



## Licorice (*Glycyrrhiza glabra* Linn) As a Valuable Medicinal Plant

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### ABSTRACT

*Glycyrrhiza glabra*, family Leguminosae, is a plant which grows in Egypt and other countries of the world. Its roots possess some nutritive value and medicinal properties. *Glycyrrhiza glabra* Linn, a commonly used herb in ayurvedic medicine. Studies indicate that *Glycyrrhiza glabra* Linn possesses antibacterial, antioxidant, antimalarial, antispasmodic, anti-inflammatory and anti hyper glycemic properties. Various other effects like antiulcer, antiviral, antihapatotoxic, antifungal and herpes simplex have also been studies. One of the most commonly reported side effects with licorice supplementation is elevated blood pressure.

**Key word:** *Glycyrrhiza glabra*, Anti-bacterial, Antioxidant Activity

### INTRODUCTION

*Glycyrrhiza glabra*, family Leguminosae, is a plant which grows in Egypt and other countries of the world. Its roots possess some nutritive value and medicinal properties. They are widely used as a cold beverage, in preparing some pharmaceutical preparations such as haematonic pills and to disguise the bitter taste of other remedies (Fenwick et al., 1990). *Glycyrrhiza glabra* Linn is one of the most widely used herb from the ancient medical history of Ayurveda, both as a medicine and also as a flavoring herb. It is a very sweet, moist, soothing herb that detoxifies and protects the liver and is also a powerful anti-inflammatory, being used in conditions as varied as arthritis and mouth ulcers. Phytochemical analysis of *Glycyrrhiza glabra* root extract showed that it contains saponin triterpenes (glycyrrhizin, glycyrrhetic acid and liquiritic acid), flavonoids (liquirtin, isoflavonoids and formononetin) and other constituents such as coumarins, sugars, amino acids, tannins, starch, choline, phytosterols and bitter principles (Fukai et al., 1998; Arystanova et al., 2001). *Glycyrrhiza glabra*, also known as licorice and sweetwood, is native to the Mediterranean and certain areas of Asia. Historically, the dried rhizome and root of this plant were employed medicinally by the Egyptian, Chinese, Greek, Indian, and Roman civilizations as an expectorant and carminative. In modern medicine, licorice extracts are often used as a flavoring agent to mask bitter taste in preparations, and as an

expectorant in cough and cold preparations. Licorice extracts have been used for more than 60 years in Japan to treat chronic hepatitis, and also have therapeutic benefit against other viruses, including human immunodeficiency virus (HIV), cytomegalovirus (CMV), and Herpes simplex. Deglycyrrhizinated licorice (DGL) preparations are useful in treating various types of ulcers, while topical licorice preparations have been used to soothe and heal skin eruptions, such as psoriasis and herpetic lesions.

### Pharmacognosy

*Glycyrrhiza glabra* Linn is a hardy perennial shrub, attaining a height up to 2.5 m. The leaves are compound, imparipinnate, alternate, having 4-7 pairs of oblong, elliptical or lanceolate leaflets. The flowers are narrow, typically papilionaceous, borne in axillary spikes, lavender to violet in colour. The calyx is short, campanulate, with lanceolate tips and bearing glandular hairs. The fruit is a compressed legume or pod, up to 1.5 cm long, erect, glabrous, somewhat reticulately pitted, and usually contains 3-5 brown, reniform seeds. The taproot is approximately 1.5 cm long and subdivides into 3-5 subsidiary roots, about 1.25 cm long, from which the horizontal woody stolons arise. These may reach 8 m and when dried and cut, together with the root, constitute commercial liquorice. It may be found peeled or unpeeled. The pieces of root break with a fibrous fracture, revealing the yellowish interior with a characteristic odour and sweet taste.

