil percentage and total phenolic content, although carvacrol concentration was minor in *Satureja khuzistanica* Jamzad (Mumivand *et al*., 2021). $ZnSO_4$ had a favorable effect on the essential oil percentage, flavonoid content, total phenolic content, and anthocyanin in *Lavandula stoechas* L. (Vojodi Mehrabani *et al*., 2017). Zinc fertilizers may cause an increase in essential oil content, including eugenol, 1,8-cineole, and methyl chavicol. However, there was no significant change between the 1.5 g/L nano-zinc chelate and 1.5 g/L $ZnSO_4$ (conventional Zn) treatments. Foliar application of 1.5 g/L zinc sulfate is advised for *Ocimum sanctum* L. (Moghimipour *et al*., 2017). Zn-nano chelates in *Ocimum basilicum* L. increased phenol concentration, essential oil content, and major components such as linalool, 1,8-cineol, Eugenol, a-terpineol, epi-α-muurolol, E-β-ocimene, and carvone (Danaee & Abdossi, 2021). Zinc increased the overall phenolic content in *Mentha piperita* L. (Jahani *et al*., 2021). According to Kiani *et al*. (2014), the vitamin zinc positively increases the anthocyanin and rosmarinic acid concentration in *Melissa officinalis* L. Nano-Zn foliar spray boosted overall phenolic and flavonoid content. Nano-Zn foliar spray increased the salinity stress tolerance of *Rosmarinus officinalis* L. (rosemary) by lowering H_2O_2 and MDA levels (Hassanpouraghdam *et al*., 2020).

Manganese (Mn)

Manganese enhances chlorophyll synthesis and phosphorus availability (Zewide & Sherefu, 2021). Mn is an essential micronutrient with numerous functional roles in plant metabolism. It acts as an activator and co-factor for hundreds of metalloenzymes in plants and is involved in a wide range of enzyme-catalyzed reactions such as redox reactions, phosphorylation, decarboxylation, and hydrolysis. Mn plays all of these roles because of its ability to rapidly change oxidation state in biological systems (Schmidt & Husted, 2019). Using micro element Mn increased the percentage of essential oil, camphor, α-pinene, and 1.8-cineole in *Rosmarinus* *officinalis* L. as compared to the control (Massoud *et al*., 2016). The essential oil, menthofuran, menthol, menthone, menthyl acetate, pulegone, and limonene were increased in *Mentha piperita* L. as a result of foliar application of Mn (Asle-Mohammadi *et al*., 2023).

Nano-Mn foliar spraying significantly increased the essential oil percentage of *Marjorana hortensis* M. compared to non-sprayed plants. Sabinene% and P-cymene levels increased significantly across all treatments, while Cis sabinene hydrate increased only at 100ppm Mn (El-Khateeb *et al*., 2020).

Foliar application of micronutrient Mn at four concentrations in *Thymus vulgaris* L. significantly affected flavonoids, phenols, carotenoids, carvacrol, and thymol %, with the maximum concentration obtained from 400 ppm micronutrient foliar treatment (Yadegari, 2015). Mn^{2+} foliar application to Lemon balm (*Melissa officinalis* L.) increased caryophyllene oxide, e-caryophyllene, geranial, geraniol, chavicol, and neral levels (Yadegari, 2017).

Cupper (Cu)

Copper is a vital mineral nutrient for plant growth, playing various roles in morphology, physiological aspects, biochemistry, enzyme cofactors, photosynthesis, respiration, electron transport chain, and defense gene structure (Shabbir *et al*., 2020; Mir *et al*., 2021). Cu is essential for the proper functioning of superoxide dismutase and ascorbate oxidase, both vital components of the antioxidant defense system (Viehweger, 2014). Yadegari (2015), found that Cu micronutrients significantly impacted flavonoids, phenols, carotenoids, carvacrol, and thymol% in *Thymus vulgaris* L when applied at four concentrations. The highest concentration of these secondary metabolites was observed in 400 ppm treatment. Yadegari & Shakerian (2014), found that foliar application of micronutrient (Cu^{2+}) at concentrations of (0, 150, and 300 ppm) has a substantial effect on the essential oil content in *Melissa officinalis* L. Yadegari's (2017), study found that copper application can increase the levels of caryophyllene β, citronellal, geranial, geraniol, geranyl acetate, linalool, and neral in lemon balm. Lafmejani *et al*. (2018), found that foliar application of copper nanoparticles in *Mentha piperita* L. increased essential oil percentages and menthol, menthone, and menthofuran levels.

