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The Effects of Fertilization on Secondary Metabolite Production İn Medicinal and Aromatic Plants: A Review Study

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ABSTRACT:
The quality and quantity of active compounds in plants are influenced by both environmental and agricultural practices. Fertilization not only enhances the growth and yield of medicinal and aromatic plants but also significantly impacts the quantity and quality of their active compound content. This review comprehensively and interdisciplinarily examines the effects of fertilization practices on secondary metabolite production in medicinal and aromatic plants, as well as the changes in the quality and quantity of these metabolites.

Plant secondary metabolites encompass bioactive compounds such as essential oils, phenolic compounds, flavonoids, and alkaloids. The value of these phytotherapeutic compounds is largely affected by the environmental and agricultural inputs plants receive during their development. Specifically, fertilization acts both as a practice supporting plant growth and as a metabolic influencer, enhancing secondary compound production by affecting plant metabolic processes at a molecular level.

Based on the current literature findings reviewed, it is concluded that there is a need to develop dose-controlled fertilization strategies that are plant-species specific, aim to maximize target active compounds, and consider environmental sustainability. It is emphasized that such precise fertilization approaches are strategically important not only for increasing agricultural productivity but also for ensuring the standardization and quality of pharmacologically valuable plant compounds used in medicine. Further research at the molecular level is suggested to contribute to a better understanding of the effects of fertilization on secondary metabolism.

KEY WORDS: Fertilization, Secondary metabolite, Medicinal and aromatic plants, Essential oils, Macro and micro nutrient elements, Sustainable agriculture.

INTRODUCTION

Throughout human history, medicinal and aromatic plants have played a crucial role in nutrition and healthcare [1]. The sustainable management of medicinal and aromatic plants is of great importance both nationally and internationally, considering macroeconomic structures, environmental conditions, healthcare services, employment opportunities, and the conservation of genetic resources [2].

The increasing awareness of the negative effects of chemical and synthetic substances has led to the 21st century being referred to as the "age of medicinal plants" [3]. Furthermore, the contribution of medicinal plants to biodiversity and ecological stability in agricultural ecosystems, along with the preservation of product quality and production sustainability, are also noteworthy aspects [4].

Due to the bioactive compounds they contain, medicinal and aromatic plants have gained significant importance in the pharmaceutical, cosmetic, and food industries. Plant active compounds form the basis of the pharmacological efficacy of medicinal and aromatic plants. Secondary metabolites such as alkaloids, flavonoids, terpenoids, and essential oils found in these plants are synthesized in relation to the plant's defense mechanisms. The quantity and quality of these compounds are directly influenced by the plant's genetic makeup, as well as environmental and agricultural factors [5].

In the cultivation of medicinal and aromatic plants, fertilization is one of the fundamental agricultural practices that directly affect plant development, biochemical compound content, and essential oil yield. The type and dose of applied fertilizer significantly shape the functioning of plant metabolism and the synthesis of secondary metabolites. Organic, mineral, and bio-fertilizer applications can impact quality parameters such as yield, phenolic compound levels, antioxidant capacity, and essential oil content at varying rates. Particularly, organic and biological fertilizers are reported to support sustainable agricultural production by reducing the negative environmental impacts of chemical fertilizers. In this context, determining appropriate fertilization strategies is of great importance for both improving product quality and ensuring environmental sustainability [6].

Macro (N, P, K) and micro (Fe, Zn, Mn) nutrient elements used in fertilization play fundamental roles in regulating primary and secondary metabolic processes. The application dose, timing, and method of these elements are critically important in determining the yield and quality of active compounds, especially in medicinal and aromatic plants [7]. Recent studies indicate that fertilization can have positive effects on plant active compound synthesis, but this effect may vary depending on the plant species and the type of fertilizer used [8].

