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Aslussoos (*Glycyrrhiza glabra* Linn): A root with immense pharmaceutical potential and its utilization in Unani system of medicine

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Abstract
The root of the plant Aslussoos (*Glycyrrhiza glabra* Linn) has been used since prehistoric times, and is well documented in written form starting with the earliest Greeks. The roots and rhizomes of licorice (*Glycyrrhiza* species) have long been used globally as a medicine and natural sweetener. According to classical Unani text *Aslussoos* acts as a demulcent, concoctive of phlegm, expectorant etc. It is widely used for cold (Catarrh), cough, pharyngitis, hoarseness of voice etc. Some of the Unani compound formulations containing *Aslussoos* are *Lauq-e-Sapistan Khiyar shambar, Mufeed Joshanda, Sharbat Nazla Safoof Asl-us-Soos, Sharbat-e-Aijaz, Jawarish Aslussoos* etc. It is used mainly for the treatment of peptic ulcer, pulmonary and skin diseases. Clinical and experimental studies suggest that it has several other useful pharmacological properties apart from their traditional indications. It includes antitussive, anti-inflammatory, antiviral, antimicrobial, immunomodulatory, antioxidative, gastroprotective, hepatoprotective and cardioprotective effects. A large number of components have been isolated from licorice root, including saponins, triterpene, flavonoids, isoflavonoids, phenolics, chalcones etc. Glycyrrhizin (glycyrrhizic acid) is normally being the main biologically active component.

Keywords: *Aslussoos, Glycyrrhiza glabra* Linn, pharmaceutical, pharmacological activity, Unani Medicine, *mulethi,* Liquorice sugar

1. Introduction
The drug *Aslussoos* in Unani medicine is correlated with *Glycyrrhiza glabra* Linn. It consists of dried stolen and roots of *Glycyrrhiza glabra* Linn. It belonged to family Leguminosae. [1, 2] The name *Glycyrrhiza glabra* is a Greek word, *Glycyrrhiza* means sweet and *glabra* means smooth. Liquorice is widely used in Indian traditional medicines for various respiratory ailments and also as a flavouring agent in pharmaceutical industry [3]. *Glycyrrhiza glabra* is the principal source of commercial drug, Liquorice, is distributed in sub-tropical and warm temperate regions of the world. The underground part throws off a large number of perennial roots. Liquorice is dried peeled or unpeeled underground stems and roots of the plant. The roots are ready for harvesting in 3-4 years after planting. Liquorice is soft, flexible and fibrous having light yellow colour internally and it has a faint characteristic smell and sweet taste. Liquorice is used in the form of powder, extract etc. but extract has been proven most potent form of this drug. *Rubb-e-soose / Rubb al-Soos* and *Sat-mulethi* are the names of *Aslussoos* extract sold in Indian bazaars. These are used for taste masking of syrups and elixirs, which contains nauseous medicines. Liquorice extract is used as an essential constituent of cough syrups and lozenges. Liquorice is used in the form of decoction, infusion or lozenges in traditional medicine [4]. Powdered drug is extensively used as a pill excipient and the aqueous extract is also used to mask the nauseous taste of various pharmaceutical preparations [5]. A good crop yields 75-80 quintals of dried roots per hectare of the crop [6]. The main active constituent of the plant is Glycyrrhizin which is also known as Liquorice sugar [7].

2. Historical Background
Shaofarastus and *Diascoroids* described it in the name of Glycyrrhiza. *Shusrut* also described [8]. Liquorice, It is known since the period of *Sushrutha* [3]. *Abu Hanifeh* describes *Sus* as a well known plant, which is used for medicine [9]. *Glycyrrhiza glabra* is one of the most widely used herb from the ancient medical history of traditional medicines, both as a medicine and also as a flavouring herb. Liquorice has been used in medicine for more than 4000 years. The earliest record of its use in medicine is found in "code Humnubari" (2100 BC). Liquorice was also one of the important plants mentioned in Assyrian herbal drugs (2000BC). Hippocrates (400BC) mentioned its use as a remedy of ulcers and quenching of thirst and Theophrastus and Dioscorides described it as a expectorant and demulcent [10]. The first documented medicinal

use of Liquirice is mentioned in Assyrian, Chinese, Egyptian and Indian cultures. Plinius suggested Liquirice as a highly significant remedy for Mailases of throat, Asthma, Mouth Ulcers and even in Sterility. Dioscorides and Avicenna treated the diseases affecting voice, lung diseases and cough, with Liquorice. Plinius and Claudius, Galen found the Liquorice a very effective drug in genitor-urinary diseases such as Kidney stones, Kidney and bladder pain and as diuretic to treat various ailments of Urinary system [11].

