GLYCYRRHIZA GLABRA: FOR TRADITIONAL USES AND PHARMACOLOGICAL ACTIONS

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Abstract: Glycyrrhiza glabra Linn. belonging to family Fabaceae, known as mulaiti or licorice. It is used in many systems of medicines including Unani, Ayurveda. Homeopathy, Chinese and Siddha to cure various types of complications like hepatitis, ulcers, pulmonary, skin diseases etc. Traditionally mulaiti is used as mild laxative, anti-arthritic, anti-inflammatory, anti-biotic, anti-viral, anti-ulcer, memory stimulant (being MAO inhibitor), anti-tussive, aphrodisiac, anti-myotic, estrogenic, anti- oxidant, anti-caries agent, anti-neoplastic, anti-cholinergic, anti-diuretic, hypolipidemic agent. It constituted phytoconstituents such as glycyrrhizin, glycyrrhizinic acid, glabrin A&B, glycyrrhetol, glabrolide, isoglabrolide, isoflavones, coumarins, triterpene sterols. Modern botanical applications of the herb continue this tradition with recommendations including the treatment of gastric ulcers, bronchitis, cough, and dyspepsia. Medicinal uses of Glycyrrhiza glabra Linn through the millennia as well as drug-botanical interaction, side effect and toxicity. As the roots of the plant comprised glycyrrhizin which is 50 times sweeter than sugar. Hence it may be used as a sweetening agent for various dosage forms.

Key Words: Dosage forms, Glycyrrhizin, Helicobacter pylori, Licorice.

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INTRODUCTION

Glycyrrhiza glabra L. (Fabaceae) generally known as mulaithi, sweet wood or liquorice is a small perennial herb native to the mediterranean region, central and southwest asia. This herb is cultivated in various parts of the world including Italy, Russia, France, UK, USA, Germany, Spain, China and Northern India. It has provided us some of important bioactive constituents for life saving drugs, used in the armamentarium of modern medicine. However, among the estimated 250,000-400,000 plant species, only 6% have been studied for biological activity, and 15% have been investigated phytochemically. It is widely used in ayurvedic formulations. Plants have been one of the important sources of medicines since the beginning of human cultivation. There is a growing demand for plant based medicines, health products, pharmaceuticals, food supplements etc. Medicinal plants are of great importance to the health of individuals and communities. It constituted various phytoconstituents like triterpenoidal saponin, flavonoids, tannins, alkaloids and phenolic compounds. There is a need for planned activity guided
phyto-pharmacological evaluation of herbal drugs. The dried rhizomes and roots of the plant are used as carminatives in various parts of world like Egypt, Chinese, Greek, Indian, and Roman. It has extensive pharmacological effects for human being $^{3,4}$.

**Classification** $^{5}$

<table>
<thead>
<tr>
<th>Kingdom</th>
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**Regional names** $^{6}$

| Sanskrit    | Yashti-madhuh, Madhuka    |
| Bengali     | Jaishbomodhu              |
| Gujarati    | Jethimadhu                |
| Hindi       | Mulhatti                  |
| Kannada     | Jastimadhuka, atimaddhu   |
| Malayalam   | Iratimadhuram             |
| Marathi     | Jeshtamadha               |
| Oriya       | Jatimadhu                 |
| Tamil       | Atimaduram                |
| Telugu      | Atimadhduranu, Yashtimadhukam |
| English     | Licorice, Liquorice, Sweet wood |
| Arab        | Aslussiesa                |
| Persia      | Ausareha mahaka           |
| Part used   | Root and Rhizomes         |

**Morphology**

**Leaves stem and root:** It was shrub, erect, branched either from the base or from further up, and are generally rough at the top. It is 1 to 2 m high and had a long sturdy primary taproot. The tap root was 15 cm long and subdivided into 3 to 5 subsidiary roots, 1.25 m in length. There was several horizontal woody stolen which may reach 8 m $^{7}$. Leaves was alternate, odd pinnate and 10 to 20 cm long. The leaf lets was in 3 to 8 pairs. The stipules were very small and drooping $^{7}$.

