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Review Article

A REVIEW ON SIDERITIS PLANT**¹Shaik. Sofiya*, ²Dr. V. Jayasankar Reddy, ³Dr. K. Venu Gopal,
⁴Dr. C. Bhuvaneswara Roa**¹Final year B Pharmacy, Krishna Teja Pharmacy College, Tirupati, 517506.²Professor, Vice Principal, Krishna Teja Pharmacy College, Tirupati, 517506.³Professor, Principal, Krishna Teja Pharmacy College, Tirupati, 517506.⁴Professor, HOD of Pharmacology, Krishna Teja Pharmacy College, Tirupati, 517506.**Abstract:**

Sideritis, a genus of flowering plants, has been employed for centuries in traditional medicine, folklore, and culinary practices. This review provides a comprehensive overview of Sideritis plants, encompassing their botany, phytochemistry, pharmacological activities, traditional uses, and future research directions. Sideritis plants are characterized by their aromatic leaves, stems, and flowers, containing bioactive compounds such as flavonoids, phenolic acids, terpenes, and essential oils. The genus comprises approximately 100 species, with Sideritis scardica, Sideritis raeseri, and Sideritis clandestina being the most extensively studied. Sideritis plants exhibit antimicrobial, antioxidant, anti-inflammatory, and antifungal properties, positioning them as valuable resources for addressing various health concerns. Their potential in neuroprotection, immunomodulation, and anticancer therapy warrants further exploration. Traditional knowledge and cultural significance of Sideritis plants have been well-documented. Preservation of traditional knowledge and cultural heritage is crucial for sustainable development of Sideritis-based products. Future research should focus on standardization, quality control, and clinical trials to fully elucidate Sideritis's therapeutic potential. This review highlights the multifaceted properties and applications of Sideritis plants, underscoring their potential as natural remedies for various health challenges. Further investigation is necessary to unlock the full therapeutic and commercial potential of Sideritis plants, offering opportunities for pharmaceutical, cosmetic, and food industries.

Keywords: Pharmacological activities, Neuro-protection, Immunomodulation, Bioactive compounds

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1.INTRODUCTION:

Sideritis, commonly known as ironwort, is a genus of flowering plants belonging to the Lamiaceae family. Native to the Mediterranean region, Sideritis species have been employed for centuries in traditional medicine, folklore, and culinary practices. The plant's versatility and therapeutic potential have garnered significant attention from researchers, scientists, and healthcare professionals. This review aims to provide a comprehensive overview of Sideritis plants, encompassing their botany, phytochemistry, pharmacological activities, traditional uses, and future research directions. Sideritis plants are characterized by their aromatic leaves, stems, and flowers, which contain a rich array of bioactive compounds. The genus comprises approximately 100 species, with *Sideritis scardica*, *Sideritis raeseri*, and *Sideritis clandestina* being the most extensively studied. Phytochemical analyses have revealed the presence of flavonoids, phenolic acids, terpenes, and essential oils, contributing to the plant's medicinal properties. Elucidating the chemical composition of Sideritis species is crucial for understanding their therapeutic potential.

The pharmacological activities of Sideritis plants have been extensively investigated, revealing antimicrobial, antioxidant, anti-inflammatory, and antifungal properties. These activities position Sideritis as a valuable resource for addressing various health concerns, including infectious diseases, oxidative stress-related disorders, and inflammatory conditions. Moreover, Sideritis's potential in neuroprotection, immunomodulation, and anticancer therapy warrants further exploration. Traditional uses of Sideritis plants date back to ancient civilizations, with records of its employment in Greek, Roman, and Turkish medicine. The plant has been utilized to treat various ailments, including digestive issues, respiratory problems, wounds, and fever. In addition to its medicinal applications, Sideritis has been used as a culinary herb, flavoring agent, and beverage. The plant's cultural significance and traditional knowledge have been passed down through generations, emphasizing its importance in folk medicine.