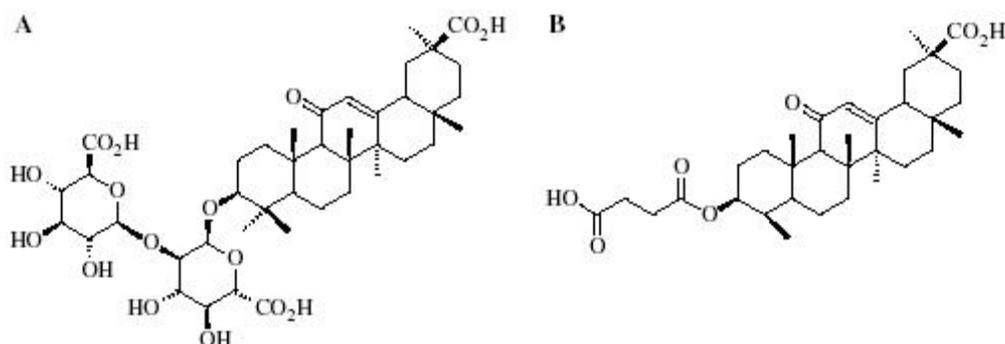


**FIGURE 1:** *Glycyrrhiza glabra* Linn

### Reported Phytochemicals

The roots of *Glycyrrhiza glabra* Linn contain glycyrrhizin, which is a saponin that is 60 times sweeter than cane sugar; Flavonoid rich fractions include liquiritin, isoliquirtin liquiritigenin and rhamnoliquiritin and five new flavonoids- glucoliquiritin apioside, prenyllicoflavone A, shinflavanone, shinpterocarpin and 1-methoxyphaseolin (Rastogi RP and Mehrotra BN) isolated from dried roots. Isolation and structure determination of licopyranocoumarin, licoaryl coumarin, glisoflavone and new coumarin-GU-12 also isolated. Four new isoprenoid-substituted phenolic constituents–

semilicoisoflavone B, 1-methoxyficifolinol, isoangustone A, and licoriphenone isolated from roots. (Rastogi RP and Mehrotra BN) A new prenylated isoflavan derivative, kanzonol R was also isolated. The presence of many volatile components such as pentanol, hexanol, linalool oxide A and B, tetramethyl pyrazine, terpinen-4-ol,  $\alpha$ -terpineol, geraniol and others in the roots is reported. Presence of propionic acid, benzoic acid, ethyl linoleate, methyl ethyl ketone, 2,3-butanediol, furfuraldehyde, furfuryl formate, 1-methyl-2-formylpyrrole, trimethylpyrazine, maltol and any other compounds is also isolated from the essential oil. The Indian roots show various 2-methylisoflavones, and an unusual coumarin, C liquocoumarin, 6-acetyl-5-hydroxy-4-methyl coumarin. Asparagine is also found. Glycyrrhizin (glycyrrhizic acid; glycyrrhizinate) constitutes 10–25% of licorice root extract and is considered the primary active ingredient. Glycyrrhizin (Figure 2) is a saponin compound comprised of a triterpenoid aglycone, glycyrrhetic acid (glycyrrhetic acid; enoxolone) conjugated to a disaccharide of glucuronic acid. Both glycyrrhizin and glycyrrhetic acid can exist in the 18 $\alpha$  and 18 $\beta$  stereoisomers.



**Figure 2: Chemical structure of Glycyrrhizin (A) and Carbenoxolone (B).**

### Mechanisms of Action

The beneficial effects of licorice can be attributed to a number of mechanisms. Glycyrrhizin and glycyrrhizic acid have been shown to inhibit growth and cytopathology of numerous RNA and DNA viruses, including hepatitis A and C, (Van Rossu et al, 1999) herpes zoster, HIV, (Hattori et al, 1989) *Herpes simplex* and CMV. Glycyrrhizin and its metabolites inhibit hepatic metabolism of aldosterone and suppress 5 $\beta$ -reductase, properties 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 mineralocorticoid and glucocorticoid activity of glycyrrhizic acid. Licorice constituents also exhibit steroidlike anti-inflammatory activity, similar to the action of hydrocortisone. This is due, in part, to inhibition of phospholipase A2 activity, an enzyme critical to numerous inflammatory processes. *In vitro* research has also demonstrated glycyrrhizic acid inhibits cyclooxygenase activity and prostaglandin formation (specifically prostaglandin E2), as well as indirectly inhibiting platelet aggregation, all factors in the inflammatory process (Okimasu et al, 1983).

