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A Review on the Phytochemical Composition and the Traditional Medicinal Uses of *Salvia argentea* (Lamiaceae)

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ABSTRACT
Salvia argentea of the family Lamiaceae, is a perennial plant, native to Mediterranean region, which spontaneously grows in Algerian highlands regions.The bioactive substances obtained from *S. argentea* have promising prospects and make it possible to propose different solutions, due to their great heterogeneity and bioactivity for such diverse applications. This article reviews the botanical characteristics, phytochemical composition and uses in traditional medicine of *S. argentea*. This study is a useful synthesis for further research and improvement of various propertiesof *S. argentea* secondary metabolites.

Keywords: *Salvia argentea*, morphology, phytochemistry, secondary metabolites

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INTRODUCTION
Salvia has always been considered as a magical plant that saves human lives. The word *Salvia* comes from the Italian "salvo" meaning "to heal" or "to save". The roots of the Chinese species *S. miltiorrhiza* have long been used to treat cardiovascular, liver and kidney diseases.[1] Diterpenoids are the main secondary metabolites responsible for the various activities of *Salvia* species.[2,3] Antituberculosis activity has been established for *S. blepharochlyna* and *S. multicaulis*, which are also known for their antifungal activity, as well as *S. prionitis*, which in addition possesses antiphlogistic and antibacterial properties.[4] The Spanish species *S. canariensis* has shown antibiotic activity, while antimicrobial activity has been demonstrated for *S. albocaerula*, *S. forskhalei*, *S. lanigera* and *S. officinalis*.[5]

The *Salvia* genus, member of the Lamiaceae family, represents a large and cosmopolitan collection of nearly 900 species,[6,7] 23 of which have been described in Algeria.[4] Figure 1 shows the worldwide distribution of *Salvia* species, including 500 species in Central and South America, 250 species in the Mediterranean countries and Central Asia and finally 90 species in East Asia.[8]

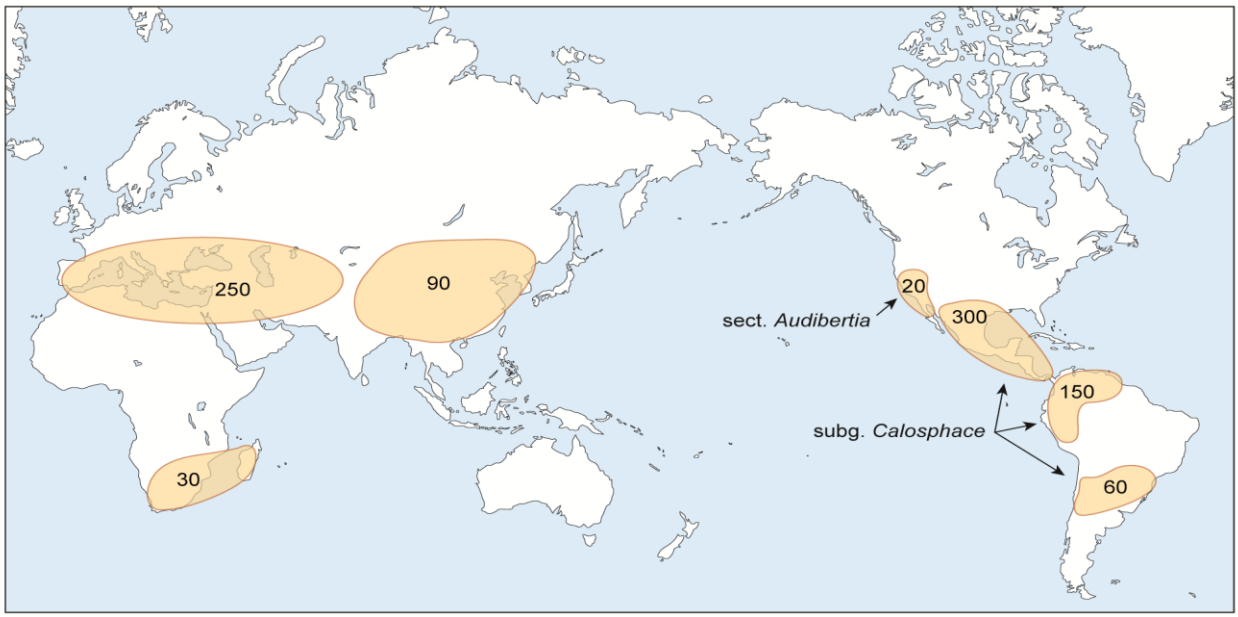

Figure 1. Worldwide distribution of *Salvia* species. Approximate numbers of species are specified in each area.

