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Review Article

## Review on *Glycyrrhiza glabra* L. (*Aşl al-Sūs*) with Unani Perspective and Modern Pharmacology

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### ABSTRACT

Traditional Unani (Greco-Arab) medicine is among the most ancient therapies founded by the father of Western medicine, the Hippocrates. Presently, most of the population worldwide depend on herbal medicines for some aspect of their primary health care needs. Treatment with medicinal plants is appraised very safely as there are no or minimal side effects. The promising fact is that herbal treatment can be used irrespective of any age group. Most of the pharmaceutical companies are currently conducting extensive research on plant materials assemble from the rain forests and other places for their potential medicinal value. *Glycyrrhiza glabra* L. (Leguminosae/Fabaceae) is best known for its use in making licorice-flavored confectionery. In Unani medicine, it is commonly known as *Aşl al-Sūs*. It is a plant of remote origin. *Aşl al-Sūs* extracts and its principle element "glycyrrhizin" have widely been used in foods, tobacco and for medicinal purposes in herbal and traditional medicines as well. It possesses multiple pharmacological and medicinal activities such as anti-ulcer, anti-inflammatory, anti-viral, and hepatoprotective actions. This review attempts to compile the data regarding its ethnobotanical actions and medicinal uses in Unani medicine along with its phyto-pharmacological descriptions.

**Keywords:** Herbal medicine, *Aşl al-Sūs*, *Glycyrrhiza glabra* L.

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### Introduction

The herbal products have extensively been used for the thousands of years for amelioration of human sufferings both in the developed and developing countries due to their natural origin and lesser side effects<sup>[1]</sup>. Even today, when the acceptance of conventional medicine is on its peak corroborated with scientific evidences, the traditional herbal treatment holds the sway among the masses due to its negligible untoward effects, effectiveness in management of chronic morbidities, lower cost, and widespread availability<sup>[2]</sup>. With the persistent demand and use of herbal medicines by the patients in various ailments, various countries have come out with political commitment and technical support for the evolution and propagation of indigenous medicines<sup>[3]</sup>.

This overwhelming support may be attributed to the development of advanced technologies for verification of phyto-chemical and pharmacological actions of plants in numerous pathological conditions<sup>[2]</sup>.

Unani system of medicine is an ancient traditional medicine founded almost 2500 years ago in islands of Cos, Greece on the hands of Hippocrates<sup>[4]</sup>. The uniqueness of this system is the individualistic but holistic approach in disease prevention and management<sup>[5]</sup>.

*Aşl al-Sūs*. is a popular herbal drug of Unani medicine. Its botanical name is *Glycyrrhiza glabra* L. of the Fabaceae family. The common names are licorice and sweet wood. Its root (*Bikh-i-Aşl al-Sūs*.) and extract (*Rub al-soos*) are widely used for the treatment of various diseases<sup>[6,7]</sup>.

According to *Ibn Baitar*, *Aşl al-Sūs*. is the drug of choice for respiratory and bladder diseases, such as burning

micturition and burning sensation in the chest. It is also used in treatment of cold-tempered ailments; *Amrād-i Balghamiyā* and *Sawdāwiā* (phlegmatic and melancholic disorders), such as *Sar'* (epilepsy), *Fālij* (hemiplegia), *Laqwa* (facial palsy), *Qabūs* (nightmare), *Tawahhush* (anxiety), *Mālikholia* (Melancholia), *Khushunat-i Halaq* (sore throat), *Bohat al-Sawt Hād* (acute hoarseness of voice), *Warm-i Luhāt* (uvulitis), *Warm-i Sho'ba al-Riyā* (bronchitis), *Dīq al-Nafas* (asthma), *Sū'al-i Yābis* (dry cough) etc<sup>[7-13]</sup>. *Aṣl al-Sūs*. has experimentally been proved for various pharmacological actions, such as anti-bacterial, anti-hepatotoxic, anti-fungal, and anti-oxidant; anti-hyper-glycemic, anti-viral, anti-ulcer, estrogenic, anti-diuretic, and immuno-stimulant activities. It has also been found effective in cure of psoriasis, eczema, and herpes simplex<sup>[14,15]</sup>.

