

Available online on 15.05.2017 at <http://ujpr.org>**Universal Journal of Pharmaceutical Research**

An International Peer Reviewed Journal

Open access to Pharmaceutical research

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Volume 2, Issue 2, 2017

REVIEW ARTICLE

A REVIEW ON CONSTITUENTS, PHARMACOLOGICAL ACTIVITIES AND MEDICINAL USES OF *GLYCYRRHIZA GLABRA*

Savita Pandey, Bipin Verma, Priti Arya

Department of Pharmacy, Government Polytechnic, Kashipur, Uttarakhand, India

*Corresponding Author's Email: savitapharma@gmail.comDOI: <http://doi.org/10.22270/ujpr.v2i2.RW2>

Received 3 April 2017; Revised 9 May; Accepted 12 May, Available online 15 May 2017

ABSTRACT

Plants have been one of the important sources of medicines for human being and animals since the ancient time. At present scenario there is an increasing demand for herbal medicines, health products and pharmaceuticals products. Herbal medicines have attained popularity at global level to replace the synthetic chemicals as they have shown less adverse reactions.

Glycyrrhiza glabra Linn is a commonly used herb for different diseases. Present review article deals with chemical constituents present in various parts of *Glycyrrhiza glabra* and pharmacological activities. Present article aim to comply all the updated information on its phytochemical and pharmacological activities, which were performed by widely different methods. *Glycyrrhiza glabra* Linn possesses antibacterial, antioxidant, antimalarial, antispasmodic, anti-inflammatory and anti-hyper glycaemic properties. Various other effects like antiulcer, antiviral, antifungal have also been discussed. This article may be useful for many researchers in discovering potential therapeutic effects and developing new formulations.

Keywords: Antibacterial, anti malarial, antioxidant, *Glycyrrhiza glabra*, glycyrrhizin.

INTRODUCTION

Human beings have used plants for medicinal purposes for centuries. It has been estimated that such use of medicinal plants possibly go back in time to around 3000 years. Today, a great percentage of the world population, particular in developing countries, uses plants for facing primary needs of medical assistance¹. Modern drugs like aspirin, atropine, ephedrine, digoxin, morphine, quinine, reserpine and tubocurarine are examples, which were originally discovered through observations of traditional cure methods of indigenous people².

Glycyrrhiza glabra has been known in pharmacy for thousands of years. In old Chinese pharmacy, it was considered to belong to drugs of the first class and to it was ascribed the rejuvenating property when consumed for long periods³. In ancient Egypt, Greece and Rome licorice was frequently used. The earliest record of its use in medicine is found in "code Humnubari" (2100 BC)⁴. It was also one of the important plants mentioned in Assyrian herbal (2000 BC). Hippocrates (400 BC) mentioned its use as a remedy of ulcers and quenching of thirsts. The drug was also mentioned by Theophrastus and Dioscorides. In traditional Siddha system of medicine, liquorice is used as a demulcent, expectorant, anti-tussive, laxative and sweetener⁵.

DISTRIBUTION/ HABITAT

This plant is cultivated in Russia, UK, USA, Italy, France, Germany, Spain, China and Northern India (Punjab and Sub-Himalayan tracts). It is distributed in Southern Europe, Syria, Iran, Afghanistan, Russia, China, Pakistan and Northern India. Large scale commercial cultivation is seen in Spain, Sicily and England¹⁰.

Table 1: Classification

Kingdom	Plantae
Subkingdom	Tracheobionta-Vascular plants ⁶
Super division	Spermatophyta-Seed plants
Division	Magnoliophyta
Class	Magnoliopsida ⁷
Subclass	Rosidae
Order	Fabales ⁸
Family	Fabaceae-Pea family
Genus	<i>Glycyrrhiza</i> licorice ⁹
Species	<i>Glycyrrhiza glabra</i> L

CULTIVATION

It is a perrineal herb/ sub shrub for subtropical and temperate zone. Young pieces of stolons having 2-3 buds of aerial shoot are used for propagation. Three to four feet deep soil having light, loamy, stone-free texture is needed for the plant¹¹. It is usually grown continuously on the same land. Licorice enjoys fertile, sandy or clay soil near a river or stream where enough

water is available for the plant to flourish in the wild, or under cultivation where it can be irrigated.

The pieces of stolons are planted in March at 2' by 3' distance. The plant attains a maximum height up to 2 m. The underground stem grow horizontally up to 2 m length, highly branched consisting of short taproot with large number of rhizomes¹². The roots are harvested 3-4 years after planting when they show sufficient growth. Dry conditions at planting time and for the next two months give best chance for a good crop. A yield of two tons of roots per acre for bailing, plus 3-4 cwt of trimmings or offal is considered satisfactory. Rhizomes and roots are dug up in October, from the plants which have not borne the fruits. Drug is washed after removal of buds and rootlets. Some pieces are peeled and divided into small pieces. The drug is dried first under sun and then in shades, during which it loses about 50 per cent of its weight¹³.