3. Scientific classification [12]

Domain	:	Eukaryota
Kingdom	:	Plantae
Phylum	:	Tracheophyta
Class	:	Magnoliopsida
Order	:	Fabales
Family	:	Leguminosae
Genus	:	*Glycyrrhiza*
Species	:	*Glycyrrhiza glabra*
Botanical name	:	*Glycyrrhiza glabra* Linn.

4. Vernacular names:- Greek: Aluqarya, Alufi and Ghalufarya, [13] Asl-us-soos, Mulethi, Rub-us- soos, [14]; Arabic: Asl-us-soos, [1] Ood-us-soos [13]; Persian: Beekh mahek [1, 4]; Hindi: Mulethi ki bel, Mulethi, Jethi madu, jeshni madu, Murti [13, 4, 1]; Urdu: Mulethi, Asl-us-soos [1, 15]; Asfahani: Masrad [16]; Latin: Abras [17]; Afghani: Khoogaoli (sweet root) [17]; Kashmiri: Sangeer [17], Multhi [1]; Turkish: Sheerin baan [17]; Firangi: Kalesarpazah [17]; English: Liquorice root, Sweetwood [1]; Bhopali: Jathon [17]; Sanskrit: Madhuka [1, 4] ; Marathi: Jeshta madha [1, 4]; Gujrati: Jethi [4], Jethimadha [1]; Telagu: Yashtimadhukam, Atimadhuramu [1, 4]; Tamil: Atimaduram [1, 4]; Kannada: Yashti mdhuka, Atimadhura [1, 4]; Bengali: Jashtimadhu [4]; Malyalam: Iratimadhuram [1, 4]; Assamese : Jesthimadhu [1]; Oriya: Jatimadhu [1]; Punjabi: Mulathi [1]; France: Bois doux [5, 18]; German: Sussholz [5, 18].

5. Habit and Habitat: Native to the Mediterranean regions [14]. *Qabaad-wa-qaya* and *Neetas* cities [16], Egypt, Iraq, Syria, Hind (India), [13] Asia minor, Persia and other central Asian countries. Successful cultivation has been done in temperate Himalayas' and the hilly places of such as Jammu, Srinagar and south India such as Anand and Bengaluru [3, 4] and also in Andaman Islands, Burma, [15] Afghanistan, Turkistan, Iran. [13]

6. Botanical description: Plant is tall perennial herb approx. 2 m. in height. [1] Plant grows well in dry and sunny climate with deep moist soil [14].

6.1 Roots and Stolons: Liquorice is the pieces of (peeled or unpeeled) underground stems and a few pieces of roots, 6 to 8 inch in length and 0.25 to 0.75 inch in diameter. Thinner rhizomes are often with alternate buds. After harvesting the underground stems and roots are cut in to pieces and dried in shade. The dried peeled or unpeeled underground stems and roots constitute the commercial drug [9, 15]. Unpeeled pieces are dark reddish to brown in colour and wrinkles are present longitudinally, while peeled pieces are smooth and yellowish. Fractured Liquorice is fibrous in the bark and splintery in the wood. Peeled drug is used for the preparation of Liquorice powder. Powdered drug is yellow in colour [4]. Stolon consists of a cambium ring with small central pith while root is without a pith [1]. Earthy odour is present in roots and stolons. Its sweet taste is due to its peculiar principles named Glycion and Glycyrrhizin [19].

6.2 Leaves: It has multifoliate leaves [9, 15]. Leaves are pinnate [20]. These are alternate with petioled, ovate, entire and pale green leaflets [5]. **Flowers**: Flowers are in axillary spikes. Colour is lavender to violet [9, 15]. Flowers are Papilionaceous [5] **Fruits**: Fruit is a compressed legume, which contains kidney shaped seeds [5].

6.3 Varieties: *Glycyrrhiza glabra* has some varieties such as G. *glabra* var. *typica* (Spanish Liquorice), *Glandulifera* (Russian Liquorice), *Violacea* (Persian Liquorice) [3], Klitaka and Klitankan were considered as aquatic varieties of Yashtimadhu [14].

6.4 Adulterants: *G. uralensis* Fisch is the source of Manchurian Liquorice. Its bark is pale chocolate brown in colour and peeled off very easily. It gives a pungent extract and contains less amount of sugar, while Liquorice of commerce is flexible and fibrous with sweet pleasant taste. Roots of *Abrus precatorius are available under the trade name of* Indian Liquorice. Roots of related genera are also used as adulterants of Liquorice [4]. The root of *Glycyrrhiza glabra* is heavy and sinks in water [9].

