The essential oils of the genus *Salvia*

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Abstract

This concise review paper aims to briefly state the current state of analysis of secondary metabolites of the genus Salvia. The research focused on the essential oils of the seventeen species published in the last two decades. The review shows that Salvia officinalis *L.,* Salvia sclarea *L., and* Salvia pratensis *L. accumulate the highest volatile compounds. We outline the major identified volatile constituents for all the analyzed Salvia species and chemical classes of the genus Salvia, with percentage composition >1% and reported by at least two independent authors. The primary types are monoterpene hydrocarbons, sesquiterpene hydrocarbons, oxygenated monoterpenes, oxygenated sesquiterpenes, and aliphatic components. The review shows that caryophyllene oxide, 1,8-cineole, germacrene D, β-caryophyllene, spathulenol, and α-humulene are characteristic for genus Salvia. These major compounds extracted from the air-dried or fresh plants were obtained from different soils, altitudes, and countries.*

Keywords

Secondary metabolites, essential oils, genus Salvia

Introduction

The phenomenon of secondary metabolites was recognized in the early days of modern experimental botany (Sachs, 1873). Secondary metabolites are chemicals produced by plants and other organisms that are not essential for their life (growth and development). In plants, they occur in small amounts in specific tissues. They are formed by the transformation of intermediates of primary metabolism. Their chemical variability depends mainly on genetic factors, but the influence of climatic conditions has also been proven. They are assumed to be protective against the adverse effects of external biotic and abiotic factors. Many secondary metabolites are biologically active substances and are used in the food, pharmaceutical, and cosmetic industries. Other secondary metabolites with a biocidal effect against phytopathogens can be used instead of classical agrochemicals (Guerriero et al., 2018).

The genus *Salvia* (sage) is the richest in the number of species of the family Lamiaceae. More than 900 species of sage represent aromatic plants, perennials blooming in various colors. Other species are woody shrubs, shrubs, semi-shrubs, rarely trees. The genus *Salvia* is widely distributed in its species diversity in Latin (Mexico) and South America, in Central and East Asia, in the Mediterranean region, which is considered

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to be its development center, from where it has spread further across Europe. It occurs in all climatic zones. There are hundreds of natural and bred hybrids in the genus *Salvia* (Whittlesey, 2014). Del Carratore et al. (1998) scientifically discuss the historical formation of sage nomenclature, citing works from the 16th century.

This concise review article outlines major essential oils found in 17 species of the genus *Salvia*. The article describes those compounds found with percentage composition >1% and reported by at least two independent authors.

Chemical Compounds in plant metabolism

Plants synthesize many different secondary metabolites (estimated at 200,000), with complex chemical compositions produced in response to various forms of environmental change to perform basic physiological tasks such as attracting pollinators, creating symbiosis, and providing structural components to woody cell walls of vascular tissues (Ncube & Van Staden, 2015). Other roles of secondary metabolites include plant protection (for example, against viruses and bacteria) and protection against external influences such as UV radiation or cold, where secondary metabolites and their composition represent a specific response to stimuli and environmental changes. Many secondary metabolites produced by plants have bioactive components which are medicinal or toxic. They are traditionally used in medicines, fragrances, flavors, or dietary supplements. They can be essential in cosmetics. Therefore, the scientific and industrial interest in secondary metabolites is enormous (Guerriero et al., 2018).

Biochemical variability

The content of chemical components in plants is not identical but is precisely organized and controlled by biogenetic metabolic processes and metabolic pathways. Most of the secondary components are produced by basic biogenetic processes leading to one or more secondary metabolites, from which numerous derivatives are usually formed by simple enzymatic transformations (Hartmann, 1996). The predisposition to chemical diversification thus forms the essence of the basic secondary metabolites. Guerriero et al. (2018) classify the secondary plant metabolites into four main classes:

1. Terpenoids
2. Flavonoids and phenolic compounds
3. Alkaloids
4. Nitrogen and sulfur compounds

Typical characteristics of secondary metabolites are biochemical variability and the "high degree of freedom" of their components and derivatives. Certain products of metabolic chains may differ qualitatively (structurally) and quantitatively (in concentration), or they may disappear without more serious consequences for plant growth and development. Thus, they differ significantly from the primary metabolites, which are essential for plants and must be strictly stable to guarantee the structural and functional integrity of the cells or organism, the synthesis of building blocks, enzymes, or hormones (Berenbaum & Zangerl, 1992; Harborne, 1993). In essence, secondary metabolites' degree of freedom (in the chemical sense) is the mechanical basis of chemical variability. Consequently, it is necessary for diversification that occurs under the specific influence of ever-changing environmental conditions (Hartmann, 1996).

