

**A COMPREHENSIVE REVIEW ON LIQUORICE
[GLYCYRRHIZAGLABRA LINN] PLANT**

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ABSTRACT

The plant known as liquorice, or *Glycyrrhiza glabra* Linn., has long been utilized in traditional medicine. Because of their cooling, demulcent, expectorant, emollient, laxative, stimulant, anti-inflammatory, antiallergic, and antibacterial qualities, the plant's dried roots are mostly utilized in medicine. Its pharmacological and phytochemical activities, which were investigated using a variety of techniques, are summarized in this review article. Hepato-protective, anti-ulcer, anti-inflammatory, anti-microbial, antioxidant, antitussive and demulcent, immunostimulatory, antidiabetic, neuroprotective, and antimalarial properties are all demonstrated by studies on *Glycyrrhiza glabra* Linn. These findings are highly promising and suggest that further research on this herb is necessary to validate these findings and uncover further possible medicinal benefits. *Glycyrrhiza glabra* Linn. should be used in clinical

trials for a range of ailments. With minimal adverse effects, licorice may be a natural substitute for existing treatments in the treatment of newly emerging illnesses.

KEYWORDS: *Glycyrrhiza glabra* root, Skin infection, Pharmacological activities.

INTRODUCTION

Glycyrrhiza glabra Linn. [GG] belongs to Fabaceae family and has been used since ancient times as a medicinal herb. It has been referred in Indian traditional medicine some 3,000 years ago. The active components of this plant have extensive therapeutic usage throughout the world and are subjected to enormous works in recent years. Licorice (*Glycyrrhiza glabra*) is also known as "sweet root". The word "Glycyrrhiza" is made from two Greek words:

Glykys, meaning "sweet" and Rhiza, meaning "root" (M. Senthil Raja, et al., 2010) Licorice is one of the most widely used medicinal herbs and is found in numerous traditional formulas. The main active constituent Glycyrrhizic acid is approximately 50 times sweeter than sugar. (Anonymous, Indian Herbal Pharmacopoeia, 2002).^[1] Herbs are very important resource for all major system of medicine, nutraceuticals and cosmetics. In the last few decades, a curious thing has happened to botanical medicine. Instead of being killed off by medical science and pharmaceutical chemistry, it has made a comeback. Botanical medicine has benefited from the objective analysis of medical science, while fanciful and emotional claims for herbal cures have been thrown out, herbal treatments and plant medicines that work have been acknowledged. And herbal medicine has been found to have some impressive credentials. No laboratory has yet produced a substitute for digitalis. The penicillin that replaced mercury in the treatment of syphilis and put an end to so many of the deadly epidemics comes from plant moulds; it was discovered accidentally as it destroyed a bacterial culture that Alexander Fleming was trying to grow in his laboratory. Belladonna still provides the chemicals used in ophthalmological preparations and in antispasmodics used to treat gastrointestinal disorders. In fact, plant substances remain the basis for a very large proportion of the medications used today for treating heart diseases, hypertension, depression, pain, cancer, aids, asthma, neurological disorder, and other ailments. Plants may offer a medical revolution for 5 billion inhabitants of the world who relies primarily on traditional medicine for their health care needs. Very recently herbal medicine has made a breakthrough in the history of medical science. During the last three decades its importance usage has increased dramatically all over the world.^[1,2]

Table no 1: Scientific Classification of Glycyrrhiza Glabra.^[4]

Kingdom	<i>Plantae</i>
Division	<i>Angiospermae</i>
Class	<i>Dicotyledoneae</i>
Subclass:	<i>Magnoliidae</i>
Order	<i>Rosales</i>
Superorder:	<i>Rosanae</i>
Family	<i>Leguminosae</i>
Genus	<i>Glycyrrhiza</i>
Species	<i>glabra Linn</i>

MORPHOLOGY

Fig: Glycyrrhiza Glabra plant.^[5]

Herb: *Glycyrrhiza glabra* Linn is a hardy perennial shrub, attaining a height up to 2.5 m. The leaves are compound, imparipinnate, alternate and 7 to 15 cm long, having 4-7 pairs of oblong, elliptical or lanceolate leaflets.^[9,10]



Fig: Glycyrrhiza Glabra Flower.^[6]

Flower: The flowers are narrow typically papilionaceous, borne in axillary spikes, pale whitish blue to purple or lavender in colour.^[11]



Fig: Glycyrrhiza Glabra Fruit.^[7]

Fruit: The fruit is a compressed legume or pod, up to 1.5 cm long, erect, glabrous usually containing 3-5 brown, reniform seeds.^[9,10]