Fig 1: *Glycyrrhiza glabra* Linn. (Aslussoos)

7. Description of Drug in Unani Medicine: *Aslussoos* is the name given to root of the plant named *Soos* [13, 21]. These are yellow and sweet roots. *Aslussoos* is of one type only. Thin and yellow is of the best quality [22]. It is a climber having branches and is two hands in length; leaves are looking like leaves of *Mastagi* plant and cuprous in color. Leaves releases sticky material. Flowers are like that of *Baraqeenas.* Flowers are soft and furfery in color. Fruits are like that of *Qalataanus* but some harder and have biconvex covering. Roots are long and same in color of the wood of *Baksees* plant found in Syria. Roots are like the roots of *Juntiyaan* also. Roots have astringent property with some sweetness. From these roots *Usarah* is obtained like *Rasou* (Dioscoroides). Most beneficent material of *Soos* is its *Usarah*, having sweetness found in its roots. Its decoction and *Usarah* both are beneficent in many type of cough [16]. It is a root of plant *Soosan*. It is of two types one is sweet and other one is bitter sweet is useful and bitter is not used as a medicine, because according to some, bitter one is toxic. Standard quality of *Aslussoos* is sweet, less fibrous, yellowish and average in girth and this is Egyptian *Aslussoos.* Its potency remains for ten years [8]. It should be used after peeling its bark [23] or

without bark, because according to some bark produces dizziness (*Ghasyan*) and vomiting [13]. Roots are externally brown and internally *yellow* easy to cut vertical and streaks. Its taste is mild irritant and somewhat bitter [8]. It is most abundantly cultivated in Spain [24]. Fresh is considered of the best quality [25].

7.1 Part used: Root, [16, 13, 8] Peeled root and Rhizome. [15, 5]

7.2 Mizaj (Temprament): *Usarah* (extract) is motadil [16] *Aslussoos*-motadil. [8, 22] Near to all the four temperament, *Murakkab al quwa*, decoction of *Aslussoos* is more motadil than its root [8] Har (hot) 2^0 - Yabis (dry) 1^0, [15, 23, 18] Har 1^0- Yabis 1^0, [13] Har - Ratab (wet). [25, 26]

8. Afa'al (Pharmacological actions in Unani medicine)*:* *Nafe khushoonat Qasaba ar-Ri'a* (Demulcent), *Buhha al-Sawt* (Hoarseness of voice), [13, 27] *Waja-i- Qasaba ar-Ri'a*, [16, 8] *Munzij-i-Akhlat-i-ghaleezah* (Concoctive of concentrated humours), *Muqawwi-i-Asab* (Nervine tonic) *Mulayyin* (Laxative), *Dafe Khushunat wa Suzash Sadar, Halaq wa Hanjara* (removes throat irritation), [13, 8, 13, 27] *Munzij-i Balgham* (Concoctive of Phlegm), *Munaffith-i balgham* (Expectorant), [21] *Mugharri* (Lubricant), [21, 26] *Jali* (Detergent), [21, 22] *Muqi* (Emetic), [21] *Mulattif, Munaqqi Sadar wa Riya* (Demulcent for chest / lungs), [22] *Munaqqi Qasba al-Ri'a*, (Cleanses respiratory passage) [16, 8, 22] *Mulayyin-i-Qasba al-Ri'a*. (Laxative for Trachea). [22]

9. Istemal (Uses as per Unani literature): *Waja-us-Sadr* (Chest pain), [16] *Humma-i-Kuhna* (Chronic Fever), *Suda*, (Headache) *Shaqeeqa* (Migrain), [8, 13] *Amraad-i-Balghami wa Saudawi*, (Diseases of Phlegm and black Bile), [21] *Rabw* (Bronchial Asthama), [13, 8, 21] *Diq-al-Nafas* (Asthma), [8, 13, 21] *Suzesh and Khushunat Ri'a wa Qasaba ar-Ri'a* (Irritation of Lungs and Trachea), [25, 21] *Sual* (Cough), [16, 25, 13] *Waram-i-Halaq* (Pharyngitis), [25] *Buhha al-Sawt* (Hoarsness of Voice), [25, 21] *Dard asab* (Neuralgia), *Nafas al-Dam* (Heamoptysis) [22] etc.

9.1 Miqdare khuraq (Dosage): 4.50 gm to17.50 gm, [13] 4.00 gm to 17.00 gm, [8] 3 - 7 gm, [1, 15, 21] 2 - 4 gm, [14] 6 - 9 masha [23, 27].