The chemical variability of secondary metabolites depends not only on genetic factors but also on climatic conditions. Recent studies have confirmed that the two most important factors of global warming - increased concentrations of CO_2 in the atmosphere and heat - have a significant adverse effect on the production of secondary metabolites in tree leaves (Holopainen et al., 2018). CO_2 increases the proportion of phenolic components in the leaves and, conversely, reduces the formation of terpenoids. The effect of warming has the opposite impact, reducing the production of phenolic compounds in the leaves and, conversely, increasing the output of terpenoids. Other non-biotic products show even more variability. Plants can cope with the stress caused by changes in the environment through changes in the formation of secondary metabolites (Jardine et al., 2017).

Essential oils of the genus Salvia

Several species of the genus *Salvia*, the most representative genus of the *Lamiaceae* family with about 900 species, are grown worldwide for their essential oils. The essential oils have various biological properties such as antimicrobial, viricidal, cytotoxic, antimutagenic, and antifungal (Russo et al., 2013). Table 1 describes major compounds of the genus *Salvia* of seventeen *Salvia* species: *Salvia aethiopis* L., *Salvia amplexicaulis* L., *Salvia austriaca* L., *Salvia chloroleuca* L., *Salvia divaricata* L., *Salvia dumetorum* L., *Salvia eriophora* L., *Salvia forsskaolei* L., *Salvia glutinosa* L., *Salvia longipedicellata* L., *Salvia nemorosa* L., *Salvia officinalis* L., *Salvia pilifera* L., *Salvia pratensis* L., *Salvia sclarea* L., *Salvia verbenaca* L. and *Salvia verticillata* L. Subsequently, Table 2 introduces their major identified volatile constituents.

The essential oils are usually extracted from the air-dried samples and then are subjected to hydrodistillation for 2–3 hours. Some authors also analyzed the fresh plants (Senatore & De Feo, 1998; Then et al., 2003; Ben Farhat et al., 2019). Šulniūtė et al. (2017) isolated the volatile compounds from just 10g of dried herbs. Other authors usually used larger samples. Šulniūtė et al. (2017) also explored supercritical fluid extraction with carbon dioxide (SFE-CO2), but the amount of volatiles isolated was 1.4–5.9 times lower compared to hydrodistillation. Gas Chromatography (GC) and Gas Chromatography-Mass Spectrometry (GC–MS) evaluated the essential oil components.

Table 1. Major compounds of the genus *Salvia* with percentage composition >1% and reported by at least two independent authors (Senatore & De Feo, 1998; Veličković et al., 2002; Anačkov et al., 2009; Then et al., 2003; Šulniūtė et al., 2017; Ben Farhat et al., 2019; Kurkcuoglu, 2019; Talebi et al., 2019).

Chemical classes	Compound
Monoterpene hydrocarbons	*α*-Pinene, *β*-Pinene, Camphene, Limonene, α-Thujene, β-Thujene, *γ*-Terpinene, Myrcene, p-Cymene, Sabinene
Sesquiterpene hydrocarbons	*β*-Cubebene, E-Caryophyllene, *α*-Humulene, δ-Cadinene, *γ*-Cadinene, Z-β-Farnesene, Bicyclogermacrene, γ-muurolene
Oxygenated Monoterpenes	1,8-Cineole, Linalool, Borneol, Thymol, Camphor, 1-α-Terpineol, Linalyl acetate
Oxygenated Sesquiterpenes	Caryophyllene-oxide, Viridiflorol, Spathulenol
Aliphatic Components	Nonanal, Hexadecanoic acid, 1-methyl ethyl ester
Others	(Z)-β-Ocimene, *α*-Copaene, *β*-Caryophyllene, Germacrene-D, epi-13-Manool, Phytol, Pentacosane

Salvia officinalis L. is the most studied species due to the antibacterial effects of secondary metabolites. It contains monoterpenes with a wide range of carbon structures, including acyclic, monocyclic, and bicyclic compounds. Three different monoterpene synthases cause the formation of the most characteristic monoterpenes of sage essential oil – according to research from Jordan:

1. Sabinene synthase catalyzes the production of sabinene, which undergoes further rearrangements leading to two major monoterpenes, *α*- and *β*-thujone.
2. 1,8-Cineole synthase produces 1,8-cineole in one step.
3. Finally, bornyl diphosphate synthase produces bornyl diphosphate, which is subsequently hydrolyzed to borneol and then oxidized to camphor (Abu-Darwish et al., 2013).