**Flower and fruit:** The axillary inflorescences were upright, spike-like and 10 to 15 cm long. The individual flowers were 1 to 1.5 cm long, bluish to pale violet and short-pedicle. The calyx is short, bell shaped and hairy. The tips of the calyx are longer than the tube, and was pointed lanceolate. Petals were narrow, the carina petals were not fused, and they were pointed but not beaked. The fruit was a pod, 1.5 to 2.5 cm long, and 4 to 6 mm wide. It was erect and splayed, flat with thick sutures, glabrous, somewhat reticulate-pitted, and usually has 3 to 5 brown, reniform seeds $^{8}$. 

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A plant of Glycyrrhiza glabra
Quantitative Standards

**Total ash** =< 6.5%, **Ash** = >3.80%, **Acid insoluble ash** =< 2%, **Sulfated ash** = <9.5%, **Water soluble extractive** = < 18.5%, **Diluted alcohol-soluble extract** = <23%, **Moisture** = 5.25%, **Woody fiber** = 5.05%, (containing sand 0.25%) \(^9,10\).

Bioactive constituents

Mullaiti roots contained glycyrrhizin, a triterpenoidal saponin glycoside which was 60 times sweeter than cane sugar; liquirtin, isoliquertin, liquiritigenin and rhamnoliquirilin type of flavonoids, and five new flavonoids- glucoliquiritin apioside, prenyllicoflavone A, shinflavanone, shinpterocarpin and 1-methoxyphaseolin. It also constituted licopyranocoumarin, licoarylcoumarin glisoflavone and new coumarin-GU-12, isoprenoid-substituted phenolic constituents – semilicoisoflavone B, 1-methoxyficifolinol, isoangustone A, licoriphenone and new prenylated isoflavan derivative, kanzonol \(^11,12\) was also included pentanol hexanol, linalool oxide A and B, tetramethyl pyrazine terpinen-4-ol, \(\alpha\)-terpineol, geraniol, propionic acid, 2,3-butanediol, furfuraldehyde, furfuryl formate, 1-methyl-2-formylpyrrole trimethylpyrazie \(^13\). Carbenoxolone(18-\(\beta\) glycyrrhetinic acid hydrogen succinate), an analog of glycyrrhetic acid, used for curing ulcerative conditions (peptic ulcers) \(^14\).

Mechanism of action

Glycyrrhizin and glycyrrhizic acid have been shown to inhibitory action on growth and cytopathology of numerous RNA and DNA viruses, including hepatitis A & C \(^15,16\) herpes zoster \(^17\), HIV \(^18,19\) herpes simplex \(^20,21\) and CMV \(^22\) and its metabolites inhibit hepatic metabolism of aldosterone and suppress 5-(beta)-reductase and was also responsible for the well-documented pseudoaldosterone syndrome. The similarity in structure of glycyrrhetic acid to the...
structure of hormones secreted by the adrenal cortex accounts for the mineral-corticoid and gluco-corticoid activity of glycyrhizic acid. Its constituents also exhibited steroid-like anti-inflammatory activity, similar to the action of hydrocortisone, to inhibition of phospholipase A2 activity, an enzyme critical to numerous inflammatory processes. In-vitro study was carried out that the inflammation & demonstrated that glycyrhizic acid inhibits cyclooxygenase activity and prostaglandin formulation as well as indirectly inhibiting platelet aggregation. *Glycyrrhiza glabra* constituents possess significant antioxidant and hepatoprotective properties. At the site of inflammation the generation of free radical atoms inhibited by Glycyrrhizin and glabridin. In vitro study was carried out that isoflavones, hispaglabridin A & B, inhibit induced mitochondrial lipid peroxidation in rat liver cells and glycyrhrizin lowers lipid peroxide levels in animal models of liver injury caused by ischemia reperfusion and also exhibit hepatoprotective activity by lowering serum liver enzyme levels.