MORPHOLOGY

Leaves- are compound, imparipinnate, alternate, having 4-7 pairs of oblong, elliptical or lanceolate leaflets covered with soft hairs on underside.

Flowers- are narrow, typically papilionaceous, axillary spikes, lavender to violet in color. The calyx is short, campanulate, with lanceolate tips and bearing glandular hairs¹⁴.

Fruit- is a compressed legume or pod, upto 1.5 cm long, erect, glabrous, somewhat reticulately pitted, and usually contains, 3-5 brown, reniform seeds¹⁵.

Root- is approximately 1.5 cm long and subdivides into subsidiary roots, about 1.25 cm long, from which the horizontal woody stolons arise. They may reach 8 m and when dried and cut, together with the root, constitute commercial licorice. It may be found peeled or unpeeled. The pieces of root break with a fibrous fracture, revealing the yellowish interior with a characteristic odor and sweet taste¹⁶.

CHEMICAL CONSTITUENTS

Flavonoid rich fractions include liquirtin, isoliquirtin, liquiritigenin and rhamnoliquiritin and five new flavonoids-glucoliquiritin apioside, prenyllicoflavone A, shinflavanone, shinpterocarpin and 1-methoxyphaseolin isolated from dried roots. The roots of *Glycyrrhiza glabra* Linn contain glycyrrhizin, which is a saponin that is 60 times sweeter than cane sugar. Both glycyrrhizin and glycyrrhetic acid can exist in the 18 α and 18 β stereoisomers¹⁷. Isolation and structure determination of licopyranocoumarin, licoaryl coumarin, glisoflavone together with a new coumarin-GU-12 are also reported. Four new isoprenoid-substituted phenolic constituents-semilicoisoflavone B, 1-methoxyficifolinol, isoangustone A, and licoriphenone had isolated from roots¹⁸. Also a new prenylated isoflavan derivative, kanzonol R was also isolated¹⁹.

The presence of many volatile components such as pentanol, hexanol, linalool oxide A and B, tetramethyl pyrazine, terpinen-4-ol, α -terpineol, geraniol and others in the roots are also reported. In addition presence of propionic acid, benzoic acid, ethyl linoleate, methyl ethyl ketone, 2, 3-butanediol, furfuraldehyde, furfuryl

formate, 1-methyl-2-formyl pyrrole, trimethyl pyrazie, maltol and other compounds are also isolated from the essential oil.

Table 2: Quantitative standards

Total ash	Not more than 4.5 %
Acid insoluble ash	Not more than 1.5%
Water soluble ash ²⁰	Not more than 1%
Aqueous extractive value	Not less than 20%
Ethanol extractive value	Not less than 15%
Chloroform extractive value ²¹	Not less than 5%
Water soluble extractive	Not less than 20%
Moisture content ²²	Not more than 7.45%

Pharmacology

After oral administration of licorice in humans, the main constituent, glycyrrhizic acid, is hydrolyzed to glycyrrhetic acid by intestinal bacteria possessing a specialized β -glucuronidase. Glycyrrhetic acid is 200-1,000 times more potent an inhibitor of 11- β -hydroxysteroid dehydrogenase (involved in corticosteroid metabolism) than glycyrrhizic acid²³. After oral dosing, glycyrrhetic acid is rapidly absorbed and transported via carrier molecules to the liver. In the liver it is metabolized to glucuronide and sulfate conjugates, which are subsequently rehydrolyzed to glycyrrhetic acid²⁴. Glycyrrhetic acid is then reabsorbed, resulting in a significant delay in terminal clearance from plasma. In the 24-hour period after oral administration, glycyrrhizin was found in the urine, indicates its partly absorption as an intact molecule²⁵.

TRADITIONAL USES

1. A decoction of madhuka or its powder is generally prescribed with honey in anemia.
2. After mixing with cow's milk it is used for promoting lactation²⁶.
3. 10g powder of it mixed with 10g sugar, pounded with rice water is commonly prescribed in menometrorrhagia.
4. A confection of rice milk, prepared with Yashtimadhu, is used treatment of hoarseness of voice.
5. Charaka prescribed 10 g madhuka powder mixed with honey, followed by intake of milk, as an aphrodisiac and as an intellect-promoting tonic²⁷.
6. Charaka prescribed paste of licorice and *Picirrhiza kurroa* with sugar water as a cardio-tonic.
7. Charaka prescribed Yashtimadhu and *Santalum album*, powdered with milk in haematemesis.
8. Sushruta prescribed the paste of Yashti madhu 10g in intrinsic haemorrhage²⁸.
9. In oedema, paste of licorice and *Sesamum indicum*, milk mixed with butter is used.
10. Warm clarified butter mixed with licorice, is used topically on wounds, bruises and burns.
11. A decoction of madhuka is used on erysipelas.
12. A decoction of the root is a good wash for falling and greying of hair²⁹.