Despite its therapeutic potential, Sideritis research remains in its infancy. Further investigation is necessary to fully elucidate the mechanisms of action, optimal usage, and safety profiles of Sideritis plants. This review aims to consolidate existing knowledge, identify research gaps, and provide directions for future studies. By exploring the multifaceted properties and applications of Sideritis, researchers and healthcare professionals can unlock the plant's

full potential as a valuable botanical resource. The medicinal properties of Sideritis plants have been validated through various in vitro, in vivo, and clinical studies. The plant's antimicrobial activity against antibiotic-resistant bacteria and its antioxidant potential in mitigating oxidative stress have garnered significant attention. Furthermore, Sideritis's anti-inflammatory properties have been explored in the context of chronic diseases, such as arthritis and cardiovascular disorders.

Sideritis plants have also been investigated for their potential in neuroprotection and cognitive enhancement. Studies have demonstrated the plant's ability to inhibit neurodegenerative pathways and improve memory and cognitive function. Additionally, Sideritis's anxiolytic and antidepressant effects have been observed in animal models, suggesting its potential as a natural remedy for mental health disorders. Despite its therapeutic promise, the quality and safety of Sideritis products remain a concern. Variations in chemical composition, extraction methods, and manufacturing processes can significantly impact the efficacy and safety of Sideritis-based products. Standardization and regulation of Sideritis products are essential to ensure consumer safety and protection.

The traditional knowledge and cultural significance of Sideritis plants have been well-documented. Ethnobotanical studies have revealed the plant's importance in Mediterranean folklore, with uses extending beyond medicine to culinary and spiritual practices. Preservation of traditional knowledge and cultural heritage is crucial for the sustainable development of Sideritis-based products. In conclusion, Sideritis plants offer a wealth of opportunities for pharmaceutical, cosmetic, and food industries. This review aims to provide a comprehensive overview of Sideritis plants, encompassing their botany, phytochemistry, pharmacological activities, traditional uses, and future research directions. By consolidating existing knowledge and identifying research gaps, this review seeks to stimulate further investigation into the therapeutic potential and commercial applications of Sideritis plants.

Synonyms:

Ironwort, Mountain tea, Greek tea and Shepherd's tea

Local names:

- 1.Kashmir: Sheetal Chini
2. Uttarakhand: Golu
3. Himachal Pradesh: Bantakdi

4. Nepal : Ghodey Jhar
5. Andhra Pradesh: Panasapoo
6. Tamil Nadu: Pannagam

2. BIOLOGICAL DESCRIPTION OF PLANT:

Sideritis plants originated from the Mediterranean region, specifically the mountainous areas of Southern Europe, Asia Minor, and North Africa. Sideritis plants are primarily found in the mountainous regions of Southern Europe, particularly in countries such as Greece, Turkey, Spain, France, and the Balkans.[1][2]. It belongs to Lamiaceae family.

2.1 Geographical Source:

Sideritis is native to the Mediterranean region, specifically the mountainous areas of Southern Europe, Asia Minor, and North Africa.[3] Key geographical sources include Greece, Turkey, Spain, France, Italy, and the Balkans. The Himalayan region, particularly India and Nepal, also harbor various Sideritis species.[4] Additional sources are Morocco and Algeria in North Africa, and Cyprus and Croatia in Europe. The plant thrives in high-altitude regions (1,000-2,500 meters) with rocky slopes, dry meadows, and woodlands.[5]

3. CULTIVATION AND COLLECTION:

3.1. Habitat and Collection

Sideritis plants are native to the Mediterranean region, thriving in well-drained soils and full sun. Harvest leaves and flowers during the flowering period (June-August) to ensure optimal bioactive compound content. Avoid over-harvesting, protect natural habitats, and promote conservation.[6]

3.2. Cultivation Requirements

The climate have to be Mediterranean-type climate with warm summers and mild winters, and the soil

have to be Well-drained, slightly alkaline soil (pH 6.5-8.5), Moderate watering, avoiding waterlogged conditions and Full sun to partial shade.[7]

3.3. Propagation Methods

Seed propagation: Sow seeds in spring or autumn, maintaining a temperature of 18-20°C.

Cuttings: Take stem cuttings in summer, using rooting hormones for enhanced success.

Division: Divide established plants in spring or autumn[8]

3.4. Pest and Disease Management

Pests: Aphids, whiteflies, and spider mites.

Diseases: Root rot, leaf spot, and powdery mildew.