The important chemical constituents are flavonoids, coumarins, volatile oils, terpenoids, and amino acids which have been isolated from the plant root<sup>[6,8,16]</sup>. However, the reported adverse effects are liver, spleen and kidney derangements. In Unani medicine, its roots are used only after peeling the bark (*Aṣl al-Sūs. Muqash'shar*) which dramatically decreases its toxic effects.

### Scientific classification<sup>[17]</sup>

Kingdom:	Plantae
Subkingdom:	Tracheobionta
Division:	Magnoliophyta
Class:	Magnoliopsida
Subclass:	Rosidae
Order:	Fabales
Family:	Fabaceae
Genus:	<i>Glycyrrhiza</i>
Species:	<i>G. glabra</i>
Botanical name:	<i>Glycyrrhiza glabra</i> L.

### Vernacular names: <sup>[6,7,9,10,16,18]</sup>

Arabic: *Aṣl al-Sūs*; Irq al-sūs; Ood al-sūs; 'Uruq al-soos

English: Licorice; Liquorice root; Sweet wood

French: Boisdoux

German: Sussholz

Greek: Glycyrrhiza

Hindi: Mulethi; Mulathi; Muleti; Jethimadhu; Jethimadhu; Mulhatti

Kannada: Atimadhura; Yeshtimadhuka

Kashmiri: Multhi; Shanger

Malayalam: Athimadhuram; Irattimadhuram; Yeshtimadhuram

Marathi: Jeshthamadha

Oriya: Jastimadhu; Jatimadhu

Persian: *Bikh-i-Mehak*; *Bikh-i-Ribas*; *'Usara-mehak*

Punjabi: Jethimadh; Mulathi

Sanskrit: Madhuka; Yashtimadhu; Sinhale: Welmi

Tamil: Athimadhuram; Antimadhuram

Telegu: Atimadhuramu; Yashtimadhukam

Urdu: Mulethi

*Dioscorides* is credited for coining the name *Glycyrrhiza* which is composed of two Greek words implying sweet root. The specific name *glabra* indicates its smooth surface without hairs.

**Distribution:** The plant is native to the Mediterranean region; it is cultivated in Iran; Afghanistan, and Europe. No liquorice yielding species is found in India; although, the cultivation of *G. glabra* L. has been undertaken at several places on an experimental basis such as Baramulla; Srinagar; Delhi; Dehradun, and hilly areas of South India<sup>[6,8,18,19]</sup>

**Description in Unani Literatures:** *Asl-ul-soos* is a dried, unpeeled or peeled root and shoot of *Glycyrrhiza glabra* L. of *Leguminosae* family. It extends up to 2-meter height; flowers vermilion blue; leaves mimic with Kasondi (*Cassia occidentalis*); small legumes arise on the branches which carry 4-5 seeds; roots spread 1 meter in soil; smell unclear and unique; taste sweet then bitter<sup>[7,9]</sup>.

### Morphology

#### Macroscopic:

**Root:** Cylindrical root pieces, 14-20 cm in length, 5-20 cm in width, surface irregular, longitudinally wrinkled, at places shows scars left by removal of the lateral roots; fracture outer fibrous and inner splintery; externally dark brown; internally golden yellow; transversally cut surface exhibits wide central xylem, cambium ring, outer narrow phloem, and wide radiating medullary rays. Taste is sweet; odor is unclear and unique<sup>[6,8,20]</sup>.

**Stolon:** Cylindrical, unbranched, straight, variable in length, 1-2 cm in diameter; it consists of yellowish brown or dark brown outer layer; externally longitudinal wrinkled with occasional small buds and encircling scale leaves; smoothed transversely; the cut surface shows a cambium ring about one-third of radius from outer surface and a small central pith<sup>[6,8,20]</sup>.

#### Microscopic:

**Stolon:** Transverse section of stolon shows cork of 10-20 or more layer of tabular cells, outer layers with reddish-brown amorphous contents, inner 3 or 4 rows having thicker; colorless walls; secondary cortex usually of 1-3 layers of radially arranged parenchymatous cells containing isolated prism of calcium oxalate; 2<sup>o</sup> phloem a broad band; cells of inner part cellulosic and outer lignified; radially arranged group of about 10-50 fibers surrounded by a sheath of parenchyma cells, each usually containing a prism of calcium oxalate about 10-35 μm long cambium form tissue of 3 or more layers of cells; secondary xylem distinctly radiate with medullary rays, 3-5 cells wide; vessels about 80-200 μm in diameter with thick, yellow, pitted, reticulately thickened walls; groups of lignified fibers with crystal sheath similar to those of phloem; xylem parenchyma of two kinds, those between vessels having thick pitted walls without intercellular spaces, the remaining with thin walls; pith of parenchymatous cell in longitudinal rows, with intercellular spaces.<sup>[6,8,20]</sup>