PHARMACOLOGICAL ACTIVITIES

1. Anti-tussive and Antidemulcent activity

The liquorice powder and extract were found to be effective in the treatment of sore throat, cough and

bronchial catarrh. Licorice 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. Glycyrrhizin is responsible for demulcent action of licorice. Liquiritin apioside, an active compound present in the methanolic extract of licorice which inhibits capsaicin induced cough³⁰.

2. Antioxidant activity

Glycyrrhiza have a significant free-radical quenching effect. Licorice flavonoids have exceptionally strong antioxidant activity. Antioxidant activity of licorice flavonoids was found to be over 100 times stronger than that of antioxidant activity of vitamin E. Thus, licorice extract can be efficiently used to formulate cosmetic products for the protection of skin and hair against oxidative damage^{31,32}.

3. Anti-malarial activity

Licochalcone A (a chalcone) present in licorice is responsible for antimalarial activity. A previous reported study against *P. yoelii* in mice with oral doses of 1000 mg kg⁻¹ have shown to eradicate malaria parasite completely³³.

4. Anti-fungal activity

Glycyrrhiza glabra possess good anti fungal activity. In a previous reported study of screening for antifungal compounds from various plant materials, licorice extract with 80% methanol (oil-based extract of licorice; OEL) was found to possess high fungicidal effect against *Arthrrium sacchari* M001 and *Chaetomium funicola* M002 and its active compound was identified as glabridin³⁴. Thus, licorice extract has a great potential in formulating cosmetic products with antiseptic activities.

5. Immunostimulatory activity

A studies proved that *Glycyrrhiza glabra* at 100µg/ml concentration, possess immunostimulatory effects. It increases production of TCD69 lymphocytes and macrophages from human granulocytes. In a previous reported study, licorice root extract was found to prevent the rise in the amount of immune-complexes related to autoimmune diseases like systemic lupus erythematosus³⁵.

6. Anti ulcer activity

Glycyrrhizinic acid, a major component of licorice, has antiulcer effect by raising the local concentration of prostaglandins that promote mucous secretion and cell proliferation in the stomach. In a previous reported study activity of Extractum liquiritiae (EL), glycyrrhizic acid, glycyrrhetic acid and a novel lipophilic derivative of glycyrrhetic acid monoglucuronide (GAMG), acetylated GAMG(aGAMG), were active against 29 *Helicobacter pylori* strains. The potent *in vitro* activity of glycyrrhizic acid against *H. pylori* concludes its beneficial effect on peptic ulcers³⁶.

7. Anti dyslipidaemic effect

In a previous reported study ethanolic (95%) extract of root of *Glycyrrhiza glabra* and its fractions were investigated for its antidyslipidaemic activity on dyslipidaemic hamsters.

The reduction in LDL-cholesterol level by ethanolic extract, ethyl acetate soluble fraction and water soluble fraction were 43.9, 31.0, 33.4 and 24.6%, respectively. The treatment with *Glycyrrhiza glabra* root ethanolic extract and its fractions significantly brought down LDL and VLDL in the HFD fed hamsters to various degrees³⁷.

8. Anti-bacterial Activity

Secondary metabolites such as; saponins, alkaloids and flavonoids present in hydro-methanolic root extract of *Glycyrrhiza glabra*, possess potent antibacterial activity against *Staphylococcus aureus*. Moreover various studies on aqueous and ethanolic extracts of licorice proved its inhibitory activity on cultures of *Staphylococcus aureus* and *Streptococcus pyogenes*³⁸.

9. Anti-viral effects

It is reported that licorice extract inhibits the growth of viruses, including herpes simplex, Varicella zoster, Japanese encephalitis, influenza virus, vesicular stomatitis virus and type A influenza virus. Glycyrrhizin does not allow the virus cell binding. Thus, it is found to have a prominent antiviral activity³⁹.

10. Antithrombotic effect

In a previous reported study the *in-vivo* effects *Glycyrrhiza glabra* extract and combined effect with Vitamin K and Heparin were evaluated in Sprague Dawley Rats. It is found that extract of *G. glabra* increased the bleeding time when given in the doses of 180 mg/kg and 360 mg/kg. Blood loss was evaluated 60 minute later as a function of absorbance at 540 nm due to hemoglobin content in water solution. Altogether data indicates that *Glycyrrhiza glabra* is an effective anti thrombotic agent⁴⁰.