Integrated Pest Management (IPM) strategies: Monitor regularly, use organic controls, and apply targeted pesticides. [9]

3.5. Harvesting and Drying

Harvest: Leaves and flowers during the flowering period.

Drying: Air-drying or freeze-drying to preserve bioactive compounds.

Storage: Store dried material in airtight containers, protected from light. [10]

3.6. Quality Control and Certification

Quality control: Monitor bioactive compound content, moisture levels, and microbial contamination.

Certification: Obtain organic or Good Agricultural Practice (GAP) certification. [11]

4. MORPHOLOGY:

4.1 Tree Structure

Sideritis plants are herbaceous perennials or small shrubs that grow up to 20-100 cm (8-39 in) in height, with erect or sprawling stems that are branched and woody at the base. The stems are often pubescent (hairy) or glabrous (hairless), with internodes ranging from 1-5 cm (0.4-2 in) long.[12]



Fig 1

4.2 Leaves

The leaves of *Sideritis* plants are simple, opposite, or whorled, with linear-lanceolate, elliptic, or ovate shapes, measuring 2-10 cm (0.8-3.9 in) long and 0.5-4 cm (0.2-1.6 in) wide. The leaf margins are entire, serrated, or crenate, with pubescent or glabrous surfaces and pinnate or palmate venation.



Fig 2

4.3 Flowers

Sideritis plants produce bilabiate, zygomorphic flowers in terminal or axillary clusters, with yellow, white, pink, or purple colors, measuring 5-15 mm (0.2-0.6 in) long. The calyx is 5-toothed or 2-lipped, while the corolla is 5-lobed with 2 lips.[13]



Fig 3

4.4 Fruits and Seeds

The fruits of *Sideritis* plants are nutlets or achenes, ellipsoidal or ovoid in shape, measuring 2-5 mm (0.08-0.2 in) long, with brown or gray colors. The seeds are small, numerous, and smooth.



Fig 4

4.5 Roots

Sideritis plants have taproots or fibrous roots that extend up to 20 cm (8 in) deep, with woody, branched, and hairy features.[14]



Fig 5

4.6 Overall Appearance

Sideritis plants exhibit a bushy, compact growth habit, with leaves and stems often pubescent, showy flowers arranged in clusters, and inconspicuous fruits hidden within leafy bracts.



Fig 6

5. MICROSCOPY:

Confocal Laser Scanning Microscopy (CLSM):

Confocal Laser Scanning Microscopy (CLSM) of Sideritis plants provides high-resolution images of plant tissues, allowing researchers to study cellular structure, cell wall composition, and distribution of bioactive compounds. CLSM helps visualize the spatial organization of tissues, such as trichomes, stomata, and vascular bundles.[15]

Polarised Light Microscopy:

Polarised light microscopy of Sideritis plants reveals the crystalline structure of cell walls, cuticles, and trichomes. This technique helps identify the orientation and arrangement of cellulose microfibrils, pectin, and other cell wall components[16].

X-ray Microscopy:

X-ray microscopy of Sideritis plants enables the study of internal tissue structure, including vascular tissue, parenchyma cells, and sclerenchyma cells. This technique provides information on tissue density, cell wall thickness, and mineral distribution.

Epifluorescence Microscopy:

Epifluorescence microscopy of Sideritis plants detects fluorescent compounds, such as flavonoids, phenolic acids, and chlorophyll. This technique helps

localize bioactive compounds within plant tissues, including leaves, stems, and roots. [17]

Transmission Electron Microscopy (TEM):

Transmission Electron Microscopy (TEM) of Sideritis plants provides ultrastructural details of cellular components, including organelles, membranes, and cell walls. TEM helps study the fine structure of trichomes, stomata, and vascular tissues.

Scanning Electron Microscopy (SEM):

Scanning Electron Microscopy (SEM) of Sideritis plants examines surface morphology, including trichome density, leaf venation, and seed coat patterns. SEM helps understand plant surface features, adaptation to environment, and potential applications.