### Chronic Hepatitis

In Japan, glycyrrhizin has been used for more than 60 years as a treatment for chronic hepatitis C. Stronger Neo-Minophagen C (SNMC), a glycyrrhizin preparation, has been extensively used with considerable success. In two clinical trials, SNMC has been shown to significantly lower aspartate

transaminase (AST), alanine transaminase (ALT), and gamma- glutamyltransferase (GGT) concentrations, while simultaneously ameliorating histologic evidence of necrosis and inflammatory lesions in the liver. In recent years, several studies have been performed supporting this action (Van Rossum et al, 1999). Presently, interferon (IFN) therapy is a predominant treatment for chronic hepatitis. Because its efficacy is limited, an alternative treatment is desirable. SNMC has profound effects on the suppression of liver inflammation and is effective in improving chronic hepatitis and liver cirrhosis. It also appears to have considerably fewer side effects than IFN (Iino et al , 2001).

### Side Effects and Toxicity

One of the most commonly reported side effects with licorice supplementation is elevated blood pressure. This is thought to be due to the effect of licorice on the renin-angiotensin-aldosterone system. It is suggested licorice saponins are capable of potentiating aldosterone action while binding to mineralocorticoid receptors in the kidneys. The phenomenon is known as “pseudoaldosteronism.” In addition to hypertension, patients may experience hypokalemia (potassium loss) and sodium retention, resulting in edema. All symptoms usually disappear with discontinuation of therapy. Many studies report no side effects during the course of treatment. (Iino et al , 2001) Generally, the onset and severity of symptoms depend on the dose and duration of licorice intake, as well as individual susceptibility. Patients with delayed gastrointestinal transit time may be more susceptible to these side effects, due to enterohepatic cycling and reabsorption of licorice metabolites. The amount of licorice ingested daily by patients with mineralocorticoid excess syndromes appears to vary over a wide range, from as little as 1.5 g daily to as much as 250 g daily (Stormer et al, 1993).

### Anti-bacterial Activity

Shirazi M.H. et al. had studied the *in vitro* inhibitory effects of *G. glabra* extract against the growth of *Salmonella typhi*, *S. paratyphi B*, *Shigella sonnei*, *S. flexneri* and enterotoxigenic *E. coli* (ETEC *E. coli*) was investigated using well and disc diffusion method. *Salmonella paratyphi B* showed no susceptibility to liquorice with concentrations lower than 7.5%, however all tested bacterial strains exhibited susceptibility to high concentration of liquorice (Shirazi et al, 2007). The antibacterial activities of the alcohol, ethyl acetate, acetone and chloroform extracts of 5 plant species were studied by Ates D. A. et al. The extracts of *Glycyrrhiza glabra Linn* (liquorice) (root), was tested *in vitro* against 13 bacterial species and strains by the agar diffusion method. The extracts of *Glycyrrhiza glabra Linn* roots showed various antibacterial activities (7-11 mm/20 µl inhibition zone) against the microorganisms tested. The alcohol extracts did not inhibit *B. subtilis* var. *niger*, *B. brevis*, *E. faecalis*, *L. monocytogenes*, *P. aeruginosa* and *Y. enterocolitica*. The ethyl acetate extracts did not inhibit *B. subtilis* or *Y. enterocolitica*, and the acetone extracts did not inhibit *E. faecalis*, *L. monocytogenes*, *P. aeruginosa* or *Y. enterocolitica*. The chloroform extracts showed no inhibition effect against *P. aeruginosa* or *Y. enterocolitica* (Ates and Erdoúrul, 2003). Alonso J. had studied the glycyrrhizin is habitually used as a vehicle in orally administered products, where it inhibits the growth of some bacteria, as well as dental plaque formation. In regards to its antibacterial action, *in vitro* studies have demonstrated inhibitory effects for licorice aqueous and ethanolic extracts on *Staphylococcus aureus* and *Streptococcus pyogenes* cultures, the first one showing the strongest inhibition with 10-15mm halo diameters (Alonso and Tratado, 2004). It exhibited antimicrobial activity against both Gram-positive and Gram-negative bacteria by Gupta V K. et al. [15]