Studies aimed at understanding the role of fertilization in plant active compound (secondary metabolite) synthesis are of strategic importance not only for an efficient production process but also for providing high-quality botanical raw materials for pharmaceutical purposes [9]. This review study aims to examine the effects of different fertilizer types and application doses on secondary metabolite synthesis in medicinal and aromatic plants, based on existing literature, and to provide a scientific contribution to sustainable, high-quality production goals.

Literature Review: In recent years, the regulation of active compound production in medicinal and aromatic plants through fertilization practices has become a significant focus of scientific research. Plant active compounds consist of secondary metabolites such as alkaloids, flavonoids, phenolic compounds, essential oils, and terpenoids. The synthesis of these compounds is largely related to the plant's nutritional status and environmental factors [8].

Fertilization is an agricultural input that can directly affect both primary and secondary metabolic pathways. However, in recent years, it has been more deeply scientifically understood that fertilization not only affects macro yield parameters but also directly influences the secondary metabolism of plants [10]. Secondary metabolites, such as alkaloids, flavonoids, phenolic compounds, terpenoids, and essential oils, are biochemical compounds that play a role in plant defense mechanisms and often determine the pharmacological value of medicinal and aromatic plants [11].

Numerous studies have investigated the effects of fertilization on the production of secondary metabolites, revealing that these effects vary depending on the fertilizer type, application dose, and timing [8, 32]. Therefore, in recent years, not only the effects of fertilization on growth and development but also its effects on the biosynthesis of these valuable compounds have been extensively researched [10].

The effect of fertilization on secondary metabolite production particularly depends on the presence of macro and micro nutrient elements that play a role in plant growth and metabolic processes. Macro elements like nitrogen (N), phosphorus (P), and potassium (K) play critical roles in fundamental physiological processes such as plant development, protein synthesis, energy transfer, and osmotic balance. Micro elements such as zinc (Zn), iron (Fe), and manganese (Mn) have direct effects on regulating enzymatic activities and the functionality of metabolic pathways [7, 10]. Specifically, nitrogenous fertilizer applications can increase the production of essential oils and alkaloids, while excessive nitrogen use can lead to metabolic imbalances and a decrease in secondary metabolites [12].

They reported that nitrogen fertilization positively affected the quality and quantity of essential oil in Mentha piperita. Similarly, deficiencies or excesses of elements like potassium and phosphorus can directly influence flavonoid synthesis pathways, leading to significant changes in the biochemical quality of the product. The perennial nature of Izmir oregano (Origanum onites L.) and its multiple harvests mean it removes high amounts of nutrients. [13] study emphasized in their study that nitrogenous fertilizers significantly increased yield and dry herb amount, especially from the second year onwards, and that applying fertilizer two or three times was beneficial for yield.

Furthermore, phosphorus fertilizer applications were recommended during planting and spring periods. [14] study reported that potassium fertilization improved oil quality in medicinal and aromatic plants. Micro elements, on the other hand, act as important cofactors in regulating enzymatic activities and the biosynthesis of metabolites.

Deficiencies of elements like zinc and iron can negatively affect flavonoid and phenolic compound production, whereas balanced micro-nutrition improves the metabolite profile [15, 16, 17]. However, excessive fertilization can lead to metabolic imbalances, oxidative stress, and even a decrease in active compounds. Therefore, determining optimum doses and strategies is critical for both productivity and environmental sustainability.

The use of organic fertilizers positively supports the accumulation of secondary metabolites by stimulating soil fertility and microbial activities, while also improving the biosynthesis pathways of plants [18, 19]. However, excessive fertilization can create metabolic stress and cause a reduction in active compound production. Organic fertilizers have been shown to improve soil structure, stimulate root development, and enhance the synthesis of secondary metabolites [19,15, 16, 17]. They reported that organic and inorganic fertilizers applied to Mentha piperita significantly affected essential oil composition. Therefore, the importance of organic and balanced fertilization within sustainable agricultural approaches is further increasing [20].