9.2 Muzir (Adverse effects): *Gurdah* (Kidney) and *Tihal* (Spleen) [8, 13, 23].

9.3 Musleh (Corrective); *Unnab*, [8, 13] *Kateera for Gurdah* and *Gule Surkh* for Tihal [8, 13, 15].

9.4 Badal (Substitute): Half of the weight of *Rub us Soos* or *Injeer* [8, 13].

10. Murakkabat (Compound Formulations): *Lauq-e-Sapistan Khiyar shambar, Lauq-e-Nazli, Lauq-e-Zeequnnafas, Sharbat-e-Sadar, Habb-e-Surfa, Dayqooza, Lauq-e-Hulba, Lauq-e- Shamoon, Qairooti-e-Arad-e-Karsana*, [1] *Safoof Asl-us-Soos, Sharbat-e-Aijaz, Qurs Sartan, Itrifal Mundi, Qurs Sartan*, [15] *Jawarish Aslussoos*, [13, 24] *Lauq-e-Amaltas*, [13, 15, 24] *Habbe Baqla*, [13, 24, 28] *Lauq-e-Badam*, [29] *Sharbat Farasiyoon, Sharbat Sual, Sharbat Char Tukhm.* [30] *Habb-e-Nazla, Qurs-e-Sartan Kafoori.* [2] *Majoon-e-Mughalliz Jawahar Wali, Arq Ma-ul-Laham Makoh Kasni Wala, Sharbat Faryad Ras, Iksier-ul-Atfal*, *Habb-e-Sual Musakkin, Qabzeen, Qurs-e-Mullayyin, Satawari, Mufeed Joshanda, Laooq Khayarshambar, Namak Sulemani, Sharbat Nazla, Surfin,* [31] *Munzij, munaffis-e-balgham, Mudirr-i-Bawl Mudir-e-haiz, kasir-e-riyah* [1].

11. Pharmacological action and uses according to ethnobotanical and other literature

11.1 Actions: Nerve tonic, Emmenogouge [15], Emollient, [7] Rejuvenating [32] Expectorant, Demulcent, [14, 15, 81] Antiallergic, Spasmolytic, Anti-stress, Antiulcer and Antidiabetic [14], Anti-inflammatory, [14,1] Mild laxative, [18,33] Antispasmodic, [3] Tonic, [18, 33,34] Astringent [18].

11.2 Uses: Irritable conditions of mucous membrane of urinary organs, gastric ulcers, [18] *Khushunat-e-halaq, Buhha al-Sawt had, Zeequn Nafas, Hirqat-ul-boul*, [1, 18] Lung diseases. [15] Catarrh, sore throat and affections of pulmonary mucus membranes. [7, 33] Tuberculosis, Mouth Ulcer, Adrenocorticoid Insufficiency, Rheumatism, Arthritis. [14] Dry Cough. [1, 14, 7] Peptic ulcer, Inflammations, Addison's disease, [3] Haemoptysis. [18] Bronchitis, Respiratory infections. [14, 18] Sore throat [18, 34].

12. Chemical constituents

12.1 Saponins: Liquorice contains triterpenoidal saponins (4-20%) [35]. **Glycyrrhizin**: Glycyrrhizin is the chief constituent of triterpenoidal saponin.[3]. It is extremely sweet and water soluble [5]. It imparts its characteristic sweetness and its concentration in different varieties is 2-14%, it is absent in aerial parts of the plants. Glycyrrhizin is present in liquorice as the calcium and potassium salt of the glycyrrhizic acid. It is 50 times sweeter than cane sugar [4]. Glycyrrhizin (main chemical constituent) - 2-9%, Glycyrrhetinic acid (glycrrhetic acid) - 0.5- 0.9%, [14] 18-alpha-glycrrhetic acid, glycyrrhetic acid methyl ester, glabric acid, glabrolide, uralenic acid [36]. Three new oleanane-type triterpenoidal saponins, namely licorice-saponin M3 (1), licorice-saponin N4 (2), and licorice-saponin O4 (3) were isolated in the form of amorphous powder from the root of *Glycyrrhiza glabra* [37].

12.2 Glycosides: Isoliquiritin is an anthoxanthin glycoside, which imparts yellow color, it partially converts in to liquiritin during drying and storage of roots. Both isoliquiritin and liquiritin are bitter with sweet after-taste. Commercial samples contain 2.2% of isoliquiritin. A steroid estrogen (estriol) is also reported to be present in liquorice [38].