**Pharmacokinetic study**

The study on glycyrhetic acid and found that it was absorbed and transported to the liver, it is metabolized to glucuronide and sulfate conjugates, which were subsequently rehydrolyzed to glycyrhetic acid and reabsorbed, resulting in a significant delay in terminal clearance from plasma. In healthy volunteer’s administration of 100 mg glycyrhrizin no glycyrhrizin, glycyrhyclic acid was found at < 200 ng/mL in plasma, and after 24-hour it was found in the urine.

**Traditional uses**

Traditionally the plant has been recommended as a prophylaxis for gastric and duodenal ulcers and in dyspepsia as an anti-inflammatory agent during allergenic reactions. In folk medicine, it was used as a laxative, emmenagogue, contraceptive, galactagogue, anti-asthmatic drug and antiviral agent. *Glycyrrhiza* roots were used for its demulcent and expectorant property. It is useful in anemia, gout, sore throat, tonsillitis, flatulence, sexual debility, hyperdypisia, fever, coughs, skin diseases, swellings, acidity, leucorrhoea, bleeding, jaundice, hiccough, hoarseness, bronchitis, vitiated conditions of vata dosha, gastralgia etc. It was an important ingredient in medicinal oils for the epilepsy, paralysis, rheumatism, hemorrhagic diseases and also used in the treatment of diarrhea, fever with delirium and anuria. Research showed that on being broken down in the gut, glycyrhrizin exerts an anti-inflammatory action similar to hydrocorticosone and other corticosteroid hormones. It stimulated production of hormones by adrenal glands and reduced the breakdown of steroids by the liver and kidneys. Glycyrrhizin also proved effective in the treatment of chronic hepatitis and liver cirrhosis. For relieving pain, discomfort and other symptoms caused by acrid matter in the stomach, *Glycyrrhiza glabra* was considered as one of the best remedies. It seems to remove the irritating effects of acids in a better way than alkalies. It was used by practitioners of the indigenous systems as tonic, as a demulcent
in catarrh of the genitor-urinary passages and as a mild laxative.

**Pharmacological activities**

The anti-inflammatory activity similar to cortisone and has been found useful for arthritis and allergies, used for mild Addison’s disease and other adrenal insufficiencies, such as hypoglycemia. It was also acted like adrenocorticotropic hormone (ACTH), caused sodium and water retention & potassium depletion. Excess consumption of licorice can lead to the classic symptoms of hypertension, with edema, increased blood pressure, potassium loss, and muscular weakness. The deglycyrrhizinated form was most often used to avoid the hypertensive side effects of the glycyrrhetinic acid in whole licorice. Licorice and deglycyrrhizinated licorice (DGL) have a mild laxative effect and can protect the intestinal lining by increasing the production of mucus, thus alleviating heartburn and ulcers.

**Thrombin inhibitor**

The thrombin induced platelet aggregation activity inhibited by glycyrrhizin but Platelet Aggregating Factor (PAF) or Collagen induced agglutination was not affected by glycyrrhizin.

**Anti ulcer activity**

Glycyrrhizinic acid showed antiulcer activity by increasing the prostaglandins concentrations that promote mucus secretion and cell proliferation in the stomach. The *in-vitro* activity was carried out against 29 *Helicobacter pylori* strains & found that the minimum inhibitory concentration of *Extractum liquiritiae*, glycyrrhizic acid, glycyrhetinic acid and a novel lipophilic derivative of glycyrhetinic acid monoglucuronide (GAMG) and acetylated by using agar dilution method.

**Antitussive activity & expectorant**

The study on glycyrrhizin was found to be effective in the treatment of sore throat, cough, bronchial catarrh. It also used as an antitussive and expectorant.

**Antioxidant activity**

Glycyrrhiza has significant free-radical scavenging activity and also reported that glabridin has potent antioxidant towards low density lipoprotein oxidation.

**Antibacterial activity and antifungal activity**

The antibacterial activities of mullati root extract in organic solvents like ether, chloroform and acetone found that it showed significant antibacterial activities against *Bacillus subtili* and *Staphylococcus aureu* and *Escherichia coli* and *Pseudomonas aeruginosa*. Investigated that oil based mulaithi extract contain glabridin (3-(2',4'-dihydroxyphenyl)-8-dimethylpyrano (8,7-e) chroman) which showed high fungicidal activity against *Arthrinium sacchari* and *Chaetomium funicola*, and reduced microorganism contamination in polyethyleneterephthalate, it means glabridin had been used for the prevention of beverage and food spoilage due to micro organisms.