Among the many species found in Algeria, we have been interested in *S. argentea*, also known under the common name "Ferrache en neda", endemic to Algerian highlands. The aim of this study was to provide an overview of the chemical profile of *S. argentea*, with a stress on the main chemical compounds and their different uses in traditional pharmacopoeia.

GEOGRAPHICAL DISTRIBUTION

S. argentea originates from north-west Africa (north of Algeria, Morocco and Tunisia), southern Europe (Spain, Portugal, Italy, Sicily, Malta, Greece and others) and the westernmost part of Asia (Turkey).[9]

This species is found in meadows, rangelands, scrub clearings, roadsides, cultivated or fallow lands. Indifferent to the substrate, it grows on rocky soils and sunny places at an altitude of between 50 and 1,700 m.

BOTANICAL DESCRIPTION

Silver Sage (*S. argentea*), has been given this name because its foliage has a woolly and silvery looking which is due to the dense hairs on both sides of the leaves.[10]It is an annual or biennial herbaceous plant of the Lamiaceae family. Native to North Africa, it adapts well to a temperate climate. It forms a rosette of leaves during the first year and flowers during the second year. The leaves are covered with a silvery down, very soft to the touch, which makes this sage popular with horticulturists. The white flowers are whorled along the stems, which are about 50 cm tall.[11]

The flowering period happens between the months of June and July with a protandrous ripening order. *S. argentea* is characterized by a dominant white colour of the flowers and Inflorescence in spiciformglomerules.

The development and survival of *S. argentea* depends on climatic conditions. Indeed, it possesses a thick and tuberous root system, and, for this reason, rainfalls and high temperatures, higher than those encountered in the regions of its origin, are considered unfavourable to the growth of the species and have even been found to be harmful.[12]

S. argentea differs from *S. patula*, according to M. Pomel, because of its non-cordate leaves at the base, the upper lip of the calyx with less uneven and larger teeth, and the connective tissue which is more highly toothed at the enlargement point. *S. patula* is considered to be a highly polymorphic species.[13]

SYSTEMATICS

According to Quezel and Santa,[11] the species *S. argentea* is classified as follows:

Reign: Plantea
Under Rule: Tracheobiontes
Branch line: Spermatophytes
Division: Magnoliophytes
Class: Magnoliopsides
Subclass: Asteridae
Order: Lamiales
Family: Lamiaceae
Genus: *Salvia*
Species: *argentea*
Vernacular names of *S. argentea*:
Arabic: Ferrache en neda
French: Sauge argentée

MORPHOLOGICAL CHARACTERISTICS

The morphological parameters of *S. argentea* have been presented by Baran et al.[14]. *S. argentea* has a perennial taproot with a thick outer layer of a dark brown colour. The stem is erect and quadrangular. The leaves are simple and differ between oval and oblong, with irregular, toothed margins and flabell-like nervations. The inflorescence is usually a whorled cyme-like form. The stem, leaves and petioles are covered with a hairy layer. The zygomorphic flowers at the base of bracts are positioned 2-4, 6 in each whorl. The upper lip of the calyx is trident, and the lower lip is bidentate.

The upper lip of the bilabiate corolla is white, pale lilac, strongly falciform. The lower lip is cream-coloured. The stigma is unevenly bifurcated and the stamens of B type. The fruit consists of four dry, light brown, triangular, mucilaginous nucules. The seeds have a reticular patterned surface and the bracts are acuminate.

The whole plant is covered with a dense layer of hairs, in some cases glandular, and in others not (Table1, Figure2).[14,15]

Table 1. Biometry of plant organs of *S. argentea*.