12.3 Flavonoids: Twenty seven flavonoids are present in Liquorice root, of these six flavonoids are isolated and three identified namely,4',7 dihydroxyflavanone also known as liquiritigenin, 4'-β-D-glucoside also known as liquiritin and 2,4'-trihydroxychalcone which is also known as isoliquiritigenin, the other three are new flavonoids, L-1, L-5, L-7. Hydrolysis of flavonoid L-1 yields aglycones, which are separated in to liquiritigenin and isoliquiritigenin. 7-hydroxy-4'-methoxyisoflavone (formonetin). Liquraside (flavonoid glycoside). Rhamnoliquiritin (flavonone glycoside) [38]. Isolicoflavonol, isoliquiritin, licoricidin [36]. Five new flavonoids - glucoliquiritin apioside, prenyllicoflavone A, shinflavanone, shinpterocarpin and 1-methoxyphaseolin are isolated from dried roots [10].

12.4 Isoflavonoids: Aglycones formononetin, glabren, glabridin, glabrol, 3-hydroxygIabrol, glycyrrhisoflavone [36]. Hispaglabridin A and B, Glyzarin, Glabron [35].

12.5 Phenolics: Semilicoisoflavone B,1-methoxyficifolinole, Isoangustone A and licoriphenone [39]. phenolic compounds glycybridins A–K (1–11), along with 47 known phenolics (12–58) was isolated by K. Li *et al.*from the Licorice root and illuminated Structures of these new phenlic compounds by the help of extensive NMR and MS analyses as well as experimental and computed ECD data [40].

12.6 Glucosides: Two new chalcone glucosides, trans-isoliquiritigenin-4'-β-D-glucopyranoside (isoliquiritin) and

trans-isoliquiritigenin-4'-β-D-glucopyranoside (neoisoliquiritin) [36].

12.7 Cumestan derivatives: Glycyrol, Isoglycyrol, Liquocoumarin [36].**Coumarins**: GU-12[39]. Liqcoumarin, Glabrocoumarone A and B, Glycyrin, Licofurano-coumarin, and Glabrocoumarin. [35]. **Hydroxycoumarins**: Herniarin, Umbelliferone, Glycycoumarin, Licopyranocoumarin.[36]

12.8 Lactones: Glabrolide, Isoglabrolide, Deoxoglabrolide 21α-hydroxy-isoglabrolide[36].

12.9 Steroids: Sterols including beta-sitosterol, stigmasterol [36].

12.10 Volatile Oil: Anethole, estragole, eugenol, hexanoic acid [36].

12.11 Sugars: Glucose, sucrose, mannite, starch [4].

13. Physicochemical Standards

Water soluble matter not less than 20%, Ash not more than 10% (unpeeled) and not more than 6% (peeled),[4] Loss on drying at 105^0C 7.94% [15]. Total ash not more than 10%, Acid insoluble ash not more than 2.5% [1]. Alcohol soluble extractive not less than 10%, Water soluble extractive not less than 20% [1, 15]. **P^H values**: 1% solution 5.8: 10% solution 5.8 [15].

14. Reported pharmacological activity

14.1 Antitussive activity: *Jahan et al.* evaluated antitussive activity of *Glycyrrhiza glabra* and *Adhatoda vasica* using a cough model induced by sulphur dioxide gas in mice. The effect of the ethanol extracts of *Glycyrrhiza glabra* and *Adhatoda vasica* on SO_2 gas induced cough in the mice have very significant effects at the level of $p<0.01$ in inhibiting the cough reflex at a dose of 800 mg/kg and 200 mg/kg body wt. in comparison with the control group. Mice showed an inhibition of 35.62%, in cough on treatment with *Glycyrrhiza glabra* and 43.02% inhibition on treatment with *Adhatoda vasica* within 60 min of the experiment. [41].

14.2 Anti-inflammatory activity: β-glycyrrhitinic acid is a major metabolite of glycyrrhizin, which has shown anti-inflammatory properties in different animal models [42].

14.3 Antiviral activity*: Crance JM et al.* estimated antiviral activity of Interferon, ribavirin, 6-azauridine and Glycyrrhizin by the reduction of the cytopathic effect of each flavivirus (flaviviruses belonging to principal antigenic complexes or individual serogroups of medical importance: dengue, Japanese encephalitis, mammalian tick-borne and yellow fever virus (YFV) groups) *in vitro* cells and by the reduction of the virus titre [43]. *Michaelis M et al*. show in this report that therapeutic concentrations of glycyrrhizin (used as clinically approved parenteral preparation SNMC) interfere with highly pathogenic H5N1 influenza A virus replication and H5N1-induced pro-inflammatory gene expression at least in part through interference with H5N1-induced ROS formation and in turn reduced activation of p38, JNK, and NFkB in lung cells [44]. *Van Rossum et al.* found that Glycyrrhizic acid inhibits the replication of several viruses *in vitro* and some mechanisms have been found also for the antiviral effects of glycyrrhizin [45].