**Root:** Transverse section of root shows structure closely resembling to that stolon except that no medulla is present; xylem tetrarch; usually principal medullary rays are at right angles to each other; in peeled drug cork shows phelloderm and sometimes without secondary phloem; all parenchymatous tissues containing abundant, simple, oval or rounded starch grains that are 2-20 μm in length<sup>[6,8,20]</sup>.

### Phytochemical Constituents <sup>[6,8,16,18]</sup>

- Amino acids
- Asparagine
- Bitters
- Coumarin

- Essential oil
- Female hormone estrogen
- Fat
- Flavonoids
- Glycosides
- Glycyrrhizin (main constituent found in the root)
- Gums
- Glycyrrhetic acid
- Mucilage (rhizome)
- Protein
- Resin
- Saponoids
- Saponins
- Sterols
- Starches (30%)
- Sugars (up to 14%) when mixed with water or used in cough drops
- Tannin
- Volatile oil.

### Pharmaco-kinetic studies

After oral administration of licorice in humans, the main constituent glycyrrhizic acid is hydrolyzed into glycyrrhetic acid by intestinal bacteria possessing a specialized  $\beta$ -glucuronidase<sup>[21,22]</sup>. Glycyrrhetic acid is 200-1,000 times more powerful inhibitor of 11- $\beta$ -hydroxy-steroid dehydrogenase involved in corticosteroid metabolism than glycyrrhizic acid. Hence, its pharmacokinetic after oral intake are too appropriate. After oral dosing, glycyrrhetic acid is promptly absorbed and transported through carrier molecules to the liver, and metabolized into glucuronide and sulfate conjugates, which are eventually hydrolyzed to glycyrrhetic acid. Glycyrrhetic acid is then reabsorbed, resulting in an important hamper in terminal clearance from plasma<sup>[23]</sup>. After oral administration of 100 mg glycyrrhizin in healthy volunteers, no glycyrrhizin was found in the

plasma but glycyrrhetic acid was found at < 200 ng/mL<sup>[23]</sup>. In the 24-hour period after oral administration, glycyrrhizin was observed in the urine which indicates that it is partly absorbed as an intact molecule.<sup>[24]</sup>

**Mechanism of Action:** Glycyrrhizin and glycyrrhizic derived from *Glycyrrhiza glabra* have been found for suppressing development of various infections including hepatitis A and C; HIV; herpes zoster; CMV, and Herpes simplex<sup>[25,26]</sup> Glycyrrhizin and its metabolites are reported to suppress the aldosterone and smother 5  $\beta$  reductase in pseudo-aldosterone disorder. The similarity in the structure of glycyrrhetic acid to the structure of hormones discharged by the adrenal cortex highlights the mineralocorticoid and glucocorticoid action of glycyrrhizin corrosive<sup>[27,28]</sup>.

**Mizāj (temperament):** Unani scholars have differed in identification of its temperament as under:

- Hot and dry<sup>[9]</sup>
- Ibn Sina and Kirmānī considered it moderate or Murakkab-ul-Quwa
- Some regarded it hot<sup>10</sup> and wet<sup>10[29]</sup>
- Hot<sup>20</sup> and dry<sup>10[9]</sup>

**Parts used:** root<sup>[29]</sup>

**Dose::** 3-7 gm<sup>[9]</sup> ; 5-10 gm<sup>[30]</sup>

**Adverse effects:** it may cause or aggravate diseases of liver, kidney, and spleen<sup>[10,30,31]</sup>

**Corrective:** Gul-e-Surkh (*Rosa demascena*) in case of splenic toxicity; *Samagh-i-Katira* (Gum *Traga cantha*) in diseases of kidney<sup>[9,30]</sup>.

**Substitute:**<sup>[10,30]</sup>

- Rubb-al-sūs (extract of root of *Glycyrrhiza glabra* L.)
- Turbud (*Ipomoea terpthum*)
- Zanjabil (*Zingiber officinale*)
- Khulanjan (*Alpinia galanga*)
- In case of headache, *Samagh-i-Katira* (Gum *Traga cantha*) is used as substitute.