Organic and bio-chemical fertilizers have been shown to increase essential oil and phenolic compounds in basil, improving its antioxidant activities. These applications support product quality and environmental sustainability by reducing chemical fertilizer use [21]. One study reported in their study that chicken manure was effective in essential oil yield and that vermicompost also increased flavonoid content and antioxidant activity [22].

Bio-fertilizer use increases essential oil percentage and yield by enabling microorganisms around the roots to produce plant growth-promoting compounds [23]. Seed inoculation with microorganisms like Azotobacter has compensated for nitrogen deficiency as an alternative to chemical fertilizer use [24]. Studies on fennel and anise show that the combined use of organic and bio-fertilizers increases essential oil yield [25].

Fertilizer applications in the cultivation of medicinal and aromatic plants, especially basil, are reported to have positive effects on fresh and dry yield and essential oil content [26,27]. However, the effects of fertilizers on phenolic compounds vary depending on the application type, with phenol content differing based on the type of fertilizer used [6, 28]. According to one study, the phenol content in plants depends on the type of fertilizer applied [28].

In a study on ginger (Zingiber officinale), increased photosynthesis through soil improvement enhanced flavonoid and phenol content, thereby boosting the plant's antioxidant activity [29]. In roselle (Hibiscus sabdariffa), bio-fertilizer inoculation increased plant diameter, and seed diameter inoculated with nitroxin was 2% higher than the control group [30]. Research on goldenberry (Physalis alkekengi) found that a combination of bio-fertilizer and bio-sulfur increased the number of lateral branches. Additionally, a combination of vermicompost and nitroxin on rosemary (Rosmarinus officinalis) was reported to increase plant dry weight and essential oil percentage [31].

In recent years, using molecular biology techniques, the effects of fertilization on gene expression and enzymatic activities have begun to be investigated in more detail. These approaches facilitate the understanding of the regulatory roles of nutrient elements in metabolic pathways and provide a basis for the development of precise fertilization strategies [11,32].

The molecular-level regulation of secondary metabolites depends on explaining the complex biochemical pathways in plant metabolism through classical and molecular biology research [11]. The contributions of molecular biology techniques to understanding the effects of fertilization on gene expression and enzymatic activities allow for more precise and effective management of secondary metabolite production [32]. These techniques are used to optimize the effectiveness of fertilization by helping to understand the regulatory mechanisms in plant metabolic processes.

The literature emphasizes that integrated and controlled fertilization strategies yield more sustainable results in increasing yield and quality in medicinal and aromatic plants [7]. At the same time, these studies facilitate the understanding of the regulatory roles of nutrient elements in metabolic pathways and provide a basis for the development of precise fertilization strategies [8].

In conclusion, the effect of fertilization on the biosynthesis of secondary metabolites is of strategic importance for increasing plant production and product quality. However, to maximize this effect, fertilization practices need to be planned more precisely and integrally in line with the principles of environmental sustainability and economic efficiency. Fertilization strategies should be customized according to the plant species, targeted metabolites, and environmental conditions to increase the production of active compounds in medicinal and aromatic plants.

Effects of Macro Nutrient Elements: Macro nutrients such as nitrogen (N), phosphorus (P), and potassium (K) form the fundamental building blocks of plant metabolism. Nitrogen is involved in protein and amino acid synthesis, phosphorus in energy transfer (ATP) and DNA synthesis, and potassium in osmotic balance and enzyme activation. For instance, two study demonstrated that nitrogen and phosphorus fertilization applied to Vitex negundo significantly increased polyphenol and essential oil content [7, 8].