Fourier Transform Infrared (FTIR) Microscopy:

Fourier Transform Infrared (FTIR) microscopy of Sideritis plants analyzes chemical composition and spatial distribution of bioactive compounds. FTIR helps identify functional groups, molecular interactions, and tissue-specific chemical signatures. [18]

6. CHEMICAL CONSTITUENTS:

Sideritis plants contain a diverse range of bioactive compounds, including:

- Flavonoids: apigenin, luteolin, quercetin, and kaempferol, which exhibit antioxidant and anti-inflammatory properties.
- Phenolic acids: rosmarinic acid, caffeic acid, and ferulic acid, which possess antioxidant and antimicrobial activities.
- Terpenes: α -pinene, β -pinene, and borneol, which demonstrate antimicrobial and anti-inflammatory effects.
- Essential oils: composed of monoterpenes and sesquiterpenes, which exhibit antimicrobial and antioxidant properties.
- Alkaloids: rare occurrence, but reported in some Sideritis species.
- Glycosides: flavonoid glycosides and phenolic glycosides, which contribute to the plant's medicinal properties.
- Saponins: triterpenoid saponins, which exhibit antimicrobial and anti-inflammatory activities.
- Tannins: condensed tannins, which possess antimicrobial and antioxidant properties. [19][20]

7. CHEMICAL TESTS:

Test 1: Flavonoid Detection using $AlCl_3$ (Aluminum Chloride) Test

The objective is to detect the presence of flavonoids in Sideritis plant extracts and the materials are sideritis plant extract (methanol or ethanol), Aluminum chloride ($AlCl_3$), Methanol and Distilled water. Prepare a 1% solution of $AlCl_3$ in methanol and add 2-3 drops of the $AlCl_3$ solution to 1 mL of Sideritis plant extract and observe the color change. The result is yellow or orange color indicates the presence of flavonoids and intensity of color depends on flavonoid concentration. [21]

Test 2: Phenolic Acid Detection using $FeCl_3$ (Ferric Chloride) Test

The objective is to detect the presence of phenolic acids in Sideritis plant extracts and the materials are Sideritis plant extract (methanol or ethanol), ferric chloride ($FeCl_3$), distilled water. Prepare a 1% solution of $FeCl_3$ in distilled water and add 2-3 drops of the $FeCl_3$ solution to 1 mL of Sideritis plant extract and observe the color change. The result is green, blue, or purple color indicates the presence of phenolic acids and the intensity of color depends on phenolic acid concentration. [22]

Test 3: Essential Oil Composition using GC-MS (Gas Chromatography-Mass Spectrometry)

The objective is to analyze the essential oil composition of Sideritis plants and the materials are sideritis plant essential oil, GC-MS instrument and

DB-5 or HP-5 column. Inject 1-2 μ L of essential oil into the GC-MS instrument and set temperature program: 60°C (5 min) to 250°C (10 min) and Record mass spectra. The result is Chromatogram shows separation of essential oil components and Mass spectra identify compounds (e.g., α -pinene, β -pinene, borneol) [23]

8. PHARMACOLOGICAL ACTIVITIES:

8.1 Antimicrobial and Antifungal activity:

Sideritis plants exhibit significant antimicrobial and antifungal activity, inhibiting the growth of various microorganisms, including bacteria (*Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Pseudomonas aeruginosa*) and fungi (*Candida albicans*, *Aspergillus niger*, and *Fusarium oxysporum*). The antimicrobial activity is attributed to bioactive compounds such as flavonoids (apigenin, luteolin, and quercetin), phenolic acids (rosmarinic acid, caffeic acid, and ferulic acid), and essential oils (α -pinene, β -pinene, and borneol). Studies have demonstrated the plant's potential against antibiotic-resistant strains, with mechanisms of action including membrane disruption, DNA damage, inhibition of enzyme activity, and antioxidant activity. Specifically, Sideritis scardica extracts showed antimicrobial activity against *E. coli* and *S. aureus*, while Sideritis raeseri exhibited antifungal activity against *Candida albicans*. These findings support the traditional use of Sideritis plants in folk medicine for treating infections and wounds, and highlight their potential as natural antimicrobial agents for pharmaceutical and biomedical applications.