Selenium (Se)

Selenium slows plant senescence by increasing antioxidant capacity in plant tissues and minimizing postharvest losses (Puccinelli *et al*., 2020). Nano-fertilizers, a nanohybrid construct, offer a sustainable alternative to traditional chemical fertilizers, delivering nutrients more efficiently, increasing crop yield, and promoting environmental sustainability (Babu *et al*., 2022). Se nano-particles significantly enhanced the essential oil yield of sage (*Salvia officinalis* L.), a plant commonly used in medicine, by 36% compared to non-NPs treated with foliar spray under lead and cadmium stress (Bakhtiari *et al*., 2023). El-Khateeb *et al*. (2020), proposed foliar application of nano microelements (Fe, Zn, and Mn) to increase the productivity of the *Origanum majorana* L. plant (herb and essential oil content, yield, and components). Se and nano-Se improved the biosynthesis of secondary metabolites in *Lippia citriodora* Kunth, including essential oils, total phenolic content, and flavonoid compounds, under non-stress and salt conditions (Ghanbari *et al*., 2023). Se spraying increased the production of essential oil and total phenolics. While anthocyanin and total flavonoids in basil (*Ocimum basilicum* L.) leaves did not differ substantially from those in control plants (Skrypnik *et al*., 2019). In the same plant, Puccinelli *et al*. (2020), discovered that Se had a substantial effect on total phenol and rosmarinic acid levels at harvest. The effects of Se foliar spraying on *Origanum vulgare* L. under drought stress conditions were investigated. Se 30 mg/l increased carotenoids and phenolic compounds significantly (Mahdavi *et al*., 2021).

Titanium (Ti)

Nano-TiO_2 can penetrate the leaf more easily than titanium dioxide particles, reduced the effects of drought stress on *Lallemantia iberica*, suggesting that it could be used to grow this plant in water-stressed locations (Shoarian *et al*., 2020). Nano TiO_2 can enhance light absorption, boost Rubisco (a crucial enzyme in photosynthesis that catalyzes CO_2 fixation) and photosynthesis enzyme activity (Li *et al*., 2019), increase nitrate absorption, and speed the conversion of inorganic to organic material (Nair & Chung, 2014). Titanium dioxide (TiO_2) nanoparticles improve plant resilience to environmental stressors and lower free radical levels (Hong *et al*., 2005). The impacts of foliar TiO_2NPs, when compared to the control, revealed a considerable increase in antioxidant enzyme activity, which may also have a role in controlling the plant's phytochemical reactions (Farahi *et al*., 2023). Titanium foliar application studies revealed that TiO_2 nanoparticles foliar spray improved the quality and quantity of *Melissa officinalis* L. essential oil rich in neral and geranial constituents (Mohammadi *et al*., 2023), and caused a significant increase in phenolic content and total flavonoid in *Lallemantia iberica* under moderate stress (Shoarian *et al*., 2020). Uddin *et al*. (2023), found that the combination of SiO_2 and TiO_2 nanoparticles significantly increased the essential oil content and bioactive components of Coleus aromatics Benth, with plants treated with Si_{100} + Ti_{100} mg/l showing the highest increase in thymol and β-caryophyllene levels.

Boron (B)

Boron is crucial for plants, influencing crop growth and yield through its regulation of cell wall and plasma membrane integrity, ion mobility, cell division, reproductive growth, biomolecule synthesis, phenol and auxin metabolism, nitrogen fixation, disease resistance, and abiotic stress management. Its bioavailability in soil and water media is essential. (Mohamed *et al*., 2016; Kohli *et al*., 2023). Boron foliar spraying in *Satureja khuzistanica* Jamzad at three dose levels (0, 2.5, and 5 mg B/L) had a significant effect on the essential oil percentage, total phenolic content, and carvacrol concentration (Mumivand *et al*., 2021). Boron foliar spray increased lavender (*Lavandula officinalis* L.) oil, essential oil proportion and yield, while Nano-boron spray enhanced monoterpene hydrocarbons and oxygenated monoterpenes, while decreasing non-oxygenated substances and sesquiterpene hydrocarbons. (Fouad *et al*., 2023). Mohamed *et al*. (2016), found that boron foliar treatment at doses of 0, 50, and 100 ppm significantly increased the essential oil % of basil (*Ocimum basilicum* L). Boric acid (17% boron) was used as a boron source in a different plant, *Dracocephalum moldavica* L., and sprayed four times during growth, resulting in an increase in the oil percentages of leaves and flowers. (Mady & Youssef, 2014).