Nitrogen Fertilization: Nitrogen, while being an essential macro nutrient for plant growth, exhibits a dual, dose-dependent effect on secondary metabolism. Recent research indicates that fertilization regimes regulate active compound concentrations, particularly in plants with high essential oil content. Many studies have found that appropriate nitrogen application can increase menthol and essential oil synthesis, while excessive doses can negatively affect this synthesis [12]. Low-dose nitrogen application, especially in medicinal and aromatic plants, enhances essential oil synthesis [12, 19, 32]. A study on Ocimum basilicum reported that moderate nitrogen application significantly increased linalool and methyl chavicol ratios [19]. Similarly, in Mentha arvensis, levels of menthol and menthone, and in Ziziphora clinopodioides, monoterpene compounds like menthone, menthol, and pulegone, were reported to increase with nitrogen döşe [11].

One study identified 612 metabolites in a metabolomic analysis of Goji berry subjected to three different nitrogen levels, with significant changes detected in 53 of them [33]. These changes were concentrated particularly in compounds such as lipids, fatty acids, organic acids, and phenolamides. The findings reveal that nitrogen fertilization affects the quality components of Goji berry at a molecular level [34].

All these findings indicate that fertilization strategies should be carefully planned not only in terms of yield but also with regard to quality parameters. Fertilization programs optimized according to plant species, soil properties, and targeted active compounds are one of the cornerstones of sustainable agriculture.

Phosphorus and Potassium Fertilization: Phosphorus and potassium are macro nutrient elements that play significant roles in plant metabolism and particularly promote the synthesis of flavonoid and phenolic compounds. Potassium plays an important role in carbon metabolism and enzymatic reactions, supporting phenolic compound production [10]. Furthermore, the positive effects of phosphorus on plant growth and metabolism are directly related to the production of phenolic compounds and essential oil composition. A recent study on Vitex negundo observed that phosphorus fertilization increased total phenolic and flavonoid content, with significant increases in the proportion of compounds like β-caryophyllene and eremophilene in the essential oil composition [7]. Similarly, one study demonstrated that phosphorus doses altered the flavonoid profile and antioxidant capacity in Lycium barbarum (goji) fruits [35].

In medicinal and aromatic plants, phosphorus fertilization shows distinct positive effects on vegetative growth, essential oil yield, and secondary metabolite production. Studies conducted on various plants have revealed that optimum phosphorus doses vary depending on the plant species and growing conditions, but applications generally ranging between 20–250 kg/ha have improved yield and quality [36, 37, 38]. Specifically, the quantities of components such as thymol, cineole, camphor, and flavonoid derivatives significantly increased with certain phosphorus doses [39, 40].

Potassium plays a critical role in the synthesis of secondary metabolites in medicinal plants and positively influences the production of metabolites such as phenolic compounds, flavonoids, and terpenoids [41]. For example, one study showed that potassium application in basil (Ocimum basilicum) increased phenolic and flavonoid content, thereby enhancing antioxidant capacity [42]. Similarly, one study reported that potassium fertilization increased essential oil components, particularly menthol content, in peppermint (Mentha piperita) [40]. These studies support that potassium promotes secondary metabolite production in medicinal plants, improving plant quality [43].

Potassium deficiency can negatively affect enzymatic reactions involved in flavonoid synthesis, thereby reducing the plant's antioxidant capacity. This directly impacts product quality, especially in plants cultivated for food and pharmaceutical purposes.

Effects of Micro Nutrient Elements: Micro elements such as zinc (Zn), iron (Fe), manganese (Mn), and boron (B) play an important role as cofactors for enzymes involved in secondary metabolite synthesis in plants. A deficiency of these elements can lead to a decrease in the production of flavonoid and phenolic compounds. Zinc and iron are associated with the phenylalanine ammonia-lyase (PAL) enzyme, which is involved in the synthesis of flavonoids and phenolic compounds. Zinc and iron deficiencies can reduce the activity of these enzymes, negatively impacting secondary metabolite production [32].
Zinc (Zn) participates in important biophysicochemical processes in plants, such as protein synthesis, gene regulation, and as a cofactor for antioxidant enzymes.

