

Therapeutic Properties and Use for Medicinal Purposes of *Agastache* Species

HORGA Vasile-Adrian, Dan-Laurențiu SUCIU*, Ionuț-Bogdan HULUJAN, Alexandru D. COSTIN, Sergiu Ștefan CIONTEA, Dan VÂRBAN, Cristina MOLDOVAN, Sorin MUNTEAN, Matei-Marcel DUDA¹

University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca,
Faculty of Agriculture Cluj-Napoca, Romania

*Corresponding author: dan.suciu@usamvcluj.ro

Abstract: Nowadays, it is proven there is an increasing interest in the study of growth and development of different medicinal and aromatic species, due to their therapeutic properties that correlate with the presence of different active compounds. *Agastache* sp. are known as aromatic plants that belong to the *Lamiaceae* family, originating from North America and East Asia. The *Agastache* genus is part of the *Lamiaceae* family and is native to North America, but one species like *Agastache rugosa*, is native to East Asia, such as Korea, Taiwan, Japan, and China. Also, the aim of recent studies is to present a summary of the few findings on the phytochemistry and biological effects of several *Agastache* sp., including both extracts and essential oil properties and characterization. The presented paper has been focused of introduction, description and use of aromatic and medicinal plants, which represent inexhaustible sources of fresh or dry materials for the pharmaceutical industry, cosmetic products and food industries. In the whole process of developing new medicines from herbal raw materials, it is important to study the spectrum of major bioactive compounds and their benefits for human health. Science have proven a significant influence of genetic traits which depends on the subspecies chosen in study, variety, the maturity of the plants, climatic conditions and cultivation features on the accumulation of bioactive compounds in harvested plants material.

Keywords: *Agastache*, essential oil, health, medicine.

Introduction

From the *Lamiaceae* family many plants are used in traditional medicine as herbal products, but also as flavourings in the

food industry (Karpinski, 2020; Lawson et al., 2021). The genus *Agastach* is part of the *Lamiaceae* family that have origin from North America and East Asia and also includes 22 species of perennial, ornamental and medicinal plants (Hashemi et al., 2017). It is known as giant hyssop and is used in traditional medicine as a remedy for pain, hypertension, gastrointestinal disorders and infections (Wesolowska, 2019; Verano et al., 2013; Najar et al., 2019). From the *Lamiaceae* family, *Agastache* sp. are less investigated compared to other medicinal plants, both from a phytochemical and therapeutic perspective. The knowledge about their benefits in alternative medicine has been passed from one generation to the next, over the centuries (Marrelli, 2021; Park et al., 2019).

In modern medicine, the health benefits of some chemical compounds from natural sources increased interest. More herbal products with a growing interest, are used as sources of bioactive compounds, such as in herbal teas, food supplements with herbal powders, essential oils, extracts from different solvents, purified isolated organic compounds, and in synergistic drug combinations (Atanasov et al., 2021; Montone et al., 2021). Many advantages were exposed after the use of some compounds from natural sources, such as chemical diversity, targeting multiple host sites through various mechanisms, displaying high biological specificity, and low side effects (Fadaka et al., 2021; Bălănescu et al., 2022). In the current context, taking into account the worldwide largest number of diseases that affect humans such as gout, cardiovascular diseases, diabetes or cancer (Khan et al., 2019; Baker et al., 2022; Al-Ishaq et al., 2019), the adapted cultivation of various plants from other geographical regions have a major importance to properly reduce the costs of cultivating, processing, and transport, and also to make more plant products with therapeutic applications (Svitlana et al., 2020) available for consumers. This innovative and sustainable approach is also able to promote the impact of natural compounds from cultivated plants on human health. Nowadays, human diseases are becoming more aggressive and resistant to classical drugs; therefore the demand for new treatments is increasingly aiming to explore new sources of natural multi-target drugs (Venugopala et al., 2019).

Plants are increasingly explored sources in the search for new drugs with positive effects in human health. According to previous studies, the efficacy of natural compounds with antioxidant activity for therapeutic purposes was demonstrated, and future studies may develop their applications in clinical therapies (Bhuyan et al., 2022).