For *Salvia officinalis* L. it was also confirmed that the extract of essential oils from mountain plants had a significantly higher content of *α*-pinene, limonene, *β*-thujone, borneol, and manool, and a lower content of *α*-thujone, camphor, and viridiflorol compared to plants grown in flat areas. According to Bedini et al. (2020), *α*-thujone was the main compound of sage, while they also found significant amounts of camphor and 1,8-cineole. Cvetkovikj et al. (2015) also studied several populations of *Salvia officinalis* L. from the Balkans and identified four different chemotypes that differ in *cis*-thujone, *trans*-thujone, and camphor content. A significant correlation of the essential oil composition with geographical variables was observed. Finally, Tundis et al. (2020) found that camphor (16.16–18.92%), 1,8-cineole (8.80–9.86%), *β*-pinene (3.08–9.14%), camphene (6.27–8.08%), and *α*-thujone (1.17–9.26%) were identified as the most abundant constituents in *Salvia officinalis* L. collected in three areas of Southern Italy. The main components of *Salvia officinalis* L. essential oils are liquid, volatile, form emulsions in water. They are soluble in organic solvents: α- and β-thujone, 1,8-cineole, camphor, and borneol (Šulniūtė et al., 2017).

Table 2. Major identified volatile constituents of *Salvia* species.

Salvia species	Major compounds and % range	References
Salvia aethiopis L. (flowers)	*α*-Thujone (21.8%), 1,8-Cineole (17.0%), Camphor (5%)	Velickovic et al. (2002)
Salvia amplexicaulis L.	Germacrene D (14.8-15.6%), caryophyllene oxide (14.7-10.5%), β-Bourbonene (3.9-4.4%)	Petrovic et al. (2009) Šulniūtė et al. (2017)
Salvia austriaca L.	Thymol (12.4%), neoiso-3-Thujyl acetate (3.4%), phytol (3.3%)	Šulniūtė et al. (2017)
Salvia chloroleuca L. (Polor population)	*β*-pinene (22.7%), *α*-pinene: (18.3%), germacrene D (7.7%), sabinene (6.6%)	Talebi et al. (2019)
Salvia chloroleuca L. (Neyshabur population)	Spathulenol (19.8%), bicyclogermacrene (11.4%), p-cymene (10.8%), *β*-pinene (10.4%)	Talebi et al. (2019)
Salvia divaricata L.	1,8-cineole (34.4%), linalyl acetate (10.3%), linalool (7.8%), *α*-pinene (6.1%), camphor (3.8%)	Kurkcuoglu et al. (2019)
Salvia dumetorum L.	Caryophyllene oxide (11.9%), Manool (9.5%), Spathulenol (2.8%)	Šulniūtė et al. (2017)
Salvia eriophora L.	Caryophyllene oxide (13.7%), heptacosane (8.9%), chavicyl angelate (8.2%)	Kurkcuoglu et al. (2019)
Salvia forsskaolei L.	Spathulenol (10%), (E)-Caryophyllene (5.1%), α-Humulene (2.3%)	Šulniūtė et al. (2017)
Salvia glutinosa L.	Caryophyllene oxide (0.5-5.6%), α-Humulene (0.6-3%)	Šulniūtė et al. (2017); Velickovic et al. (2002)
Salvia longipedicellata L.	*β*-caryophyllene (47.9%), *α*-humulene: (11.5%)	Kurkcuoglu et al. (2019)
Salvia nemorosa L.	Caryophyllene oxide (22%), p-Vinylguaiacol (5.3%), 14-Hydroxy-(Z)-caryophyllene (5.2%)	Šulniūtė et al. (2017); Then et al. (2003)
Salvia officinalis L.	(E)-Caryophyllene (58.8%), Humulene epoxide II (29%), α-Humulene (20.6%)	Šulniūtė et al. (2017)
Salvia pilifera L.	*α*-Pinene (9.4%), *β*-eudesmol (6.1%), myrcene (5.3%), *ar*-curcumene (5.1%)	Kurkcuoglu et al. (2019)
Salvia pratensis L.	Caryophyllene oxide (7.4-20%), 1,8-cineole (3.9-6.2%), *β*-Caryophyllene (1.6-8.1%)	Senatore & De Feo, (1998); Velickovic et al. (2002); Šulniūtė et al. (2017)
Salvia sclarea L.	Linalyl acetate (41%), Caryophyllene oxide (27.2%), (5E,9E)-Farnesyl acetone (23,4%)	Šulniūtė et al. (2017)
Salvia verbenaca L.	Viridiflorol (3.4–17.7%), *α*-pinene (0.7–15.9%), *β*-caryophyllene (1–15.3%), p-cymene (1.3–14.2%), 1,8-cineole: (2–12.8%)	Ben Farhat et al. (2019)
Salvia verticillata L.	Spathulenol (8,9%), Germacrene D (5,6%), Germacra-4(15),5,10(14)-trien-1-α-ol (3,7%)	Šulniūtė et al. (2017)