It also helps reduce oxidative damage under abiotic stress conditions [44]. Zinc contributes to increased essential oil production and phytochemical components by protecting plants against water insufficiency and drought stress [45, 46]. Furthermore, zinc enhances nitrogen and phosphorus efficiency in plants, mitigating the negative effects of nutrient deficiencies [47].

The impact of micro element-supported fertilization programs has been confirmed, particularly in plants like Thymus vulgaris and Salvia officinalis, by improving essential oil quality. One study highlighted that fertilization with micro nutrient elements increased secondary metabolite production and essential oil quality in these plants [32].

Effects of Organic and Inorganic Fertilizers: The effects of organic and inorganic fertilizers on secondary metabolite production in plants differ significantly. While organic fertilizers can indirectly enhance secondary metabolite production by positively influencing soil microbiota, inorganic fertilizers exhibit faster and more direct effects [48]. Organic fertilizers support soil microbiota, increasing microorganism activity and thereby stimulating plant metabolic activities. One study stated that organic fertilizers enrich soil microorganisms, enhancing biological activity, which indirectly triggers secondary metabolite production [18].

It has been highlighted in many studies that organic materials such as farmyard manure, compost, and vermicompost have distinct positive effects on secondary metabolites [18, 15, 16, 17]. A study on Melissa officinalis reported that organic fertilizers significantly increased both total phenolic content and rosmarinic acid levels [49]. Furthermore, a meta-analysis by [15, 16, 17] stated that organic fertilization increased the amount of active compounds by an average of 18%, with compost and vermicompost applications being particularly effective.

Inorganic fertilizers, on the other hand, provide nutrients to plants more rapidly and are directly utilized in metabolic

activities. However, excessive use can lead to salt accumulation in the soil and disruption of microbial balance, causing long-term negative effects [8]. The correct combination of organic and inorganic fertilizers can optimize both plant growth and the quality of active compounds.

Studies demonstrate that organic fertilizers provide more sustainable and long-term effects on plants' secondary metabolism. It has been noted that organic fertilizers, especially by increasing microorganism activities, facilitate nutrient uptake by plants, resulting in increased proportions of essential oils, flavonoids, and other phenolic compounds. These findings provide an important indication that organic fertilizers improve soil health and support biodiversity.

CONCLUSION

Fertilization is a crucial agricultural practice that directly influences the production of active compounds in plants. The balanced and strategic use of macro and micro nutrient elements regulates plant metabolic processes, thereby enhancing secondary metabolite synthesis. Recent research indicates that fertilization not only increases plant biomass but also optimizes the quality and quantity of active compounds. Particularly in medicinal and aromatic plants, the impact of fertilization improves the biochemical processes of these plants, increasing the production of compounds with high pharmacological value [48].

The integrated use of organic and inorganic fertilizers ensures the sustainable support of plant growth and soil health. While organic fertilizers have long-term positive effects on active compound production by increasing soil microbial activities, inorganic fertilizers provide short-term nutrient supply to plants [8]. However, since the dosage, timing, and type of fertilizer can affect plant metabolic activities in different ways, the development of plant-specific fertilization programs is of great importance [12,34].

Future studies at the molecular level will elucidate in more detail the mechanisms of fertilization on gene expression, enzymatic activities, and metabolite accumulation. This will enable the development of more precise and effective nutrient strategies. Concurrently, using biotechnological approaches, the optimization of active compound production in medicinal plants should be targeted. Considering sustainable agriculture and environmental impacts, the combined use of organic and inorganic fertilizers stands out as the most ideal recommended approach [11].

In conclusion, the yield and quality of active compounds in medicinal and aromatic plants can be increased not only by focusing on yield enhancement but also by supporting plant metabolism in a balanced way with nutrients. In this regard, the development of plant-specific fertilization programs will be an important step from a sustainable agriculture perspective. In the future, examining the interactions between fertilization practices and plant genetics will further contribute to increasing the efficiency of plant active compound production.

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