The potential of biological activities of *Agastache* species differ between subspecies and is known that each has a varied chemical profile. Essential oils are natural products, obtained from plant resources include steam distillation, expression, solution extraction, cold enfleurage, and supercritical extraction, from fragrant plants, historically used throughout the world as anti-inflammatory, soothing, and stimulating agents. The variation in the composition of essential oils and extracts of *Agastache* medicinal plants depends to their genetic variations, the stages of plant growth, geo-climatic conditions from the studied area, nitrogen applied fertilizers, irrigation regimes, and maturity stage at the time of harvesting (Svitlana et al., 2020). This plant is a source of bioactive compounds that could be good candidates in therapeutic applications to treat human diseases and may find use as raw material for the nutraceutical, food, pharmaceutical, and cosmetic industries, and may be synergistically used with other antioxidants and chemotherapeutic agents (Bălănescu et al., 2023).

Some of the most studied sp. of the genus are *Agastache rugosa* (Fisch. & C.A.Mey.) Kuntze, *Agastache Foeniculum* (Pursh) Kuntze and *Agastache Mexicana* (Kunth) Lint & Epling (Wesolowska, 2019; Verano et al., 2013; Najar et al., 2019). Similarly, *A. urticifolia* has received considerable attention for its strong aromatic properties and is successfully used in medicine.

The acclimatization of *Agastache* species in Romania raised the interest for the analysis of their chemical composition and biological activity, especially because was recently introduced in culture (Matei et al., 2010). The phytochemical profile can significantly vary due to many internal and external factors, including plant organs, genetic profile, environmental factors, such as growing site and soil type (Cirak and Radusiene, 2019).

Most studies carried out on Romanian cultivated *Agastache* sp. evaluated their agronomic suitability (Vârban et al., 2021), and fewer described their phytochemical profile and pharmacological properties for therapeutic applications (Bălănescu et al., 2023).

Taxonomy and physiology of the plant

The family *Lamiaceae* includes herbal plants such as *Rosmarinus officinalis* (rosemary), *A. rugosa* (Korean mint), *Salvia officinalis* (sage), *Ocimum tenuiflorum* (basil), *Origanum vulgare* (oregano), *O. majorana* (marjoram), and *Melissa officinalis* (lemon

balm) (Alfieri and Mann, 2015). They are also used as ornamental plants being the most common, making giant hyssops one of a few examples in the mint family where decorative value appears to overshadow its potential as a medicinal plant. Also, they are used as spices and as an important source of essential oils (Wesolowska, 2019; Verano et al., 2013).

Plants from *Agastache* genus are short-lived herbaceous perennial, reaching one meter or more in height. The stems can be simple or branched, erect or slightly creeping, and with an occasionally woody stem base. Their morphology is typical for *Lamiaceae*, with opposite petiolate leaves, a four-angled stem, numerous trichomes and labiate flowers with pink, purple, white, yellowish or orange corolla. These plants have prevalingly ovate or deltoid-ovate leaf shapes with serrate or crenate margins. The inflorescence is comprised by small flowers arranged in verticillasters (WFO, 2021). They exhibit a hemicryptophyte life-form in conditions of Romania (Vârban et al., 2021). The genus does not occur naturally in Europe, but species from this genus are promising medicinal plants from which herba is harvested during flowering and can be valorised as green or dried biomass as well as for essential oil production (Duda et al., 2013; Muntean et al., 2016).

Chemical Composition and nutritional value

The studies evaluated the chemical composition and showed that extracts from *Agastache* sp. contain polyphenols, such as flavonoids (tilianin) (Yuk et al., 2023) and rosmarinic acid (Nam et al., 2020).

In Romania, several *Agastache* sp. have been successfully acclimatised and introduced in culture (Matei et al., 2010; Vârban et al., 2021), raising the interest for their pharmacological and phytochemical investigation. The extracts from *Agastache* species especially contain polyphenolic compounds, such as caffeic acid derivatives (Bielecka et al., 2019; Park et al., 2019). Tilianin, acacetin and rosmarinic acid have been reported as major components (Hong et al., 2021). Extracts from *Agastache* sp. contains various polyphenols, with flavonoids and caffeic acid derivatives. Tilianin is the major compound in *Agastache* sp. extracts, followed by rosmarinic acid (Figure 1) and also chlorogenic acid. Rosmarinic acid is a caffeic acid derivative, identified mainly in *Lamiaceae* species. Rosmarinic acid has been associated with various biological actions,

with benefits in inflammation, diabetes, cancer and liver diseases (Noor et al., 2022).