Anačkov et al. (2009) describe apparent differences in the main compounds in the essential oil of *Salvia pratensis* L., which was E-caryophyllene (26.4%), while in *Salvia bertolonii* L. the essential oil was caryophyllene oxide (35.1%). The main class of substances in the essential oil of *Salvia pratensis* L. was the group of sesquiterpene hydrocarbons (53.7%), followed by aliphatic compounds (15.7%).

Interesting results were found in the quality of essential oil in *Salvia pratensis* L. in the locality of České Středohoří-Radobýl in the Czech Republic, with a very high content of linalool (43.3%) compared to plants from other Czech localities (Dušek et al., 2010). On the other hand, this sample found a shallow caryophyllene content compared to samples from other localities where it showed caryophyllene up to 86.4%; this suggests that the population from this locality is very different from the others. The composition of the essential oil of *Salvia pratensis* L. is generally characterized by a higher proportion of *β*-caryophyllene and *γ*-muurolene. Their ratio in the calyx and the leaf oils is similar, but in the essential oil of the leaves, it is reversed (Then et al., 2003). Veličković (2002) identified caryophyllene as the main compound of the essential oil of *Salvia pratensis* L.

Major essential oils compounds of the same species but different populations are usually the same, but with different percentages. For example, Talebi et al. (2019) reported that two populations of *Salvia chloroleuca* L. harvested from different altitudes 1700 and 2100 m in Iran had the same first and second main groups of compounds, monoterpene, and sesquiterpene hydrocarbons. However, the studied Polor and Neyshabur populations had different percentages of monoterpene hydrocarbons, 62.5%, and 43.9%, respectively, and 16.3% and 24.4% of sesquiterpene hydrocarbons.

Šulniūtė et al. (2017) compared the extraction of essential oils using hydrodistillation and SFE-CO_2 of ten *Salvia* species grown in Kaunas Botanical Garden at Vytautas Magnus University in Lithuania. Hydrodistillation was a considerably more effective method for the extraction of mono and sesquiterpenes (the total amount extracted was from 8 – *Salvia glutinosa* L. – to 195 times – *Salvia sclarea* L. – higher than by SFE-CO_2), which are typical essential oils constituents, whereas alkanes were better extracted by the SFE-CO_2 method (the total amount of extracted alkanes was from 3.5 – *Salvia sclarea* L. – to 40.8 times – *Salvia officinalis* L. – higher than by hydrodistillation).

The essential oil composition of the fresh and dried plant organs of *Salvia nemorosa* L. (native in Hungary) cultivated in the experimental garden of the Ecological and Botanical Research Institute of the Hungarian Academy of Sciences did not differ (Then et al., 2003). The oil composition of each *Salvia nemorosa* L. organ – leaf, calyx, and petal – was the same.

The analysis of *Salvia divaricate* L., *Salvia eriophora* L., *Salvia longipedicellata* L., and *Salvia pilifera* L., the four endemic Salvia species in Turkey, revealed that the species have monoterpene-rich oil under the α/β-pinene group. The remaining two oils contained sesquiterpenes as the main constituents (Kurkcuoglu et al., 2019).

Salvia genus contains a diversity of bioactive constituents, showing significant variations affected by the collection sites and phenophase. Ben Farhat et al. (2019) found that *Salvia verbenaca* L. harvested from 10 regions in Tunisia yielded almost equal amounts of monoterpene hydrocarbons and oxygenated monoterpenes. In contrast, the sesquiterpene fraction was influenced by the collection site.

Conclusion

This article has provided a concise review of major essential oils found in 17 species of the genus *Salvia*. The results indicate that caryophyllene oxide, 1,8-cineole, germacrene D, *β*-caryophyllene, ppathulenol, and α-humulene are characteristic for genus *Salvia*. These major compounds extracted from air-dried or fresh plants were obtained from different soils and altitudes in different countries.

Plants synthesize a vast number of secondary metabolites with a complex chemical composition. The tremendous scientific and industrial interest in secondary metabolites guarantees that knowledge about the essential oils can significantly impact the pharmaceutical and cosmetic industries, agriculture, and the production of food supplements.

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