14.4 Antimicrobial activity*: Gupta VK et al*. studied antimicrobial activity of Glabridin (obtained from the roots of *Glycyrrhiza glabra*) at 500 µ gm/ ml concentration. Bioactivity guided phytochemical analysis identified glabridin as potentially active against both *Mycobacterium tuberculosis* H37Ra and H37Rv strains at 29.16 g/mL concentration. It exhibited antimicrobial activity against both Gram-positive and Gram-negative bacteria [46]. *Fukai et al.* found in his study that Glabridin, glabrene and licochalcone A (active constituents of *Glycyrrhiza glabra* species) exhibited antimicrobial activity against *Helicobacter pylori in vitro* [47].

14.5 Memory enhancing activity: Chakravarthi KK *et al*. were designed a study to investigate the beneficial effects of *Glycyrrhiza glabra* root extract on learning and memory in 1-month-old male Wistar albino rats. Four doses (75, 150, 225, and 300 mg /kg) of aqueous extract of root of *Glycyrrhiza glabra* was administered orally for six successive weeks. Diazepam-induced amnesia provided as the interoceptive behavioral model. In this study, results showed that all the doses of aqueous root extract of Glycyrrhiza glabra notably enhanced the memory; though, in the doses of 150 and 225 mg/kg, it showed a significant enhancement in learning and memory. In addition, Diazepam-induced amnesia was reversed by the aqueous root extract of *Glycyrrhiza glabra* (150 and 225 mg/kg). Findings advocate that the memory enhancement effects of *Glycyrrhiza glabra* may be mediated by its antioxidant and anti-inflammatory activities. So the, *Glycyrrhiza glabra* appears to be a hopeful drug for improving memory in the management of impaired learning, dementia, Alzheimer's disease, and other neurodegenerative disorders [48].

14.6 Antiprotozoal activity: According to *Chen et al.* chalcones such as Licochalcone A, from Chinese Liquirice root (*G. glabra, G. uralensis, G. inflate*) are known to possess antiplasmodial activity with IC 50 values between 4.5 and 0.6 mg/ml [49].

14.7 Antimalarial activity: A study has been done by *et al*. as a part of drug discovery plan for antimalarial agents. In this study, they have been made chemical investigation of roots of Glycyrrhiza glabra and they were successful in isolation and characterization of 18β-glycyrrhetinic acid (GA) as a major constituent. The GA was tested against *P. falciparum* NF 54 (*in vitro*) and *P. berghei* K173 (*in vivo*), which were chloroquine sensitive. When *P. falciparum* was subjected to 18β-glycyrrhetinic acid in graded doses, an IC_{50} of 1.69µg/ml was derived as against 0.015µg/ml for chloroquine. The *in vitro* studies against *P. falciparum* showed significant (IC_{50} 1.69µg/ml) anti-malarial potential for 18β-glycyrrhetinic acid. Docking results revealed that 18β-glycyrrhetinic acid has moderate docking score (LibDock) of 71.18 for the target protein *pf*LDH in comparison to the standard anti-malarial drug chloroquine. On the basis of *in-vitro* and *in-silico* results, 18β-glycyrrhetinic acid was further evaluated in mice infected with *P. berghei*, which showed a dose dependent activity (6.68±2.19, 1.49±1.04 and 0±0% parasitemia at 62.5, 125 & 250mg/kg respectively) as against 20.57±3.13% parasitemia in infected but non-treated animals. This is the first ever report on the anti-malarial potential of GA (18β-glycyrrhetinic-acid) [50].

14.8 Probiotic activity: In the present study *Asha MK et al.* found that the extract of *Glycyrrhiza glabra* (rich in flavonoids) was capable with probiotic strains, (Lactobacillus fermentum, Lactobacillus casei, Lactobacillus plantarum and Streptococcus thermophilus) commercial probiotic drinks and different digestive enzymes such as pancreatic lipase, pancreatic α-amylase, α-glucosidase, xylanase and phytase. This study has been done taking patients with functional dyspepsia and demonstrates that flavonoid rich extract prepared from Glycyrrhiza glabra have some gut health-promoting properties such as antioxidant, anti-inflammatory and anti-Helicobacter-pylori-activities [51].

14.9 Immunomodulatory activity: *Zhang et al.*demonstrated that Glycyrrhizin displays a unique action to prolong the

duration of the T-cell receptor-mediated in vitro splenic T-lymphocyte growth response to anti-CD3 monoclonal antibody (mAb) or concanavalin A (Con A) through enhancement of interleukin-2 (IL-2) secretion andIL-2 receptor (IL-2R) expression [52]. *Nose et al.* investigated the effects of crude polysaccharide fractions obtained from the shoot of *Glycyrrhiza glabra* on murine peritoneal macrophage function, in order to clarify whether plants grown under aseptic conditions produce immunomodulatory polysaccharides. All crude polysaccharide fractions induced nitric oxide production by murine peritoneal macrophages *invitro* [53].