### Pharmacological actions of *Glycyrrhiza glabra* L. (Aşl al-Sūs.) in Unani medicine and Ethno-medicine

Table 1: Pharmacological action of *Glycyrrhiza glabra* L. (Aşl al-Sūs.)

S. No.	Action	Unani Reference	Ethno-botanical Reference
1.	Resolvent ( <i>Muħallil-i-Warm</i> )	[8,30]	[32]
2.	Demulcent ( <i>Mulattif</i> )	[8,10]	[17,33]
3.	Expectorant ( <i>Munaffith-i-Balgham</i> )	[8,17]	[34]
4.	Detergent ( <i>Jālī</i> )	[8,10]	[35]
5.	Carminative ( <i>Kasir-i-Riyāħ</i> )	[8,36]	
6.	Nervine tonic ( <i>Muqawwi-i-Asab</i> )	[8,17,36]	[34]
7.	Emmenagogue ( <i>Muddirr-i-ħayd</i> )	[8,17,29]	[34]
8.	Laxative ( <i>Mulayyin</i> )	[36]	[17]
9.	Diuretic ( <i>Mudirr-i-bawl</i> )	[8,10,36]	[35]
10.	Antipyretic ( <i>Daf-i-Hummā</i> )	[8,10]	
11.	Anti-anxiety ( <i>Daf-i-Tawahħush</i> ),	[10]	
12.	Emollient		[37]

## Therapeutic uses in Unani and Ethno-medicine

Table 2: Therapeutic uses of *Glycyrrhiza glabra* L. (Aṣl al-Sūs.)

S. No.	Uses	Unani reference	Ethno botanical references
1.	Gastric ulcers ( <i>Qarḥa-i-mi'da</i> )	[11,12]	[38]
2.	Duodenal ulcers ( <i>Qarḥa-i-Ashnā-i-Ashri</i> )	[11,12]	[38]
3.	Sore throat ( <i>Khashūnat al-Halq</i> )	[8,12]	[39]
4.	Bronchitis ( <i>Warm-i-Sho'ba al-Riyya</i> )	[8,12]	[39]
5.	Asthma ( <i>Dīq al-Nafas</i> )	[7,9,10]	[39]
6.	Rheumatoid Arthritis ( <i>Waj al Mafaṣīl</i> )		[40]
7.	acute hoarseness of voice ( <i>Buḥḥa al-Ṣawth</i> )	[7,9,10]	[41]
8.	Dry cough ( <i>Suāl-i-yābis</i> )	[13]	[40]
9.	Epilepsy ( <i>Sar'</i> )	[7,9,10]	[34]
10.	Hemiplegia ( <i>Fālij</i> )	[7,9,10]	
11.	Facial palsy ( <i>Laqwa</i> )	[12,13]	
12.	Nightmare ( <i>Qābūs</i> )	[12,13]	
13.	Anxiety ( <i>Tawaḥḥush</i> )	[7,10,13]	
14.	Melancholia ( <i>Malānkhūliya</i> )	[9,12]	
15.	Hemorrhoids ( <i>Bawāsīr</i> )	[7]	
16.	Burning micturition ( <i>Hurqa al-bawl</i> )	[7,9,10]	
17.	Uvulitis ( <i>Warm-i-luhāt</i> )	[7,9,13]	
18.	Stomatitis ( <i>Qulā'</i> )	[7,9,10]	
19.	Gonorrhoea ( <i>Suzāk</i> )	[12,13]	
20.	Abdominal pain ( <i>Waja al-mi'da</i> )	[9,12]	[34]
21.	Hypertension ( <i>Zaghtuddam Qawi</i> )		[42]
22.	Foul perspiration of the armpit	[7]	[34]

## Pharmacological evidence/ experimental studies

Table 3: Experimental studies on *Glycyrrhiza glabra* L.