8.2 Antioxidant activity:

Sideritis plants possess significant antioxidant activity, attributed to their rich content of bioactive compounds such as flavonoids (apigenin, luteolin, and quercetin), phenolic acids (rosmarinic acid, caffeic acid, and ferulic acid), and essential oils (α -pinene, β -pinene, and borneol). These compounds scavenge free radicals, reduce oxidative stress, and protect against cell damage, inflammation, and oxidative-related diseases. Studies have demonstrated the plant's antioxidant potential through various assays, including DPPH, ABTS, FRAP, and ORAC, revealing IC_{50} values comparable to standard antioxidants [29]. Specifically, Sideritis scardica extracts exhibited antioxidant activity against hydrogen peroxide-induced oxidative stress in human cells, while Sideritis raeseri showed protective effects against lipid peroxidation and DNA damage. The antioxidant activity of Sideritis plants supports their traditional use in folk medicine for treating oxidative-related ailments and highlights their potential as

natural antioxidants for pharmaceutical, cosmetic, and food industries. [30]

8.3 Analgesic activity:

The ethanol extract and chloroform fraction of *Sideritis lhotskyi* have anti-nociceptive effects. An oral dose of 400 mg/kg of petroleum ether extract from *Sideritis taurica* has an analgesic activity similar to that of 400 mg/kg acetylsalicylic acid at 45 and 60 min.

8.4 Anti-ulcerogenic activity:

The in vivo anti-ulcerogenic activity of *Sideritis* species is well known. Hypolaetin-8-O- α -D-glucoside, a flavonoid present in several *Sideritis* species, reduces gastric lesions and ulcers in rats. Decoctions prepared from aerial parts of *Sideritis caesarea* have a gastroprotective effect against ethanol-induced gastric ulcer in rats. *Sideritis italica* essential oil also has strong activity against *Helicobacter pylori*. These findings confirm the traditional gastroprotective use of *Sideritis* species.

8.5 Antitumor activity:

Methanol extract from *Sideritis libanotica* ssp. *linearis* is reported to have anti-proliferative activity against three human cell lines: C6 cells, Vero cells and HeLa cells. *Sideritis* aqueous extracts have selective estrogen receptor modulator activity: indeed *Sideritis euboea* and *Sideritis clandestina* induce osteoblast differentiation of KS483 cells and suppress breast cancer cell growth.

8.6 Antiviral activity:

Study of the anti-HIV activity of these plants showed that 26 semisynthetic derivatives of linearol inhibit virus replication. The dichloromethane extract showed antiviral activity against herpes simplex viruses, an important result in view of the emergence of drug-resistant (e.g. acyclovir-resistant) HSV mutants

9. Toxicity and safety:

Sideritis plants are generally considered safe for consumption and therapeutic use, with minimal reported toxicity. Acute toxicity studies in animals have shown that *Sideritis* extracts exhibit low toxicity, with LD50 values exceeding 2,000 mg/kg[31][32]. Subchronic and chronic toxicity studies have also revealed no significant adverse effects. However, high doses (>5g/day) of *Sideritis* tea consumption have been linked to gastrointestinal upset, allergic reactions, and interactions with medications, particularly blood thinners and diabetes medications. [33] Pregnant and breastfeeding women should exercise caution due to limited studies on fetal

and infant safety. Topical application of *Sideritis* essential oils may cause skin irritation or allergic reactions in sensitive individuals. To ensure safety, it is recommended to consult with a healthcare professional before using *Sideritis* products, especially for individuals with underlying health conditions or taking medications. [34]

Despite its generally considered safe profile, *Sideritis* plants may interact with certain medications, exacerbating underlying health conditions. For instance, the plant's flavonoids and phenolic acids may potentiate anticoagulant effects when combined with blood thinners, increasing the risk of bleeding. [35] Additionally, *Sideritis*'s hypoglycemic properties may interact with diabetes medications, leading to hypoglycemia. Individuals with kidney or liver disease should also exercise caution due to potential nephrotoxicity and hepatotoxicity. Furthermore, allergic reactions to *Sideritis* have been reported, manifesting as skin rash, itching, or respiratory issues[36][37]. To minimize risks, it is essential to consult with a healthcare professional before using *Sideritis* products, especially for prolonged periods or in combination with other medications. Standardized extracts and products with established quality control measures can also help ensure safe consumption. [38]

10. Traditional Uses:

Sideritis plants have been employed for centuries in traditional medicine across the Mediterranean region, particularly in Greece, Turkey, and Italy. The plant's therapeutic properties have been utilized to treat various ailments, including digestive issues, respiratory problems, and wounds. [24] In Greek traditional medicine, *Sideritis* tea is consumed to alleviate digestive problems such as bloating, indigestion, and diarrhea. Additionally, the plant is used to treat respiratory issues like bronchitis, coughs, and colds.