11. Hair growth stimulation

Licorice has a significant hair growth activity and it can be safely used in herbal formulations in treatment of various types of Alopecia. In a previous reported study hydro-alcoholic extract of licorice showed good hair growth promoting activity. Comparison between licorice extract and the standard drug used (Minoxidil 2%) showed that, 2% concentration of licorice extract showed better hair growth stimulatory activity than 2% Minoxidil⁴¹.

12. Skin lightening activity

The extract of licorice is reported to be an effective pigment lightening agent. Glabridin in the hydrophobic fraction of licorice extract inhibits tyrosinase activity in cultured B16 murine melanoma cells. Some other active compounds in licorice extract like glabrene, Licochalcone A, Isoliquiritin are also responsible for inhibition of tyrosinase activity. Liquiritin present in licorice extract disperse melanin, thereby inducing skin lightening⁴².

13. Anti-inflammatory activity

It is reported that glycyrrhetic acid in licorice extract gives anti-inflammatory effect similar to glucocorticoids and mineralocorticoids. Licorice root (*Glycyrrhiza*) extract promotes the healing of ulcers of the stomach and mouth and this fact was known for over 2000 years.

According to studies, glycyrrhizic acid inhibits all factors responsible for inflammation. It inhibits

cyclooxygenase activity and prostaglandin formation. It is also responsible for indirectly inhibiting platelet aggregation⁴³.

14. Anti-diabetic activity

In a previous study Kuroda M *et al.* reported that ethyl acetate extract of licorice exhibited a significant PPAR- γ (peroxisome proliferator-activated receptors) that function as transcription factors regulating the expression of genes involved in glucose and lipid metabolism binding activity. Finally reduces the blood glucose level in knockout diabetic mice⁴⁴

15. Hepatoprotective activity

Glycyrrhizin induced a significant reduction in serum aminotransferases and improved the liver histology⁴⁵. It has also been implicated that long-term usage of glycyrrhizin prevents development of hepatocellular carcinoma in chronic hepatitis C. *In vitro* studies have indicated that glycyrrhizin modifies the intracellular transport and suppresses hepatitis B virus (HBV) surface antigen (HbsAg)⁴⁶.

16. Anticancer activity

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.

CONCLUSION

At present scenario there has been an increase in demand for the phytopharmaceuticals all over the world because of the fact that the allopathic drugs have more side effects. This forms a basis for the selection of plant for further phytochemical and pharmacological investigation.

The pharmacological activities reported in the present review confirm the therapeutic value of *Glycyrrhiza glabra*. The plant has been used since centuries for asthma, bronchitis, ulcers, and an anti-inflammatory. It is reported to contain essential oil, coumarins, alkaloids and flavonoids. Extract of root can be found in various herbal preparations that are in market today. Presence of chemical compounds indicates that the plant could serve as "lead" for development of novel agents for disorders in the coming years.

In this regard, further studies need to be carried out to explore *Glycyrrhiza glabra* Linn for its potential in preventing and treating diseases. So, the present review gives a direction for future investigators to carry out research on the plant so that they could get some medicinally important drugs or may design new dosage form of active constituents.

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Figure 1: Leaves, flower, root and powder of *Glycyrrhiza glabra*

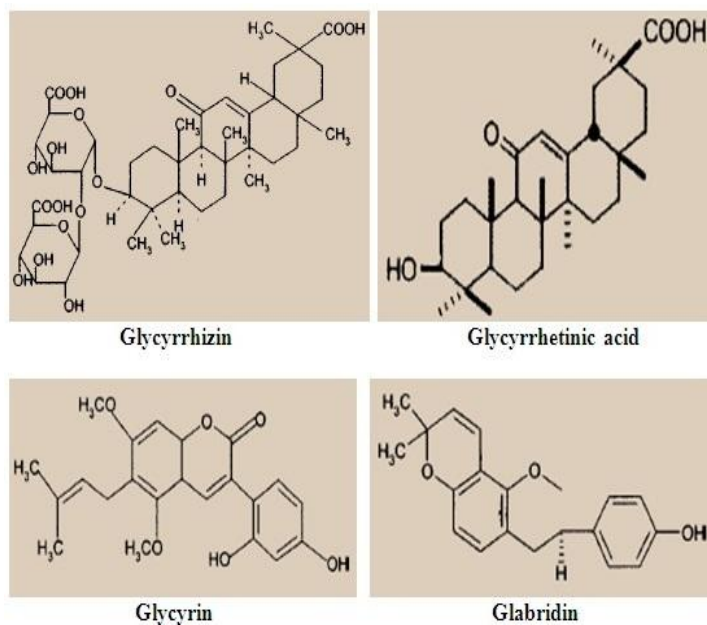


Figure 2: Chemical structure of some active constituents of *Glycyrrhiza glabra*



Cite this article-

Pandey S, Verma B, Arya P. A review on pharmacological activities of *Glycyrrhiza glabra*. Universal Journal of Pharmaceutical Research. 2017; 2(2): 6-10.