S. argentea organs		Min-Max (cm)	Mean ± S.D.[c](Cm)
Root[a]		15 – 55	29.3 ± 15.3
Stem[a]		20 - 56	42.5 ± 10.8
Leaf[a]		2 - 19.5	8.2 ± 3.9
Leaf[b]		1 -12	4.6 ± 2.5
Petiole[a]		0.8 - 9.5	3.7 ± 2.5
Flower	Pedicel[a]	0.3 - 0.6	0.42 ± 0.08
	Calyx[a]	0.8 - 1.7	1.14 ± 0.22
	calyxteeth[a]	0.02 - 0.5	0.27 ± 0.14
	Corolla[a]	1.7 - 3	2.29 ± 0.4
	Filament[a]	0.4 - 0.6	0.49 ± 0.05
	Anther[a]	0.4 - 0.5	0.41 ± 0.03
	Pistil[a]	4 - 4.6	4.28 ± 0.2
Bract[a]		0.6 - 1.8	1.08 ± 0.32
Bract[b]		0.6 - 1.5	1.06 ± 0.22
Seed[a]		0.3 - 0.4	0.35 ± 0.05
Seed[b]		0.22 - 0.4	0.29 ± 0.05

[a] Length; [b] Width; [c]Standard Deviation.

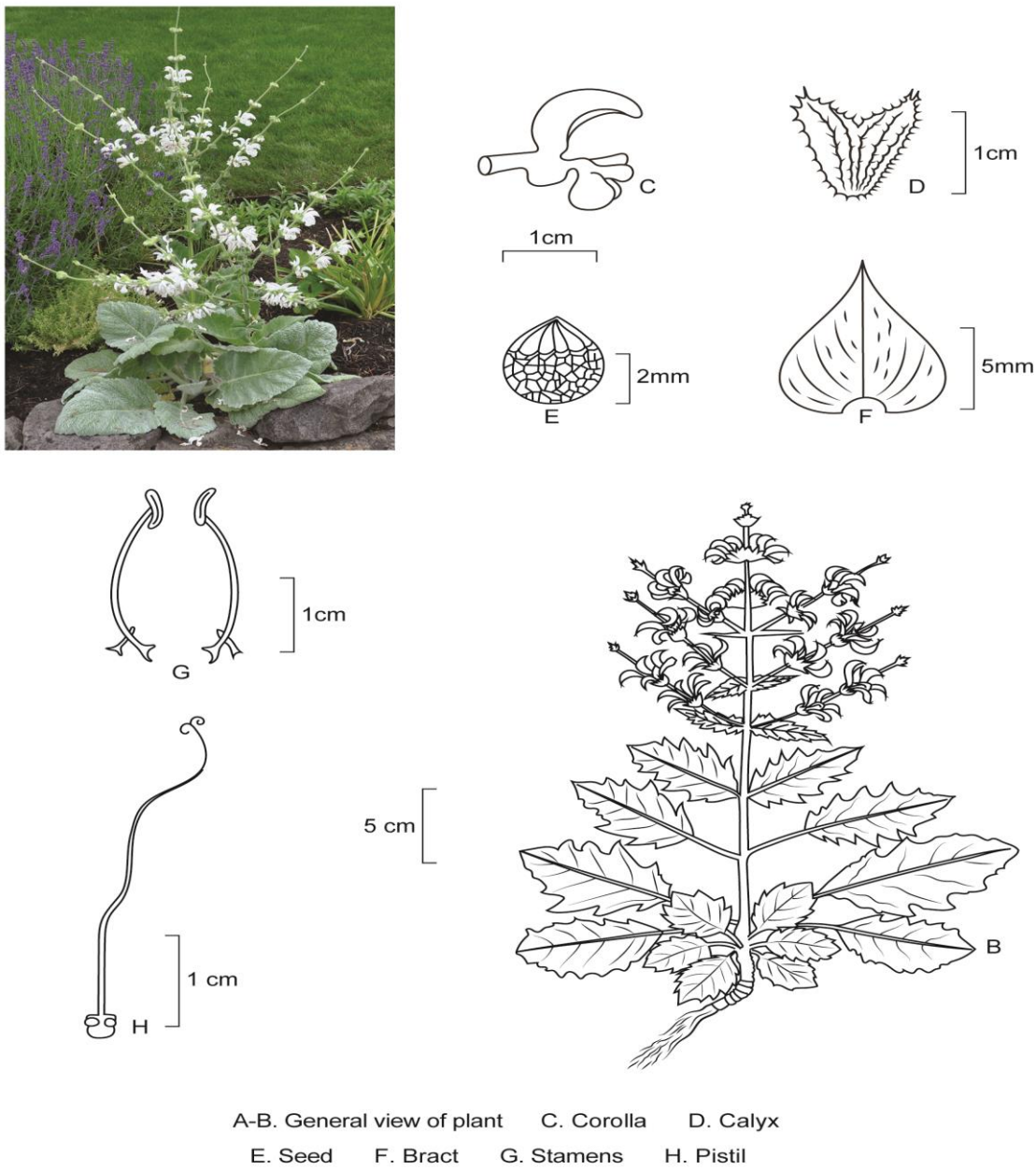

Figure 2. General view and some parts of *S. argentea*.

Glandular trichomes of *S. argentea*

Glandular trichomes are widely distributed on the aerial parts of Lamiaceae. They are the main secreting organs of these plants, and their structures can vary considerably from one species to another.[16]

The glandular trichomes of *S. argentea* have been studied morphologically and anatomically and their distribution on aerial organs have been described. Two main types of morphologically distinct glandular trichomes were determined according to the classification of Werker et al.[17] and Özdemir and Şenel[18]:

1- Trichomes forming a base consisting of 1 to 7 cells with a stem of 1 to 5 cells; they can be stemless and have a uni- or bi-cellular head with different shapes. It has been shown that the neck cell plays an important role, particularly in xeromorphic plants, acting to prevent the reflux of the secreted substances through the apoplast.

2- Glandular trichomes with a large secretory head that may contain 5 to 8 central cells and 8 to 14 peripheral cells. Peeled trichomes are present on all aerial organs except the petiole and are more abundant on the calyx and the corolla.[19]

The essential oil produced by the glandular trichomes is one of the characteristic traits of the Lamiaceae family.[20] Glandular trichomes that develop from epidermal cells are generally considered to be the site of biosynthesis or accumulation of essential oils.[21,22]