Silicon (Si)

Foliar sprays containing silicon compounds, first used in 1990, have evolved into silicic acid sprays in 2003 and silica nanoparticles in recent years. These sprays are effective insecticides, while silicic acid promotes growth and yield while reducing biotic and abiotic stress. Studies show that silica-Nano sprays reduce biotic stress while increasing growth and production. (Laane, 2018). Silicon is crucial for agricultural plant growth and productivity as it enhances their nutritional state. Exogenous use of silicon under well-watered or drought conditions can mimic sweet basil plant development and biochemical features like photosynthetic pigment, ion percentage, antioxidant solutes, and organic osmolytes (Farouk & Omar, 2020). Furthermore, Si promotes plant defense and phytohormone signaling pathways in response to biotic and abiotic stresses (Khan *et al*., 2023). Different plant metabolic pathways generate byproducts that cause cellular oxidative stress. The presence of Si in the plant body is almost essential for reducing such physiological stresses (Frew *et al*., 2018; Kim *et al*., 2019). Si presence in leaves also improved leaf retention and delayed leaf senescence by up-regulating cytokinin production in both Si-accumulating and non-Si-accumulating plant species (Markovich *et al*., 2017). Silicon nano-particles (NPs) increased essential oil yield by 37% compared to non-NPs of sage (*Salvia officinalis* L.) treated with foliar application under lead (Pb) and cadmium (Cd) stress (Bakhtiari *et al*., 2023). *Satureja hortensis* L., under moderate Cd stress, was treated with Si-NPs, resulting in the highest total phenolic content, flavonoid content, antioxidant capacity, and essential oil % (Memari-Tabrizi *et al*., 2021). Si-NPs were used to enhance the physio-biochemical condition of summer savory plants under Cd stress. The application of silicon at 5 g/L under magnetite of *Majorana hortensis* L. resulted in the highest volatile oil content, 1-4-terpineol (29.55%), followed by trans-sabinene hydrate (21.28%), α-terpinene (16.45%), sabinene (6.99%), P-cymene (3.29%), linalyl acetate (2.97%), trans-carophyllene (2.93%), L-linalool (1.59%), α-pinene (1.3%), and d-limonene (1.01%) (Badawy *et al*., 2014). Silicon foliar spray can enhance the essential oil content of *Satureja hortensis* L. plants under salinity stress levels (0 and 100 mM), making it a useful management tool for plant growth, protection against abiotic stresses, and increasing yield potential and secondary metabolites in medicinal plants. (Mohammadi *et al*., 2019). Under mild drought conditions, 250 mg/L Na_2SiO_3 sodium metasilicate (Si) produced the highest essential oil output from sweet basil (*Ocimum basilicum* L.). The use of Si has been shown to mitigate the distortion and lysis of cell organelles resulting from severe drought damage. It increased drought tolerance and essential oil yield by accelerating antioxidant system, osmoregulation, and maintaining organelle ultrastructure, resulting in herb growth and essential oil yield (Farouk & Omar, 2020). Spraying Nano-Si (60 and 90 ppm) on the Basil Plant (*Ocimum basilicum* L.) boosted the essential oil percentage (Mahmoud *et al*., 2017).

Cerium (Ce)

CeO_2NPs foliar treatment in *Salvia miltiorrhiza* B. enhanced phytochemical properties, including total phenol and flavonoid levels, and achieved maximum root rosmarinic acid and tanshinone concentration (Paryan *et al*., 2020). The foliar application of cerium oxide-salicylic acid nanocomposite enhanced protein, carbohydrate, phenolics, flavonoids, essential oil percentage, and antioxidant capacity in spearmint under salt stress. The essential oil contained various compounds, and the CeO_2-SA nanocomposite effectively reduced salt stress effects (Shiri *et al*., 2023). The study found that the use of cerium dioxide nanoparticles (CeO_2NPs) or their interaction with different drought stress intensities, field capacity moisture, and post-stress re-watering significantly impacted the physio-phytochemical characteristics of *Salvia mirzayanii* Bunge. The essential oil samples contained various oxygenated monoterpenes and sesquiterpenes, with the combination of CeO_2NPs and re-watering under drought stress potentially enhancing drought resistance, growth, and phytochemical content in *S. mirzayanii* plants (Imani *et al*., 2023).