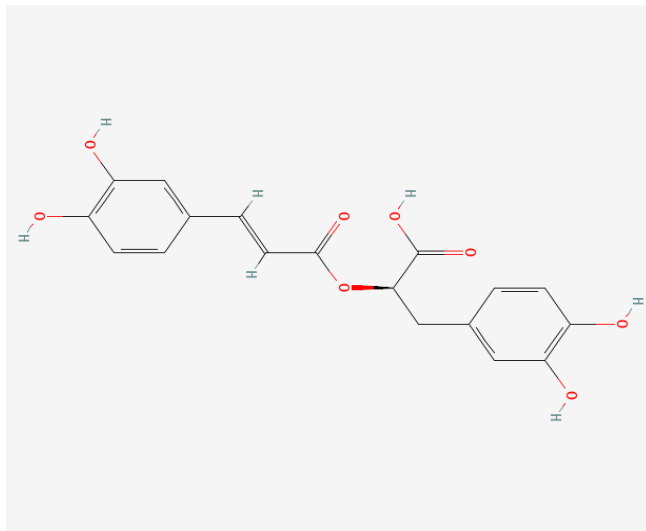


Figure 1. Rosmarinic acid chemical structure
Source: <https://pubchem.ncbi.nlm.nih.gov>

The main property of this plant is to improve metabolism and activate the immune system. The essential oil is able to decrease blood pressure and has bactericidal properties, and the presence of bioflavonoids suggests its use as an antioxidant agent (Choi et al., 2016). The essential oil obtained by steam distillation from *Agastache* plants is characterized by a high content of estragole (41.1%) and pulegone (20.4%). Estragole determines the strong antibacterial effect of the oil and its phytotoxic properties. Its presence gives the anise-like smell. Pulegone, gives the essential oil insecticidal properties, therefore, it can be recommended in the biological protection of plants. Rosmarinic acid is a naturally occurring phenolic carboxylic acid that is commonly found in the *Lamiaceae* family. Essential oils have potential use in the modern application of experimental medicine.

Methyl chavicol (80.24%), also known as 4-allylanisole (Kim, 2008), is the primary component of the essential oil from *A. rugosa* leaf extract. In addition, 31 compounds were determined from this plant (Kim, 2008), while only six compounds were characterized in this study. Another study was conducted on the dried flower and leaf

of *A. rugosa* with a similar method and illustrated 21 components in the flower oil, representing 99.7% of the total oil (Gong et al., 2012).

Uses of *Agastache* species in medicinal purposes

Agastache species are traditionally used for the treatment of anorexia, vomiting, cholera, diarrhoea, anxiety, miasma, nausea and bacterial infections (Park et al., 2016; Yeo et al., 2021). *Agastache* sp. extracts have a wide range of therapeutic properties, including antioxidant (Bălănescu et al., 2023; Shtereva et al., 2016), anti-adipogenic (Hwang et al., 2021), anti-osteoporotic (Hong et al., 2021; Jang et al., 2021), gastroprotective (Nam, 2020), anti-inflammatory (Lee et al., 2020) and antihypertensive properties (Hernández-Abreu et al., 2013).

Essential oils are traditionally used for treating different diseases in the digestive, nervous systems, respiratory tract, and skin (Park et al., 2016). Often, essential oils including those used to treat diseases were extracted by steam distillation method. Essential oils are generally utilized and produced in the cosmetic, food, and medicinal industries as natural alternatives to synthetic products for preventing and treating infectious diseases. The content and yield in the steam distillation process depend on the component acquisition and the extraction method (Seify et al., 2018; Song et al., 2020). Tilianin possess antioxidant capacity, and it is also well-known for its health benefits such as modulating oxidative stress-related inflammation (Nam et al., 2006) and apoptosis and cardio-protective and anti-hypertensive behaviours (Hwang et al., 2021). 4-Allylanisole possesses many pharmacological and biological activities, including antioxidant, antimicrobial, and anti-inflammatory properties, and its flavours can be also used in the pharmaceutical, cosmetic, and antimicrobial fields for food preservation. Tilianin has various biological and therapeutic impacts (Nam et al., 2005). There are various mechanisms contributing to the protective activity of tilianin such as free radical scavenging and inflammation modulation. Tilianin is used to treat a variety of ailments, and to modulate health and longevity. It is a potential treatment for many different diseases via several therapeutic pathways (Akanda et al., 2019).