14.10 Anti-ulcer activity (Gastric): The anti-ulcer activities of aqoueous liquorice extract was done by *Aly et al*., Indomethacin induced ulceration technique in rat stomach were investigated. The results obtained showed that the stomach of rats treated with intra-gastric indomethacin (20 mg/kg) developed gastric ulceration after 4 hours of administration. Results of this *in vivo* demonstration show that licorice has similar anti-ulcer activity to FT (famotidine) [54].

In a study, the hydroalcoholic extract of *Glycyrrhiza glabra* L. was evaluated for antiulcerogenic activity and acute toxicity profile in mice by *Jalilzadeh-Amin G et al.* Various doses of HEGG (hydroalcoholic extract of *Glycyrrhiza glabra*) (50-200 mg/kg) were administered orally to animals of different groups. Omeprazole and cimetidine at doses of 30 and 100 mg/kg were used as positive controls, respectively. Greater curvature of the stomach was used for determination of the ulceration index in the inner lining of stomach. There was no toxic symptoms and mortality in mice on the oral administration of the extract at 1600 mg/kg. and 2950 mg/kg was determined as the oral LD50. The HEGG (50-200 mg/kg) showed a noteworthy reduction in ulcer index in HCl/Ethanol-induced ulcer, and at the doses of (50-150 mg/kg) showed antiulcer activity against indomethacin-induced gastric lesions dose dependently. The extract was effectively capable to inhibit gastric lesions formation induced by ethanol. The extract (200 mg/kg) was more potent than omeprazole (30 mg/kg). The results indicated that HEGG exerted an antiulcerogenic effect that could be associated with increase in gastric mucosal defensive factors [55].

14.11 Gastroprotective activity: Bhama dhanabalan *et al.* evaluated gastroprotective effects of Glycyrrhiza glabra Linn. aerial root extract in 150 and 300 mg/kg body weight orally in the rats, once daily for 14 days for prevention from asprin induced gastric ulcers and results of the study displayed significant gastroprotective activity [56]. *Nugroho AE et al.* made an investigation of gastroprotective effect of the combination of hot water extract of Licorice (*Glycyrrhiza glabra*), Pulasari stem bark (*Alyxia reinwardtii*) and Sembung leaf (*Blumea balsamifera*), against aspirin-induced gastric ulcer model in rats. The number and area of gastric ulcers were evaluated macroscopically, whereas, histo-pathological observation were used for evaluation of mucosal damage score, and the number of eosinophils and mast cells. In this study, herbal extracts combination markedly exhibited protective effects indicated by less number and smaller area of gastric ulcers in comparison to those of aspirin group. The score of mucosal damages were also decreased in herbal extracts combination groups. The number of eosinophils and mast cells of herbal combination groups were also smaller than those of aspirin group. In conclusion, herbal combination of Licorice (*Glycyrrhiza glabra*), Pulasari stem bark (*Alyxia reinwardtii*) and Sembung leaf (*Blumea balsamifera*) have potential to develop as a gastroprotective agent [57].

14.12 Hepatoprotective activity: Various hepatotoxins were added by *Nakamura T. et al*. to the medium of primary cultures of adult rat hepatocytes and the release of the cytosolic enzymes lactic dehydrogenase, glutamic-oxaloacetic and glutamic-pyruvic aminotransferases were measured 24 h later. In this *in vivo* study glycyrrhizin was found hepatoprotective, probably by preventing changes in cell membrane permeability [58].

14.13 Cytotoxic activity: According to *Fukai et al.* four known favonoids, medicarpin, liquiritigenin, (aR)-a,2', 4, 4' tetrahydroxydihydrochalcone and licuraside (isoliquiritigenin 4-O-apiosylglucoside) were isolated from a methanol extract (by *Mosher's method*) of the roots of G. glabra cultivated in Japan. Licorice phenols using a recombination, less mutant of Bacillus subtilis M45, seven compounds showed induction activities of DNA damage [59].

14.13.1 Anticancer activity: *Li K et al*. conducted a study in which, enzyme or cell based bioactivity of phenolic compounds of *Glycyrrhiza glabra* has been demonstrated. After screening of these phenolic compounds (11 new and total 58), they found that a number of compounds significantly activate Nrf2, inhibit tyrosinase and inhibit the proliferation of human cancer cells (HepG2, SW480, A549, MCF7). They also studied that Glycybridin D showed moderate toxicity against the four cancer cell lines. They also found in their study that, these compounds decrease tumour mass by 39.7% on an A549 human lung carcinoma xenograft mice model with minimal toxicity [40].