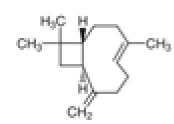
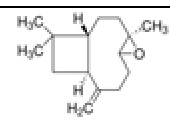
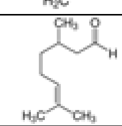
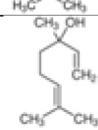
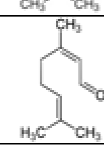
Mixture of micronutrients

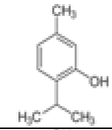
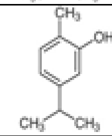
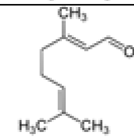
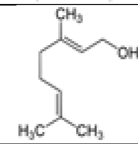
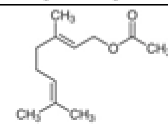
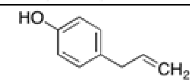
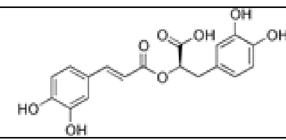
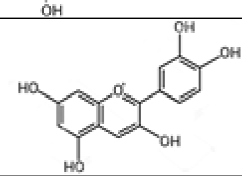
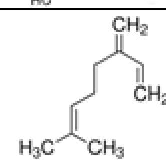
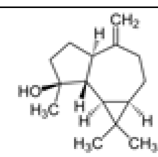
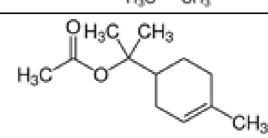
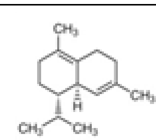
When micronutrients (Fe, Zn, and Mn) were added to *Rosmarinus officinalis* L., the percentage of essential oil, camphor, α-pinene, and 1.8-cineole rose in comparison to the control group (Massoud *et al*., 2016). Hanafy *et al*. (2018), found that oil components terpine-4-ol and α-pinene increased, while linalyl acetate, linallool, and limonene increased only at low concentrations. β-Phyllandrene increased only at high concentrations. Said-Al Ahl *et al*. (2010), revealed that a mixture of (Zn, Fe, and Mn) produced the maximum levels of essential oil (%) and total flavonoids in *Dracocephalum moldavica* L. under 90 Kg/fed nitrogen fertilizer, followed by a mixture of (Zn, Fe, and Mn) with compost tea. Geranial and geraniol levels increased with micronutrients, with or without compost tea, however geranyl acetate levels fell. Yadegari (2015), showed that foliar application of a mixture of micronutrients (Fe, Zn, Cu, and Mn) at four concentrations (0, 200, 400, and 600 ppm) had a favorable effect on essential oil, flavonoids, phenols, carotenoids, carvacrol, and thymol % in *Thymus vulgaris* L. These findings highlight the importance of applying the four foliar fertilizers in increasing the total essential oils in medicinal plants. Using four foliar fertilizers (Fe, Cu, Mn, and Zn) increased the total essential oils in medicinal plants. Perhaps micronutrients, by their effects on absorption and transfer of important nutrients, altered metabolism, growth, and development, resulting in an increase in phytochemicals (Yadegari, 2017). The micronutrient mixture (Zn, Cu, Fe, and Mn) greatly enhanced essential oil, phenol, and flavonoids when compared to the control. Plants treated with Mn, Fe+Mn, Fe+Zn, Mn+Zn, Fe+Mn+Zn, and Fe+Mn+Zn+Cu produced more essential oil (%) than other treatments, with the control treatment yielding the lowest percentage. Spraying Fe+Mn+Zn+Cu on lemon balm leaves (*Melissa Officinalis* L.) enhanced the essential oil of this medicinal plant by 73.64% compared to the control treatment (Yadegari, 2017). The usage of Zn-Salicylic acid Nano-complexes has a stronger effect than their non-Nano form in *Ocimum basilicum* L., with the largest level of α-Cadinol and trans-α-Bergamotene in the essential oil at 0.2% Zn-Salicylic acid Nano treatment. In example, 0.2% Zn and Salicylic acid-Nano treatments considerably raised the percentage of phenolic and flavonoid components in the extract (Tavallali *et al*., 2020). Jahani *et al*. (2021), discovered that Zinc-Salicylic acid produced a higher percentage of essential oil in *Mentha piperita* L. than the non-treated control; however, moderate drought stress increased oil compound synthesis, while foliar zinc and salicylic acid applications alleviated this effect. Said-Al Ahl & Mahmoud (2010), found that basil plants treated with Zn+Fe showed higher essential oil percentages under soil salinity conditions, while untreated plants had lower yields. Soil salinity treatment reduced linalool and methylchavicol levels, with Linalool levels increasing in saline soils after applying Fe, Zn, and Fe+Zn treatments. However, Fe+Zn reduced methylchavicol levels compared to the control group, indicating the potential benefits of these treatments. The combination foliar spraying of Se and Si has been shown to improve the physiological properties of *Origanum vulgare* (Mahdavi *et al*., 2021).

