

Phytochemistry and Pharmacological effects of *Smyrniium cordifolium* Boiss. (Apiaceae): A review

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ABSTRACT

Background and aims: Belonging to the Apiaceae family, *Smyrniium cordifolium* Boiss. Is commonly known as Avandul in Iran. However, there is limited information about this plant and *S. cordifolium* has been regrettably neglected in Iran. This review was an effort to provide detailed information on phytochemistry and pharmacological effects of *Smyrniium cordifolium* growing in Iran, aimed at taking the first steps towards introducing the species for further future investigations.

Methods: The information of this review was obtained by searching for keywords Apiaceae, *Smyrniium cordifolium*, pharmacological effects and phytochemistry in scientific articles and books published in search engines Scopus, Google Scholar, Science Direct, PubMed, and Web of Science.

Results: This plant is aromatic owing to the presence of essential oil. The Sesquiterpens, monoterpenes and flavonoids were reported as the major constituents of essential oil, and in the traditional medicine of Iran, it was used to treat anxiety, pain, insomnia and as vegetables. Curative application of this national wealth has only been considered from ethnobotanical point of view among indigenous people of the country.

Conclusion: With regard to medicinal and nutritional importance of *S. cordifolium*, it can be used in the pharmaceutical and food industry, and also may be effective for diseases of the bladder and kidneys. Despite that, the bioactivities of *S. cordifolium* have been confirmed in vitro and in vivo studies; however, more studies clinical are required on the bioactivities.

Keywords: Medicinal plants, Phytochemistry, *Smyrniium cordifolium* Boiss., Avendol.

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INTRODUCTION

Smyrniium is a genus of flowering plants in the celery family Apiaceae. *Smyrniium* includes biennial plants with a height of 80 to 120 cm, with a thick and robust stem which becomes hollow and grooved with age, bearing greenish-yellow flowers in umbrella-like clusters with a pungent, myrrh-like scent. The leaves are bright green and toothed, arranged in groups of three at the end of the leaf stalk. The globular fruit is ridged and ripen to a blackish color. The genus comprises about 38 species¹, of which only one species, *Smyrniium cordifolium* Boiss. (an unresolved name), has been reported in the flora of Iran¹⁻² (Fig 1). *S. cordifolium* is well-adapted to the uplands, foothills and associated plains of the Zagros range in the northwest and southwest regions of Iran³, mainly through Kohgiluyeh & Boyer-Ahmad and Chaharmahal & Bakhtiari⁴ and Lorestan⁵, three provinces with a remarkable share of the distribution.

Along with being well appreciated as an aromatic plant, members of the genus have also found a wide range of applications as either functional foods or nutraceuticals. Traditionally, these plants have been used as a fresh vegetable, with a preference being shown for their leaves, young shoots and leaf stalks, which impart a pleasant flavor similar to celery, although somewhat sharper⁶. The raw or cooked roots are served at table, the fleshy stems are eaten raw or cooked as celery and asparagus, the leaves are used as an herb, the flower buds are used raw in salads or can be steamed and eaten in place of broccoli, and the fruits are used to flavor meat, soups and salads^{7,8}. It was also used as an herbal medicine in the treatment of inflammation of internal organs, especially for bladder and kidney⁸. This review evaluates report of phytochemistry and pharmacological



Fig 1. Root (left), leaves at vegetative stage (right), and the whole plant at flowering stage (middle) of *Smyrniium cordifolium* (Photos by Sadegh Doodman, Yasouj-Kohgiluyeh & Boyer-Ahmad, 2018, Identified by Shirmardi, Hamzeh Ali, PhD., Research Center of Agriculture and Natural Resources, P.O. Box 415, Shahrekord, IRAN).

activity to clearer initiate on future perspective about *S. cordifolium*.