Fig: Glycyrrhiza Glabra Root.^[8]

Root: The taproot is stoloniferous and approximately 1.5 cm long and subdivides into 3-5 subsidiary roots, about 1.25 cm long, from which the 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.^[9,10,11]

PHARMACOLOGICAL ACTIVITIES

Anti-tussive & expectorant activity: The liquorice powder and extract was found to be effective in treatment of sore throat, cough and bronchial catarrh. The specific mechanism of action is not known. Liquorice has been shown to work as efficiently as codeine in sore throat. It decreases irritation and produces expectorant effects. Carbenoxolone (a semi synthetic compound derived from Glycyrrhiza) stimulates gastric mucus secretion. Likewise, liquorice extract may also be able to stimulate tracheal mucus secretions producing demulcent and expectorant effects.^[12,13] Glycyrrhizin is responsible for demulcent action of liquorice. Liquiritin apioside, an active compound present in the methanolic extract of liquorice which inhibits capsaicin induced cough.^[14] Ethanolic extract of *G. glabra* was found to be responsible for inhibition of 35.62% SO₂ gas induced cough in experimental animals (mice).^[15]

Skin lightening and skin tightening activity: The extract of liquorice is reported to be an effective pigment lightening agent. It is the safest pigment-lightening agent known with least side effects. Glabridin in the hydrophobic fraction of liquorice extract inhibits tyrosinase activity in cultured B16 murine melanoma cells. It does not affect DNA synthesis. Some other active compounds in liquorice extract like glabrene, Licochalcone A, Isoliquiritin are also responsible for inhibition of tyrosinase activity. Liquiritin present in liquorice extract disperse melanin, thereby inducing skin lightening.^[16] Also the antioxidants present in extract may contribute to decrease in skin melanin content.^[17] In vitro tyrosinase enzyme inhibition studies has showed that 21.2 µg/ml of methanolic extract of liquorice caused 50% tyrosinase enzyme inhibition. The inhibition of tyrosinase enzyme and reduction in enzyme activity is caused due to modification of action site of the enzyme. Due to good tyrosinase inhibition activity, liquorice extract can be used to formulate cosmetic formulations with depigmenting activity.^[18] Ethanolic extract of *Glycyrrhiza glabra* is reported to show improvement in the viscoelastic and hydration properties of the skin. Synergistic effect of UV protective, antioxidant and anti-inflammatory properties of liquorice extract might be responsible for giving beneficial effects on skin.^[19]

Antioxidant activity: High content of phenolic component in ethanolic extract of Liquorice (*Glycyrrhiza glabra* L) is responsible for its powerful antioxidant activity by means of

significant free radical scavenging, hydrogen-donating, metal ion chelating, anti-lipid peroxidative and reducing abilities.^[20] Liquorice flavonoids have exceptionally strong antioxidant activity. Antioxidant activity of liquorice flavonoids was found to be over 100 times stronger than that of antioxidant activity of vitamin E. A dose of 2.58 mg/ml liquorice flavonoids can scavenge more free radicals (20.6% scavenging) than 258 mg/ml of vitamin E (11.2% scavenging). Ju, H.S. reported that flavonoids from liquorice are currently the strongest natural antioxidants known.^[21] Thus, liquorice extract can be efficiently used to formulate cosmetic products for the protection of skin and hair against oxidative damage.^[22]

Anti-bacterial Activity: Because of the presence of secondary metabolites such as; saponins, alkaloids, flavonoids in hydro-methanolic root extract of *Glycyrrhiza glabra*, the extract exhibits potent antibacterial activity.^[23] In vitro studies have proved that aqueous and ethanolic extracts of liquorice show inhibitory activity on cultures of *Staphylococcus aureus* and *Streptococcus pyogenes*.^[22]

Anti-malarial activity: Licochalcone A (a chalcone) present in liquorice has reported to possess very good antimalarial activity. All *Glycyrrhiza* species have this compound in different amounts and it can be isolated from them. In vivo studies against *P. yoelii* in mice with oral doses of 1000 mg kg⁻¹ have shown to eradicate malarial parasite completely. Also no toxicity was observed.^[24]

Anti hyperglycemic activity: The effect of liquorice extract on serum lipid profile and liver enzymes was studied in albino mice. Root extract of *Glycyrrhiza glabra* was found to have antilipidemic and antihyperglycemic activity at low doses.^[25]