### Antioxidant Activity

Ashawat M.S. et al. had studied the relative reducing activity in terms of antioxidant activity of extracts was determined by using individual extract (15mg) as well as its combination with equal amount of ascorbic acid. The extracts and ascorbic acid were dissolved separately in 1.0 ml of deionised water with

phosphate buffer. The mixture was incubated at 50 °C for 20 min. aliquot of trichloroacetate acid were added to the mixture and centrifused at 3000 rpm for 10 min. the upper layer of solution was mixed with distilled water and a freshly prepared FeCl<sub>3</sub> solution. The absorbance was measured at 700nm by making 500µg mL extract aliquot. Increased absorbance of the reaction mixture indicated increased antioxidant activity via reducing power with reference to equal amount of standard ascorbic acid (Ashawat et al, 2009). Visavadiya N. P. et al. showed antioxidant property of *Glycyrrhiza glabra* Linn root extracts using *in vitro* models. The dosedependent aqueous and ethanolic extracts demonstrated the scavenging activity against nitric oxide (concentration that caused 50% inhibition of nitric oxide radicals [IC<sub>50</sub>]=72 and 62.1 µg/ml, respectively), superoxide (IC<sub>50</sub>=64.2 and 38.4 µg/ml, respectively), hydroxyl (IC<sub>50</sub>=81.9 and 63 µg/ml, respectively) radicals. Further, both extracts showed strong reducing power and iron-chelating capacities. In the Fe<sup>2+</sup>/ascorbate system, both extracts were found to inhibit mitochondrial fraction lipid peroxidation. In copper-catalyzed human serum and low-density lipoprotein oxidation models, both extracts significantly ( $P<0.05$ ) lengthened the lag phase along with a decline in the oxidation rate, conjugated dienes, lipid hydroperoxides and thiobarbituric acid reactive substance formation. So, ethanolic extract of *G. glabra* possess considerable antioxidant activity and protective effect against the human lipoprotein oxidative system (Visavadiya et al,2009).

### Anti malarial Activity

The Chinese pharmacopoeia accepts three species of *Glycyrrhiza*, *G. glabra*, *G. uralensis* and *G. inflata*, as sources of Gan Cao. The chalcone licochalcone A can be isolated from all *Glycyrrhiza* species in different amounts and has been shown to exhibit good antimalarial activity. In *in vivo* tests against *P. yoelii* in mice, oral doses of 1000 mg kg<sup>-1</sup> resulted in the complete eradication of the malaria parasite and no toxicity was noted (Sianne and Fanie ,2002) . The burden of this disease is getting worse, mainly due to the increasing resistance of *Plasmodium falciparum* against the widely available antimalarial drugs. There is an urgent need for new, more affordable and accessible antimalarial agents possessing original modes of action. Natural products have played a dominant role in the discovery of leads for the development of drugs to treat human diseases. This present review covers most of the recently-published nonalkaloidal natural compounds from plants with antiplasmodial and antimalarial properties, belonging to the classes of terpenes, limonoids, flavonoids, chromones, xanthenes, anthraquinones, miscellaneous and related compounds. (Batista et al,2009). Licochalcone A inhibited *in vitro* growth of both chloroquine-susceptible (3D7) and chloroquine-resistant (Ddz) strains of *Plasmodium falciparum* to same extent in [3H] hypoxanthine uptake assay (Rastogi and Mehrotra, 1990) .