S. No.	Activity	Part/Extract	Cell lines/Animal model
1.	Anti-inflammatory	Hydroalcoholic extract	Carrageenan induced rat paw edema at dose levels of 100,200,300 mg/Kg. The extract showed a maximum of 46.86% inhibitory action <sup>[43]</sup>
2.	Immunomodulatory	Aqueous extract	<i>In vivo</i> phagocytosis, determination of cellular immune response hemagglutination antibody titer & plaque forming cell assay using sheep RBCs <sup>[44]</sup>
3.	Antiulcer	Aqueous, acetone, ethanolic extracts of leaves	Micro-organism used: <i>Helicobacter pylori</i> by agar well diffusion method <sup>[45]</sup>
4.	Anti-tussive	Ethanol extract	SO <sub>2</sub> gas induced cough in experimental animals. Mice showed an inhibition of 35.62% in cough on treatment with <i>G. glabra</i> extract <sup>[46]</sup>
5.	Chronic fatigue stress	Hydroalcoholic extract	The extract showed the protective effect on mice on exposure to chronic fatigue stress <sup>[47]</sup>
6.	Antimicrobial	Ether, Chloroform, acetone	Micro-organisms used: <i>E. coli</i> , <i>B. subtilis</i> , <i>P. aerogenosa</i> , <i>S. aureus</i> <sup>[48]</sup>
7.	Cytotoxic	CHCl <sub>3</sub> , methanol & aqueous extract	<i>In vitro</i> cytotoxic activity using two different cell lines MCFT-cancerous & Vero-normal cell line <sup>[49]</sup>
8.	Anticonvulsant	methanol extract of leaves	Fractions were evaluated intra-peritoneally in mice using maximal electroshock (MES) & pentylenetetrazol (PTZ) seizure tests <sup>[50]</sup>
9.	Antiviral	Aqueous extract	Herpes simplex 1 & vesicular stomatitis virus <sup>[51]</sup>
10.	Anticancer	Licorice extract	Ames test, Trp-p-1, Trp-p-2 in <i>S.typhimurium</i> TA 98 revertants <sup>[52]</sup>
11.	Enzyme inhibiting	Methanolic extract	<i>In-vitro</i> inhibition of tyrosinase enzyme <sup>[53]</sup>
12.	Hepatoprotective	Aqueous extract of roots	PCM induced rats' hepatocytes damage <i>in vivo</i> . Rabbit models with acute liver injury induced by CCl <sub>4</sub> <sup>[54]</sup>
13.	Memory enhancing	Aqueous extract of roots	Three-month-old Wistar albino rats. Elevated -plus maze and Morris water -maze test were conducted <sup>[55]</sup>
14.	Antioxidant	Methanol extract	The method based on scavenging activity & reduction capability of 1,1-diphenyl-2-picrylhydrazyl radical; Also against nitric oxide & superoxide radicals <sup>[56]</sup>
15.	Anti-stress activity	Alcoholic & aqueous extract	Reduce stress in <i>Drosophila melanogaster</i> induced by Methotrexate at different conc <sup>[57]</sup>

**Compound formulations:** Various compound formulations have been mentioned in Unani medicine containing *Aṣl al-Sūs*, and these compounds are:

*Dayaquza; Ḥabb-i-Baqḷa; Ḥabb-i-Sū'al Musakkin; Ḥabb-i-Ghariqun; Ḥabb-i-Nazla; Ḥabb-i-Surfa Qawi; Jawarish Aṣl al-sūs; Joshandah Munzij; Lauq Sapistan; Lauq Amaltas; Lauq Khiyar Shmabar; Lauq Sapistan; Lauq Shamoon; Lauq Hulba; Lauq Ziq-un-Nafas; Majun Mughalliz Jawaharwali; Majun Mundi; Marham Kafoor; Namak Sulemani; Qabzeen; Qurs-i-Gul; Qurs-i-Su'al; Qairūtī Aarad Karsana; Qurs-i-Mullayyin; Qurs-i-Sartan Kafoori; Qurs-i-Zarishk; Roghan Sanan; Satawari; Sharbat Sadar; Sharbat Aijaz* <sup>[58-60]</sup>

### Conclusion:

*Aṣl al-Sūs* is one of the most important plant *Glycyrrhiza glabra* L. (Leguminosae/Fabaceae) which has been used by Unani physicians for the treatment of various diseases. The modern experimental and clinical pharmacological studies confirmed also anti-inflammatory, immuno-modulatory, antiulcer, anticonvulsant, memory-enhancing activities etc.

From this evidence-based review it can be concluded that new research avenues may validate scientifically the use of *Glycyrrhiza glabra* L. in amelioration of various diseases as described by Unani scholars.

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