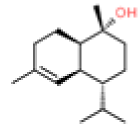
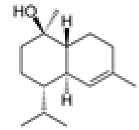
CONCLUSION

Recent studies showed a growing interest in foliar application of micronutrients, which can be used alone or in combination. These micronutrients are more readily available, have a positive effect with immobilized nutrients, and increase efficient nutrient absorption. Foliar sprays are also more affordable and environmentally friendly. Foliar application with bulk nutrients or nano-nutrients is an excellent option for sustainable medicinal plants, especially Lamiaceae because of its reduced application amount, faster nutrient absorption than soil application, and low environmental impact. Nano-fertilizers outperform conventional one due to their small particle size, stable physical qualities, and increased surface area to volume ratio, high reactivity and high density. Nano-nutrients can control nutrints release, overcoming technical limitations. Studies confirm this for micronutrients in Lamiaceae plants. Several genera, like *Lavandula*, *Satureja*, *Origanum*, *Lippia*, and *Hyssopus*, have received little attention and need focus studies in future, but *Melissa* and *Ocimum* are intensively investigated. Studies focusing on micronutrients, particularly when combined, have demonstrated enhancements in the biochemical and physiological conditions of various Lamiaceae plants, resulting in elevated levels of flavonoid and phenolic compounds, antioxidant capacity, essential oil percentage, and oil components. This minireview emphasizes the need for further research on Cerium (Ce), Titanium (Ti), and Boron (B). Currently, there is a growing interest in nano-nutrients and foliar nutrition, however, research on the foliar use of nano-nutrients is not as prominent as research on their use in soil. Hence, further research should be carried out on plant nutrition from the Lamiaceae family by foliar application method, utilizing nano-nutrients or conventional ones.

Table No. 1
Secondary metabolites (description, structure and formula) found in Family Lamiaceae

No.	Secondary metabolites	Description	Chemical structure	Formula
1	β- caryophyllene	Bicyclic sesquiterpene		$C_{15}H_{24}$
2	Caryophyllene oxide	Bicyclic sesquiterpene		$C_{15}H_{24}O$
3	Citronellal	Monoterpenoid		$C_{10}H_{18}O$
4	Linalool	Noncyclic monoterpenoid (monoterpene alcohol)		$C_{10}H_{18}O$
5	Neral (citral B)	Acyclic monoterpene aldehyde		$C_{10}H_{16}O$

6	Thymol	Monoterpenoid phenol derivative of p-Cymene		$C_{10}H_{14}O$
7	Carvacrol	Monoterpenoid phenol		$C_{10}H_{14}O$
8	Geranial (citral A)	Acyclic monoterpene aldehyde		$C_{10}H_{16}O$
9	Geraniol	Acyclic monoterpenoid alcohol		$C_{10}H_{18}O$
10	Geranyl acetate (acetate ester derivative of geraniol)	Monoterpenoid.		$C_{12}H_{20}O_2$
11	Chavicol (p-allylphenol, 4-Allylphenol)	Phenylpropanoid		$C_9H_{10}O$
12	Rosmarinic acid	A phenolic compound and ester of caffeic acid		$C_{18}H_{16}O_8$
13	Anthocyanin (pigments)	A flavonoid (polyphenol)		$C_{15}H_{11}O_6$
14	β-myrcene	A monoterpene		$C_{10}H_{16}$
15	Spathulenol	A tricyclic sesquiterpenoid		$C_{15}H_{24}O$
16	α-terpinyl acetate	A monoterpene ester		$C_{12}H_{20}O_2$
17	δ-Cadinene	A sesquiterpenes		$C_{15}H_{24}$

18	Tau-muurolol	A cadinane sesquiterpenoid		$C_{15}H_{26}O$
19	α-Cadinol	A sesquiterpenoid alcohol		$C_{15}H_{26}O$
20	Eudesm-7(11)-en-4-ol	A sesquiterpenoid		$C_{15}H_{26}O$

ACKNOWLEDGMENT
The authors extend their appreciation to the Deanship of Scientific Research at Northern Border University, Arar, KSA for funding this research work through the project number “NBU-FFR-2024-56-01”.

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