### Anti hyper glyceic Activity

Kalaiarasi P. et al. had studies the antihyperglycemic effect of 18β-glycyrrhetic acid, aglycone of glycyrrhizin, on streptozotocin-diabetic rats. Diabetes was induced in adult male albino rats of the Wistar strain, weighing 180–200 g, by administration of streptozotocin (40 mg/kg of body weight) intraperitoneally. Diabetic rats showed increase of plasma glucose and glycosylated haemoglobin (HbA1c) and a decrease of plasma insulin and haemoglobin (Hb). Activities of gluconeogenic enzymes such as glucose 6-phosphatase, fructose 1, 6-bisphosphatase increased and glucokinase, glucose 6-phosphate dehydrogenase decreased in the liver along with glycogen. Oral administration of 18β-glycyrrhetic acid (50, 100, or 200 mg/kg/body weight) or glibenclamide (600 µg/kg/body weight) in 5% dimethyl sulfoxide, for 45 days, prevented the above changes and improved towards normalcy. (Kalaiarasi and Pugalendi, 2009) .

### Anti fungal activity

Hojo A and Sato J. were screening for antifungal compounds from various plant material, licorice (*Glycyrrhiza glabra Linn*) extracts with 80% methanol (oil-based extract of licorice; OEL) was found to have high fungicidal effect against *Arthrimum sacchari* M001 and *Chaetomium funicola* M002, and its active compound was identified as glabridin (3-(2',4'- dihydroxyphenyl)-8-dimethylpyrano [8,7-e]chroman). OEL was effective against not only filamentous fungi but also some bacteria, especially thermo-resistant bacilli such as genera of *Bacillus* and *Alicyclobacillus* (Hojo and et al,2002). Glabridin to be active against both yeast and filamentous fungi and also showed resistance modifying activity against drug resistant mutants of *Candida albicans* at a minimum inhibitory concentration of 31.25-250 microg/mL by Fatima A. et al. (Fatima et al, 2009). In regards to its antifungal action, *in vivo* inhibition of *Mycobacterium smegmatis* and *Candida albicans* has been reported, which was attributed to the action of isoflavonoids such as glabridin, glabrol and derivatives of these. A recent study demonstrated the inhibitory effects of a licorice root aqueous extract (CIM=1.56 mg/ml) on cultures of *Candida albicans*, which had been obtained from mouth lesions of 5-months old infants. These results support the use of licoricebased mouthwash to treat candida-induced lesions in HIV patients (Alonso and Tratado, 2004). Therefore, licorice-eco extract is of great use to formulate cosmetic products with purifying and antiseptic activities.

### Enzyme Inhibitory Activity

Zuidhoff H. W. et al. had studies licorice methanolic extract has shown *in vitro* inhibition of the tyrosinase enzyme, with 21.2 µg/ml inducing 50% inhibition. Active principles able to inhibit tyrosinase act by modifying the action site of the enzyme, thus reducing its activity. Licorice root extract is known to inhibit tyrosinase. Most of tyrosinase inhibitors are reducing agents, which produce their effects through their reducing capacity. Thus, licorice-eco extract is of great use to formulate cosmetic products with depigmenting activity. (Zuidhoff and et al, 2001) Isoliquiritigenin inhibited rat lens aldose-reductase using DL-glyceraldehyde as substrate. Licochalcones A and B, licopyranocoumarin ,licoarylcoumarin, licocoumarone, glycyrrhisoflavone and glisoflavone inhibited xanthine oxidase (Rastogi and Mehrotra, 1990) .

### CONCLUSION

Licorice (*Glycyrrhiza glabra Linn*) root and its extract such as glycyrrhizin have a long history of use in traditional medicines, folk remedies, and as a sweetening and flavoring agent. Pharmacological studies have evaluated several of the traditional health claims behind licorice use although many of these reports have produced inconsistent results. Carbenoxolone, an analog of glycyrrhetic acid, has shown success in clinical trials for gastric and duodenal ulcers, but the potential development of pseudoaldosteronism has limited its use. Deglycyrrhizinated licorice has also shown some effect in the treatment of gastrointestinal ulcers, suggesting the presence of active ingredients other than glycyrrhizin, although other studies have shown it has no beneficial effects.

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