14.14 Cardioprotective activity: *Ojha et al*. evaluated the cardioprotective effect of *Glycyrrhiza glabra* against ischemia-reperfusion injury, induced by ligation of left anterior descending coronary artery (LADCA) in rat model. In this study ligation of LADCA was done for 45 minutes, followed by 60 minutes of reperfusion has induced considerable heart dysfunction evidenced by significant decrease in mean arterial pressure, heart rate, contractility dtmax, relaxation and increased left ventricular and diastolic pressure. So the all results of this study clearly suggest the cardioprotective potential of *G. glabra* against myocardial infarction by amelioration of oxidative stress and positive modulation of cardiac function [60].

14.15 Antiatherosclerotic activity: *Curcuma longa* and *Glycyrrhiza glabra*, which are traditional medicines in Asia, have been reported to exhibit preventive effects against atherosclerosis. In this study *Lee JJ et al.* demonstrated the anti-atherosclerotic effects and possible molecular mechanisms of Kiom-18 (Kiom-18 is a new composition of *Cinnamomum cassia, Pinus densiflora, Curcuma longa* and *Glycyrrhiza glabra*) using vascular smooth muscle cells (VSMCs). Kiom-18 inhibited platelet-derived growth factor (PDGF)-BB-stimulated-VSMC proliferation and DNA synthesis. Kiom-18 also arrested the cell cycle transition of G0/G1 stimulated by PDGF-BB and the proteins which was related to its cell cycle. The level of p27(kip1) expression was upregulated in the presence of the Kiom-18 extract. Furthermore, in an atherosclerotic animal model of LDLr knockout mice, Kiom-18 extract showed a preventive effect for the formation of atherosclerotic plaque, fat weight and triglyceride level [61].

15. Utilization of *Glycyrrhiza glabra* as an pharmaceutical excipient: In many European countries such as Germany, Austria, Norway, Netherland, etc, *Glycyrrhiza glabra* radix is used as an excipient, in various types of herbal teas and as an

extract in other pharmaceutical products [62]. Its use as a Pharmaceutical excipient is mentioned below.

15.1 Sweetening agent: Glycyrrhizin is 50 times sweeter than sucrose and is perhaps the sweetest natural chemical used commercially. It is used as a substitute as well as a synergistic sweetness enhancer with sucrose [63]. Non-saccharide natural sweetening agents such as glycyrrhizine have low calorific value and can overcome the problems of sucrose and synthetic sweeteners. This natural sweetener (glycyrrhizine) is useful sugar substitute for diabetic patients and in other cases of calorie restrictions [64].

15.2 Flavouring agent: Ammoniated glycyrrhizin has the characteristic licorice flavour and used as flavoring agent in pharmaceutical products as well as in confectionaries. The amount required for sweetening also imparts the characteristic licorice flavor so the glycyrrhizin is used as a sweetening as well as a flavouring agent [63].

15.3 Foaming agent: Glycyrrhizin has also been used in very minute quantities as a foaming agent in various beverages [63].

16. Discussion and conclusion

G. glabra is uses as demulcent, concoctive of phlegm, expectorant etc and is used for cold (Catarrh), cough, pharyngitis, hoarseness of voice etc. Its reported pharmacological activity are antitussive, antiinflammatory, antiviral, antimicrobial, antiprotozoal, anti malarial, immunomodulatory, antioxidative, gastroprotective, hepatoprotective cardioprotective, anti-ulcer, Cytotoxic, anticancer, probiotic memory enhancing activity etc. Several Pharmacological activity and uses in Unani medicine are been validated such as Dafe suaal (anti tussive) [16,25], *Muqawwi-i-Asab* (Nervine tonic) *Munzij-i Balgham* (Concoctive of Phlegm), *Munaffith-i balgham* (Expectorant), *Nafe khushoonat Qasaba ar-Ri'a* (Demulcent), *Mugharri* (Lubricant), *Buhha al-Sawt* (Hoarseness of voice), *Jali* (Detergent) etc.

Review clearly indicates that there is further scope of research and immense therapeutic potential owing to its activity and medicinal uses mentioned in classical Unani text. These activities which are yet to be validated can be evaluated by sophisticated contemporary tools in the light of Unani principles. Present review can be a handy in this direction as it is an attempt of updating the recent phyto-pharmacological profile of the drug and is also revealing the rich medicinal literature mentioned in Unani medicine about licorice.

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