Phytochemistry

The plants from the genus *Smyrniium* are aromatic owing to the presence of essential oils, predominantly constituted by furanosesquiterpenoids⁹. Studies by Ulubelen and his colleagues on several species of the genus *Smyrniium* have led to the identification of several compounds belonging to different classes of terpenes, e.g. sesquiterpenoids and furanosesquiterpenoids¹⁰⁻¹⁵ (Fig 2). Their occurrence can be explained by the fact that these molecules are considered to be precursors of sesquiterpene lactones¹⁶, which are known as marker compounds in the genus *Smyrniium*^{17,18}. The parent compound of this class of molecules is isofuranodiene, a thermosensitive molecule which undergoes cope rearrangement to its corresponding element derivative curzerene during distillation¹⁹.

Isofuranodiene has shown promise for anticancer activity, along with analgesic effects, due to its activity on brain opioid receptors²⁰. One of the

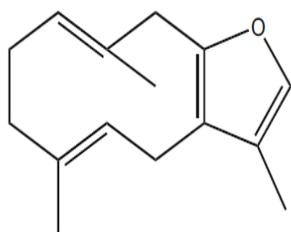


Fig 2. Chemical structure of isofuranodiene (C₁₅H₂₀O; CAS No.: 57566-47-9), an oxygenated sesquiterpene (furanosesquiterpenoid), from *S. cordifolium* essential oil.

most important compounds derived from the *Smyrniium* drug is linolenyl alcohol, an unsaturated fatty alcohol type with the chemical formula C₁₈H₃₂O. The monoterpene section of this plant is very small and includes α -pinene and β -pinene²¹, other compounds of *Smyrniium* include flavonoids and folic acid²².

Amiri et al. (2007) characterized the essential oil composition of *S. cordifolium* from northwestern Iran, and results were as follows: The major constituents of the leaf and root essential oils were two oxygenated sesquiterpenes (curzerenone and curzerene), while a reverse order was found in the stem and fruit oils. Hexadecanoic acid was another major compound in the stem and leaf oil samples²³. In another study, Esmaeili and Amiri (2006) reported curzerene and curzerenone, followed by germacrene-D, isopimarol and phyllocladanol as the major components of the essential oil of *S. cordifolium*³. Abbasi et al. (2017) showed that the main components of essential oil of the *S. cordifolium* were curzerene (65.26%), δ -Cadinene (14.39%), and γ -elemene (5.15%), which comprised approximately 85.28% of essential oil²⁴. Armand and Jahantab (2019) in studying to compare the essential oil composition of *S. cordifolium* reported that the chemical compounds of essential oil of the species include curzerene, with curozurenone as a major component in the essential oil²⁵.

Pharmacological effects

The use of plants for treating the diseases dates back to the mankind birth on earth. During the past decade, traditional systems of medicine have become a topic of global importance. In many developing countries, a large proportion of the population relies heavily on traditional systems of medicine to meet primary health care needs for historical and cultural reasons²⁶. The genus has long been traditionally used around the world for the treatment of various disorders and diseases, e.g. urinary system and prostate problems, gynaecological diseases, and indigestion and stomachic^{3,4}. *Smyrniium* taxa are constantly considered as plants with diuretic, depurative and aperient properties, particularly through their roots. One of the most important medicinal qualities of the genus is perhaps its antiscorbutic property because of high vitamin C content²⁷. However, there is limited information on the taxa belonging to this genus. The antioxidant and antimicrobial activity of the genus *Smyrniium* and its species has been shown in several studies^{28,29}. Tabaraki and Ghadiri (2013) showed that the aqueous and methanolic extracts of leaf and stem of *Smyrniium* have strong antioxidant properties and can be a potent natural antioxidant source. Significant relationship between the antioxidant capacities and phenolic compounds included antioxidant activities of these plants²⁹. Minareci & Kalyoncu (2012) investigated several taxa belonging to the genus *Smyrniium* in Turkey for their antioxidant

properties and found strong activity thorough the taxa tested⁶.