**Anti inflammatory acvtivity**

Glabridin was effective in melanogenesis and inflammation by inhibiting the tyrosinase activity of melanocytes.
glycyrrhetinic acid exhibits anti-inflammatory activity by inhibiting glucocorticoid metabolism \(^{48, 49}\).

**Hepatoprotective activity**
The hepatoprotective activity of glycyrrhizin showed that by preventing changes in cell membrane permeability, inhibiting phospholipase A2 (PLA2) and increasing survival rate of hepatocytes \(^{50, 51}\).

**Anticancer**
*G. glabra* extract has been used in herbal formulations for combating cancers like PC-SPES, a polyherbal composition used for prostate cancer. The licorice extract induced the Bcl2 phosphorylation and G2/M cycle arrest in tumour cell lines as done by clinically used anti-microtubule agent Paclitaxel. \(1-(2,4\text{-dihydroxyphenyl})\text{-3-hydroxy-3-(4'}\text{-hydroxyphenyl})\text{1-propanone}(\beta\text{-hydroxy –DHP})\) was identified in the licorice extract, which induced Bcl2 phosphorylation in breast and prostate tumour cells, G2/M cell cycle arrest, apoptosis demonstrated by Annexin V and TUNEL assay, decreased cell viability demonstrated by tetrazolium (MTT) assay, and altered microtubule structure \(^{52}\). \(70\%\) Methanol soluble fraction of licorice acetone extract was found to induce apoptosis in human monoblastic leukaemia U937 cells. The compound was identified to be licocoumarone also responsible for antioxidant and antimicrobial activity \(^{53}\). Blocking of tumour promoter induced AP-1 activity could be used to arrest the induced cellular transformation. It was found that Glycyrrhizin induced AP-1 activity in untreated cells whereas inhibited TPA (12-O-tetradecanoylphorbol-13-acetate) induced AP-1 activity in TPA treated cells.

**Anti-diabetic**
Licorice has also been traditionally used as an artificial sweetening agent and could be helpful in insulin resistance syndrome prevalent in the modern society \(^{54}\).

**CONCLUSION**
*Glycyrrhiza glabra*, also known as sweet wood, belonging to family Fabaceae/Leguminaceae is native to the Mediterranean and certain areas of Asia. Glycyrrhizin a pentacyclic triterpenoid \(\beta\text{-amyrin}\) compound, accounts for the sweet taste of liquorice root. This compound represents a mixture of potassium-calcium-magnesium salts of glycyrrhizinic acid that varies within a 2-25% range. Traditional applications across diverse cultures include as both a demulcent and an anti-inflammatory, often used to soothe respiratory or gastrointestinal (GI) symptoms. The parts of G. glabra used traditionally is a prophylaxis (for gastric and duodenal ulcers and in dyspepsia) in Indian system of medicine. It also recommended as a laxative, anti-ralumpementic and anti-viral agents. It also exhibited anti-inflammatory activity & can be used in Addison’s disease, arthritis etc. Both the traditional & pharmacological effects of G. glabra may be
due to pharmaceutical constituents (glycyrrhyzin etc.). Future sophisticated techniques may help to explore scientific proof which can help to prove its efficacy in commercial formulations.

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**REFERENCES**

7. https://www.google.co.in/search?q=glycyrrhiza+glabra+PLANT&biw=1366&bih=667&source=lnms&tbm=isch&sa=X&ved=0ahUKEwjwvNLikP7kAhXUxY4KHeBuCnEQ_AUIBigB#imgrc=g3NVf8waspupjM%3A
16. Rossum V, Vulto TG, Hop AG, Brouwer WC, Niesters JT, Schalm
48. Okimasu E, Moromizato Y, Watanabe S, Sasaki J, Shiraishi N, Morimoto YM, Miyahara M, Utsumi K. Inhibition of phospholipase A2 and platelet aggregation