Essential oil produced by the glandular trichomes of the Lamiaceae family is important for the pharmaceutical and cosmetic industry, and its valorization as a bio-pesticide is very promising.[16,23] This oil, which gives a special fragrance, is characteristic of many species of the genus *Salvia*.[24] The latter has the richest and most diversified glandular trichomes of the family.[25]

CHEMICAL COMPOSITION

Physico-chemical characterization

Benabdesslem et al. have previously characterized the physico-chemical parameters of *S. argentea* leaf powder (moisture, ash, pH and titratable acidity).[26] The powder revealed a similarly low average water content of 12.89 %. This low content leads to the conclusion that *S. argentea* leaf powder can be stored for a long period of time without causing significant damage due to microbial contamination.[27] On a dry basis, for better reproducibility of results, the ash obtained after incineration represents approximately 17.61%. Indeed, similar results were found in *Spinacia oleracea* (Spinach) with 20.6 % and in *Nasturtium officinale* (Watercrese) with an average of 16.5 %.[28] The average pH value is 8.05. These values can be explained by the chlorophyll characteristics of the leaves of *S. argentea*, which tend to confer alkalinity. The titratable lactic acid value is also related to the pH value determined. Their average value is 0.74. Houndji et al. observed the same tendency in *Moringa oleifera* (Moringa) leaf powder. [29]

Phytochemical screening

Phytochemical screening of *S. argentea* leaf powder shows the presence of chemical groups, which in turn have interesting biological activities. These include alkaloids, flavonoids (such as anthocyanins, saponins, coumarins, sterols and triterpenes), tannic acid (catechins and gallic acid) and reducing sugars. It does not contain any derivatives of hydrocyanic acid (HCN), which significantly reduces the toxicological risks associated with the use of *S. argentea*.[26] Potentially active chemical groups, such as polyphenols (such as two forms of tannin) and anthocyanins, may justify the use of this plant in traditional medicine mainly because of their pharmacological properties.[30.31] Therefore, because of its interesting biological activity, this plant has become the material of choice for enriching conventional medicines.