In Turkish folk medicine, *Sideritis* is used to treat digestive and respiratory issues, as well as to reduce fever and alleviate pain. The plant's anti-inflammatory and antimicrobial properties make it an effective remedy for wounds, cuts, and skin conditions. In some regions, *Sideritis* is applied topically to accelerate wound healing, reduce swelling, and prevent infection. [25]

Beyond its medicinal uses, *Sideritis* plants have culinary significance in Mediterranean cuisine. The leaves and flowers are used to prepare a soothing herbal tea, while the plant's essential oil is employed as a flavoring agent in soups, stews, and salads. In Greece, *Sideritis*-infused oil is used in cooking,

particularly in traditional dishes like stews and braises.

Sideritis plants also hold cultural significance in the Mediterranean region. In Greece, the plant is associated with traditional remedies passed down through generations. In Turkey, Sideritis is used in cultural rituals and ceremonies to promote health, prosperity, and good fortune. [26] The plant's cultural importance is reflected in its inclusion in traditional medicine practices, folklore, and culinary traditions. In terms of preparation, Sideritis plants can be consumed as infusions, decoctions, tinctures, or ointments. Infusions involve steeping dried leaves and flowers in hot water, while decoctions involve boiling plant parts. Tinctures are concentrated liquid extracts, and ointments are used for topical application. However, it is essential to consult healthcare professionals before using Sideritis for medicinal purposes, particularly during pregnancy, breastfeeding, or when taking medications [27].

11. Research and future directions:

Research on Sideritis plants has unveiled their potential therapeutic applications, including antimicrobial, antioxidant, anti-inflammatory, and antifungal activities. However, further investigation is necessary to fully elucidate the mechanisms of action and optimal usage. Future research directions include clinical trials to validate traditional uses, bioavailability and pharmacokinetic studies to optimize dosing regimens, and investigations into synergistic effects with conventional medications. [39] Additionally, characterization of Sideritis's chemical composition and standardization of extracts will enhance product quality and consistency.

Future directions for Sideritis research also encompass exploration of its potential in addressing emerging health concerns, such as antibiotic resistance and neurodegenerative diseases. Investigating Sideritis's antimicrobial properties against multidrug-resistant bacteria and its neuroprotective effects against Alzheimer's and Parkinson's diseases could yield valuable insights. [40] Moreover, studies on Sideritis's potential in cosmeceuticals, functional foods, and agricultural applications could expand its commercial utility. Collaboration between researchers, industries, and regulatory agencies will facilitate the translation of research findings into tangible products and therapies, ultimately unlocking Sideritis's full potential as a versatile and valuable botanical resource. [41]

To fully harness the potential of Sideritis plants, interdisciplinary research collaborations are essential. Scientists from fields like pharmacology, botany, microbiology, and biochemistry should work together to elucidate the plant's bioactive compounds, mechanisms of action, and optimal extraction methods. Moreover, clinical trials and epidemiological studies will provide valuable insights into Sideritis's efficacy and safety in human populations. [42] Investigation of Sideritis's potential in preventive medicine, such as chemoprevention and immunomodulation, may also reveal new applications.

Future research should also focus on sustainable cultivation and production of Sideritis plants, ensuring environmental stewardship and economic viability. Studies on optimal cultivation conditions, genetic diversity, and breeding programs will enhance crop yields and quality. [43] Furthermore, development of standardized extraction and processing methods will facilitate large-scale production of high-quality Sideritis products. Exploration of Sideritis's potential in veterinary medicine and animal health may also open new avenues for research and commercialization. By addressing these research gaps and directions, the scientific community can unlock the full therapeutic and economic potential of Sideritis plants. [44]

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