In the traditional medicine of Iran, *S. cordifolium* is also used to treat anxiety, pain, insomnia and withdrawal syndrome³⁰. Additionally, various locally produced preparations are still being used, e.g. anti-helminthic and antiparasitic, antipyretic and antiseptic ailments. *S. cordifolium* is also used in treatments of internal organ edema, especially in bladder and kidney problems³¹. Khanahmadi et al. (2010) studied the antioxidant and antibacterial activity of ethanol extracts from the aerial parts of fresh plants of *S. cordifolium* and reported potent antioxidant activity³². Also, the extract inhibited Gram positive bacteria significantly higher than Gram-negative bacteria. Observed antioxidant and antibacterial properties of ethanolic extract of the *S. cordifolium* in this study showed that this plant might be a useful source for the development of new and more potent natural antioxidants and antibacterials³². In another study, Amiri et al. (2006) studied the antibacterial activities of stem, leaf, root and fruit essential oils of *S. cordifolium* against seven Gram-positive and Gram-negative bacteria, and reported that oil essential oils of root and fruit inhibited the growth of *Salmonella typhi* and the stem oil inhibited the growth of *Escherichia coli* and *Pseudomonas aeruginosa*³³. Research has shown that unsaturated alcohols such as linolenyl alcohol prevent the growth of bacteria and linolenyl alcohol prevents the growth of all Gram-positive bacteria³⁴. Regarding

the main oil constituents, isofuranodiene attracted attention of scientists in recent years for its anticancer effects. Notably, it was proven to suppress proliferation of many cancer cell lines such as hepatocellular carcinoma, leukaemia, breast and lung cancer cells, showing synergism with some chemotherapeutic agents, namely tamoxifen and paclitaxel¹⁸.

Adhamian et al. (2015) evaluated the effect of ethanolic extract of *S. cordifolium* root on prevention of calcium oxalate nephrolithiasis in rats, and showed that *S. cordifolium* extract was able to reduce urine oxalate. Therefore, the action of the extract may be beneficial on human kidney stones³⁰.

In a study, Abbasi et al. (2017) evaluated the anticonvulsant effects of the essential oil of *S. cordifolium* and curzerene on the seizure on mice and reported that flumazenil and naloxone could suppress the anticonvulsant effects of essential oil and curzerene; this effect may be related to their effects on GABAergic and opioid systems²⁴. Abbasi et al. (2014) investigated the hypnotic characteristics of *S. cordifolium* plant extract on the mice and reported the extract as a natural product showing hypnotic effects even better than diazepam³⁰. Nazari et al. (2018) studied the effect of *S. cordifolium* hydroalcoholic extract on addiction withdrawal syndrome in mice in comparison with clonidine and found that the extract was capable of reducing the signs of opiate withdrawal in morphine-dependent mice³⁵. In another study, Nazari et al. (2020) investigated the effects of *S. cordifolium* extract on the Muopioid receptors of mice

compared to clonidine and reported that *S. cordifolium* extracts such as clonidine relieve pain caused by addiction withdrawal syndrome³⁶.

FUTURE PERSPECTIVE

Medicinal and nutritional importance of *S. cordifolium* has been regrettably neglected in Iran and curative application of this national wealth has only been considered from the ethnobotanical point of view among indigenous people of the country. To the best of our knowledge, few ethnobotanical important taxa have been scientifically evaluated for their possible medical application. Furthermore, in most countries the herbal medicines market is poorly regulated, and herbal products are often neither registered nor controlled. To bridge this information gap, this is an attempt to provide additional evidence for the reconsideration of this species in the human diet and the drug industry.

CONCLUSION

This review concludes that *S. cordifolium* is a nutritionally and medicinally popular functional food in its normal range through Zagros range. This plant as an edible and a medicinal plant is a rich source of isofuranodiene, a furanosesquiterpenoid with numerous medicinal properties, including hypnotic effects and antioxidant and antibacterial activity. With regard to medicinal and nutritional importance of, it can be used in the pharmaceutical and food industry, and also may be effective for diseases of the bladder and kidneys. Despite that, the bioactivities of

S. cordifolium have been confirmed through *in vitro* and *in vivo* studies however, clinical effectiveness of this plant on aforementioned diseases awaits further substantiation from future experiments.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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