Memory enhancing activity: The effects of *Glycyrrhiza glabra* on learning and memory was investigated in mice. Elevated plus-maze and passive avoidance paradigm were used to test learning and memory. Three doses of aqueous extract of liquorice were administered [75, 150 and 300 mg/kg p.o.]. The study was conducted for 7 successive days in separate groups of animals. Significant improvement in learning and memory of mice was reported at the dose of 150 mg/kg. But, the exact mechanism of action is unknown and needs further investigation.^[26]

Hepatoprotective activity: Glycyrrhizin significantly inhibits the CCl₄- induced release of AST and LDH at concentrations of 25–200 µg/ml. Alteration of membrane fluidity by the

glycyrrhizin or inhibition of CCl₄-induced membrane lipid peroxidation might be responsible for the activity. 18 β -glycyrrhetic acid (an aglycone of glycyrrhizic acid) shows hepatoprotective activity by inhibiting both free radical generation and lipid peroxidation.^[27] Glycyrrhizin is useful in treating acetaminophen-induced hepatotoxicity.^[28] Liquorice extract is proved to show hepatoprotective activity against diclofenac –induced hepatotoxicity in rats.^[29]

Anticoagulant: Glycyrrhizin is the first plant based inhibitor of thrombin. It is found to prolong the thrombin and fibrinogen clotting time. It also increases plasma recalcification duration. Glycyrrhizin causes inhibition in thrombin induced platelet aggregation. But there was no effect of glycyrrhizin on Platelet Aggregating Factor (PAF) and Collagen induced agglutination.^[30, 31]

NUTRITIONAL VALUE

Table no 2: Nutritional Value Of *Glycyrrhiza Glabra* L.^[32]

Chemical composition(g/100g)	
Protein	7.19 \pm 1.55
Crude fat	2.21 \pm 0.61
Sugars*	40.47
Crude fiber	38.41 \pm 0.54
Moisture	4.11 \pm 0.19
Ash	7.61 \pm 0.14
Food energy value (Kcal/100g)	210.53
Minerals contents (g/100g)	
Calcium, Ca	112.2
Iron, Fe	1.70
Zinc, Zn	0.5
Copper, Cu	0.14

Data represented are the mean \pm standard deviation, n=3. * Sugars estimated in this fashion includes fiber.

HEALTH BENEFITS OF LIQUORICE

- 1. May ease digestive issues:-**Liquorice root is promoted as a health aid for digestive issues including heartburn and peptic ulcers.
- 2. May help manage menopausal symptoms:-**Often taken as a natural alternative to hormone replacement therapy, liquorice may help manage menopausal symptoms, through a mild oestrogenic effect.

3. May help ease symptoms of coughs and sore throats:- Liquorice appears to ease coughs, sore throats and other symptoms of viral infections. The active component of liquorice, called glycyrrhizin, has also shown promise in test tube studies against the SARS-CoV-2 virus.

4. May help manage bone loss:-Glycyrrhizin may help manage bone loss and tissue ageing in the elderly, according to research with animals. The mechanisms behind this include reducing inflammation, reducing bone breakdown and increasing protective compounds, called sirtuins.

5. May support adrenal function:-One mechanism responsible for some of the health implications of liquorice is its ability to inhibit an enzyme that inactivates the stress hormone, cortisol. This may be helpful for those with adrenal fatigue, because it helps the body regulate cortisol and supports normal adrenal function. However, in a similar fashion, this same action may lead to heightened cortisol levels, disruption to electrolyte balance and the reabsorption of salt and fluids, which may elevate blood pressure, promote oedema (excess tissue fluids) and more. For this reason, liquorice should be taken with caution if you are predisposed to high blood pressure, fluid retention or stress-related conditions.

6. May help manage atopic dermatitis:-The natural compounds in liquorice (glycyrrhizic acid and glycyrrhetic acid) are responsible for the root's protective, antimicrobial and anti-inflammatory properties and are the reason it is used in a range of products, including topical skin products, that are used to manage conditions like atopic dermatitis.

7. May protect against dental cavities:-Liquorice root may protect against high levels of the bacteria that promote dental cavities. A short three-week study examining the effects of liquorice (in the form of a twice-daily sugar-free lollipop) on pre-school children suggested a reduction in *Streptococcus mutans*, a bacteria known to be a cause of cavities. More research is needed to evaluate the optimal dose and form of liquorice that may provide this protection.

8. May ease upper respiratory conditions:-Liquorice root extract as well as tea made from the root may ease respiratory conditions. Animal studies also suggest glycyrrhizin may help relieve asthma, especially when combined with modern asthma treatments. However, human studies are limited and more research is needed to assess these benefits.^[33]

SIDE EFFECTS

When taken by mouth: Licorice is likely safe for most people when eaten in typical food amounts. Licorice that has had the chemical glycyrrhizin removed is possibly safe when taken in doses up to 4.5 grams daily for up to 4 months.