Three methods have been separately used to extract the essential oils from the aerial parts of *S. argentea:* steam distillation and extraction with petroleum ether and with dichloromethane. The three fractions were analysed by gas chromatography coupled with a mass spectrometer. Analysis of the steam distillate revealed hydroxy-α-humulene as the major compound (40.1%), followed by 1,3,8 -*p*- menthatriene (12.1%), globulol (7.4%) and β-sesquiphellandrene (5.8%). In the organic solvent (petroleum ether and dichloromethane) extracts, tritriacontane (9.9% and 14.1%), heptacosane (8.4% and 10.5%), hentriacontane (8.3% and 10.9%), tetradecanal (8.4% and 10.2%) and methyldotriacontane (7.9% and 7.6%) were recognized as the main constituents. These two extracted fractions were then treated with diazomethane in ether oxide and analysis of the products revealed the presence of methyl linolenate (36.6% and 13.5%) and methyl myristoleate (10.5% and 18.5%).[9]

Other bioactive chemicals of the genus *Salvia*

Many species of the *Salvia* genus have been studied for their biologically active constituents and chemical compounds. Flavonoids, triterpenoids and volatile substances, especially monoterpenes, are the main compounds in the aerial parts, while in the roots, diterpenoids are generally more abundant.[32] However, many classes of phenolic acids, including caffeic acid derivatives,, have also been found in this genus.[33]

The genus *Salvia* contains salvinorins, mainly salvinorin A and salvinorin B. It also contains the following psychoactive parent components: salvinorin TGA, salvinorin F (unknown activity), divinatorins A, divinatorins D, divinatorins E, salvicinase A.

Only salvinorin A appears to cause psychotropic effects, so it is commonly and simply referred to as salvinorin. It is a diterpene with the chemical formula $C_{23}H_{28}O_8$. Unlike most known psychoactive components, salvinorin A is neither an amine nor an alkaloid, which means that it does not contain any functional nitrogen groups. Nor does it act on conventional (5-HT2A) receptors.[34]

It has been shown that the effects of salvinorin A are blocked by kappa opioid receptor antagonists.[35] This means that the effects of *Salvia* can be largely, if not entirely, attributed to kappa antagonism. Salvinorin A is believed to be unique, as it is the only known natural substance that induces a hallucinogenic state via this mode of action.[36]

TRADITIONAL USE

The different species of *Salvia* are widely used medicinal plants and have not lost their importance for many years. As indicated by their name *Salvia* means "Saviour" in Latin and is a plant that is used to cure many diseases.[14]

Salvia has multiple uses such as condiment, food additive, seasoning, spice and is also used as a herbal tea.[37] The seeds of *Salvia* species form mucilages, due to their high content in polysaccharides, which swell in the presence of water and form a gel that is used to produce pleasant drinks and deserts.[38] Otherwise, in Eastern countries, these same mucilages are used to treat eye diseases.[39]In Algeria, herbalists recommend *S. argentea* leaves with different preparation methods for the treatment of respiratory tract diseases.[26,40] Previously, *S. argentea* leaves have also been used as a hemostatic.[41]

In addition to their medicinal properties, *Salvia* species are also used in gardens as ornamental plants.[42]

CONCLUSION

Salvia argentea is a medicinal plant which is widely used by the local population in Algeria. Our interest in this species lies, on the one hand, in the fact that it is still relatively little studied and, on the other hand, because it does not appear in the collections of medicinal plants in Algeria and therefore has no application in conventional medicine.

This work is a very valuable source of information on national and international medicinal plants. It can be further developed for new research in the fields of phytochemistry and pharmacology, with the aim of looking for new natural bioactive compounds with therapeutic interests.

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