Previous studies revealed that *A. rugosa* has antiatherogenic, antimicrobial, antitumor, and anti-inflammation effects and may mitigate hyperlipidaemia, and postmenopausal osteoporosis symptoms (Hong et al., 2021). *A. rugosa* leaves and flowers have a

unique aroma, and so it has been used as a deodorant, spice, and tea throughout East Asia (Desta et al., 2016; Kim et al., 2013). *Agastache* species are a unique food ingredient and a folk medicinal herb with multiple potencies (Oh et al., 2016). These compounds have protective effects on human health, especially related to their antioxidant activity (Dwivedi et al., 2016), their anti-inflammatory, antibacterial, antiviral, anti-skin ageing, anti-cancer properties, and to osteoporosis, insulin sensitivity, obesity, and cardiovascular disease (Matsumura et al., 2023; Mutha et al., 2021). It is a plant source containing both bioactive compounds (Desta et al., 2016) used to treat anxiety, cholera, infections, nausea, and gastrointestinal problems (Cao et al., 2017; Gong et al., 2017), and antimicrobial and antifungal agents (Desta et al., 2016) (Table 1). It also possesses HIV integrase inhibitory activity and is a potential drug candidate against COVID-19 (Adhikari et al., 2021).

Table 1

Health benefits and associated compounds found in the most studied species of *Agastache*

Species	Main compounds	Health benefits	References
<i>Agastache rugosa</i> (Fisch. & C.A.Mey.) Kuntze	Tilianin Rosmarinic acid Caffeic acid Ferulic acid Methyl chavicol	Treat abdominal pain (malaise, chills, and diarrhea) Antimicrobial, Antiatherogenic	Park et al., 2021; Hong et al., 2021
<i>Agastache foeniculum</i> (Pursh) Kuntze	Tilianin Derived flavonoids Terpenoids Estragole	Treat cardiovascular diseases Treat abdominal pain Treat burns and fever	Duda et al., 2013; Fálticeanu and Munteanu., 2006; Matei et al., 2010
<i>Agastache urticifolia</i>	Tilianin Menthone Limonene	Immunostimulant tonic Anti-inflammatory Antispasmodic	Bogdan et al., 2021
<i>Agastache mexicana</i> (Kunth)	Tilianin Methyleugenol Estragole Pulegone Acacetin	Reduce hypertension Anti-inflammatory Vasorelaxant effects Antihypertensive activity	Verano et al., 2013; Palma-Tenango et al., 2021

Natural antioxidants, including phenolics and flavonoids found in a diverse array of plant-based foods such as fruits, vegetables, cereals, and spices, offer protective roles against oxidative stress (Shahidi & Zhong, 2015). The increased interest in natural antioxidants over synthetic ones underscores the exploration of plant-based sources for new antioxidant compounds, driven by their potential health benefits and minimal adverse effects (Lim et al., 2024). Due to their bioactive components, *Agastache* species could be promising therapeutic agents for human health with antioxidant, anti-inflammatory, analgesic, antimicrobial, antihypertensive, vasorelaxant, antiviral, nutraceutical, anticancer, and anti-diabetic properties (Ivanov et al., 2019; Lashkari et al., 2020; Palma-Tenango et al., 2021).

Conclusion

- Studies carried out and experimental research from the species of *Agastache* demonstrated the fact that a lot of chemical compounds present in plants have many benefits for human health. Not only does the herba have benefits on human health, but also essential oil obtained from it, prevents and cures some diseases.
- The *Agastache* species have a wide range of therapeutic properties, and antihypertensive properties, which is why recent studies have highlighted the effects of the chemical compounds existing in plants, to precisely develop treatment possibilities for more and more diseases.
- The plant presents more interest because it is a relatively recently cultivated plant, especially in Romania where several *Agastache* sp have been successfully acclimatised and introduced in culture.
- Deepening the effects of existing chemical compounds, as well as discovering new therapeutic effects for each *Agastache* species existing in culture, represents an important step that studies in the field have taken in this direction.
- It is known that these plants have therapeutic properties for most of common diseases but the importance of them significantly increased after the studied has shown the fact that it can prevent or even treat some serious conditions such as cancer, heart disease, HIV, and even COVID-19.

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