Licorice that contains glycyrrhizin is possibly unsafe when consumed in large amounts or for a long time. Eating licorice 5 grams or more daily for several weeks can cause severe side effects including heart attack. People who have heart disease, kidney disease, or high blood pressure are more sensitive to it. Ingesting large amounts of licorice from candy, lozenges, or tea might also cause serious side effects.^[34]

When applied to the skin: Applying gel with licorice root extract 2% is possibly safe for up to 2 weeks. It is possibly safe to use a licorice mouth rinse for up to one week.^[34]

EXTRACTION METHODS

Extraction is the separation of the medicinally active component from its parent source using selective solvents through suitable standard procedures. A lot of extraction methods have been employed to extract glycyrrhizin from licorice which includes analytical, solvent based dipping/percolation/maceration, microwave-assisted, Soxhlet, etc. A new technique involving ultra-sound was employed and the product yield was compared with other existing procedures.^[35]

1. Analytical method

Analytical method mainly comprises of extraction of the principle component glycyrrhizin from the licorice roots using the combination of all the three individual analytical extraction methods, namely, acid precipitation, alcohol and ammonia extraction.^[35,36] This method starts with heating of the shredded roots of licorice for 4 to 6 hours in ten times its volume of distilled water at 60°C at a neutral pH. The suspension is centrifuged, and the supernatant is evaporated in vacuum to about 75% of its volume. Crude glycyrrhizic acid is then precipitated by addition of 10% concentrated sulphuric acid (H₂SO₄) at constant stirring. This crude powder is taken up in fresh distilled water and stirred for 4 to 6 hours to bring the pH at 4 by using NH₄OH/ sodium carbonate/potassium carbonate. Stirring is continued followed by centrifugation till a clear supernatant is obtained. Similar washing steps are continued with fresh distilled water to neutralize the pH of the precipitate. Finally, the crude is completely dried and extracted in absolute ethanol which is further evaporated on water bath and dried in

vacuum oven to obtain active glycyrrhizic acid. The recovery of active glycyrrhizic acid by analytical method is 7-8% only.^[36]

2. Microwave-assisted extraction

In this method, microwave energy is used to facilitate the breaking of analytes from the sample matrix into the extraction solvent. Microwave radiation interacts with the dipoles of the polar and polarizable materials in the solvent and the sample causing heating. This heat is transferred through conduction promoting solvent penetration into the sample thereby enhancing migration of the active constituents into the extraction solvent.^[37]

3. Ultrasound assisted extraction or Sonication method

This method involves use of ultrasound using a sonicator probe ranging from 20 kHz to 2000 kHz.^[38] The vibrational and acoustic effect from the ultrasound increases the surface contact between the solvent and samples thereby increasing the permeability of the plant cell walls. Thus, the physical and chemical properties of the plant cell wall is disrupted and altered which results in the mass transportation of the solvent into the plant cell. It facilitates release of the active constituent in the desired solvent of extraction.^[39]

CONCLUSION

One of the best herbal remedies for lowering toxicity and boosting the effectiveness of other herbal remedies when used in combination is licorice. Although licorice's biochemical properties and natural makeup have been thoroughly investigated, further work is still required to confirm its effectiveness in treating a range of illnesses. To understand the mechanism of action, research on the many licorice constituents and their biological targets is necessary. To determine the synergy between the toxicity and efficacy of additional ingredients in combination preparations, more research is required. The benefits of eating licorice typically don't outweigh the possible drawbacks. Licorice extract is still used by many individuals in underdeveloped nations to treat a variety of illnesses. Researchers have used licorice to create a variety of medications. The biological significance of this herb's active ingredients has been thoroughly tested and investigated, and in vitro, in vivo, and human clinical trials give us important evidence to move on to the next stage of our investigation. In order to treat various illnesses, licorice must be taken according to a precise dosage schedule. In this way, licorice may be used more frequently in pharmaceutical businesses, but only under strict control. The integration of licorice's isolated phytochemical ingredients, their biological significance in combating a range of physiological illnesses, and

their secondary metabolites to create promising pharmaceutical formulations was the conclusion of this review. Licorice can therefore be beneficial for a variety of ailments. The present review concludes that licorice extracts and licorice flavonoids have been used for hepatoprotective, antibacterial, anticancer, respiratory tract infection, and cardiovascular disease purposes. To extend their method of action to various biological processes, however, further research is required.

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