



Phytochemistry & Pharmacological Studies of Glycyrrhiza glabra: A Medicinal Plant Review

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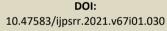
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ABSTRACT

Plants have been one of the important sources of medicines for human being and animals since the ancient time. 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 herb belonging to the family Leguminosae, also known as Liquorice 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. It is widely used in ayurvedic formulations and herb for different diseases. Present review article deals with chemical constituents present in various parts of Glycyrrhiza glabra and pharmacological activities. Present article object 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 glycemic properties. Various other effects like antiulcer, antiviral, antifungal have also been discussed. A large number of components have been isolated from liquorice including triterpene saponins, flavonoids, isoflavonoids and chalcones, glycyrrhizic acid normally being considered to be the main biologically active component. This will be helpful to create interest towards liquorice and may be useful in developing new formulations with more therapeutic and economical value.

Keywords: Antibacterial, Pharmacological action, Glycyrrhiza glabra, Liquorice.

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INTRODUCTION

erbal medicines are also in great demand in the developed world for primary health care because of their efficacy, safety and lesser side effects. They also offer therapeutics for age-related disorders like memory loss, osteoporosis, immune disorders, etc. for which no modern medicine is available. India despite its rich traditional knowledge, heritage of herbal medicines and large biodiversity has a dismal share of the world market due to export of crude extracts and drugs. WHO too has not systematically evaluated traditional medicines despite the fact that it is used for primary health care by about 80% of the world population. However, in 1991 WHO developed guidelines for the assessment of herbal medicine.¹

Herbal medicines are in great demand in both developed and developing countries as a source of primary health care owing to their attributes having wide biological and medicinal activities, high safety margins and lesser costs. Traditional use of medicine is recognized as a way to learn about potential future medicines. Researchers have identified number of Compounds used in mainstream medicine which were derived from "ethnomedical" plant sources. Plants are used medicinally in different countries and are a source of many potent and powerful drugs.²

Glycyrrhiza glabra is one of the most popular medicinal plants belonging to the Fabaceae family (also known as Leguminosae), and its members are now commonly used as feed and food. The genus Glycyrrhiza is derived from the Greek words glykos (sweet) and rhiza (root). This species is a native of Mediterranean areas, but it is now also present in India, Russia, and China. The extracts are currently used in pharmaceutical and food industries, as well as in the manufacture of functional foods and food supplements.³ In traditional Chinese medicine, for example, the plant is recommended as a common remedy for gastrointestinal problems, cough, bronchitis, and arthritis. In particular, it is still widely used to treat gastritis, peptic ulcers, respiratory infections, and tremors in folk medicine. Commonly, G. glabra root is employed to prepare a tea that is an excellent thirst quencher. The dried root has been described as a tooth cleanser.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 thirds. 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 sweetener.⁵



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hypolipidemic. cardiovascular, central nervous. respiratory, immunological, antiinflammatory, analgesic antipyretic and many other pharmacological effects. The phytochemical screening of the Glycyrrhiza glabra root revealed the presence of alkaloids, glycosides, carbohydrates, starches, phenolic compounds, flavonoids, proteins, pectin, mucilage, saponins, lipids, tannins, sterols and steroids. It showed memory enhancement, antidepressant, antimicrobial, anticancer, antioxidant, protective, antiinflammatory, antiulcer, antidiabetic, hypolipidemic and many other pharmacological effects.⁶⁻⁹ This review can be considered as a bird's eye view highlighting the current progress of *Glycyrrhiza alabra* in pharmacological and pharmacognostical field with its prominent folk uses.

Botanical Descriptions

G. glabra is a typical herbaceous perennial, growing to 1 m in height, presenting pinnate leaves with a length of 7 to 15 cm. The flowers are purple to pale whitish blue, being arranged in a hermaphrodite inflorescence, whereas the fruit is an oblong legume with 2 to 3 cm of length and containing several seeds. The genus Glycyrrhiza (Fabaceae) consists of about 30 species, such as G. glabra, G. uralensis, G. inflata, G. aspera, G. korshinskyi, or G. eurycarpa. Like the other plants of Fabaceae, G. glabra is able to fix nitrogen, due to symbiosis with bacteria of the genus Rhizobium, at the root level, being suitable for sandy and clay soils, though preferring humid soils. Since the Egyptian age, the therapeutic properties of G. glabra are well documented. The roots are the most used parts whereas leaves are considered an agrochemical waste. However, in the last years different authors studied the phytochemical composition of G. glabra leaves demonstrating that certain compounds present in the roots are also identified in leaves although in smaller quantities.^{10,11} The Scientific Classification of *Glycyrrhiza glabra* shown in Table 01.¹³⁻¹⁵

Habitate

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 England.¹²

Table 1: Scientific Classification of Glycyrrhiza glabra

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



Figure 1: (A) Leaves (B) Flower (C) Root and powder of *Glycyrrhiza glabra* Linn.

Common / Vernacular Name

Glycyrrhiza glabra has been known by various names according to regional languages and areas, which are as follows-

Sanskrit	: Yashti-madhuh. Madhuka	
Bengali	: Jashtimadhu, Jaishbomodhu	
Gujarat	: Jethimadhu	
Hindi	: Jothi-madh, Mulhatti	
Kannada	: Yastimadhuka, atimaddhura	
Malayalam	: Iratimadhuram	
Marathi	: Jeshtamadha	
Oriya	: Jatimadhu	
Tamil	: Atimaduram	
Telugu	: Atimadhuranu, Yashtimadhukam	
English	: Licorice, Liquorice, Sweet wood	
Arab	: Aslussiesa	
Persia	: Ausareha mahaka	
France	: Boisdoux	

Traditional Uses

Traditional Uses of G. glabra Traditionally licorice has been reported to treat many diseases such as asthma, tonsillitis, sore throat, hyperdipsia, flatulence, epilepsy, fever, sexual debility, paralysis, coughs, stomach ulcers, heartburn, colic, swellings, rheumatism, skin diseases, acidity, leucorrhea, bleeding, hemorrhagic diseases and jaundice.¹⁶⁻²⁰ Moreover it was traditionally used as an insecticide, laxative, anti-inflammatory, anti-ulcer, antibiotic, anti-arthritic, antiviral, memory stimulant due to its action as a monoamine oxidase (MAO) inhibitor, anticholinergic, antitussive, anti-caries, hypolipidemic, anti-mycotic, estrogenic, antioxidant, anticancer, and antidiuretic agent.²¹ It is used in the confection industry such



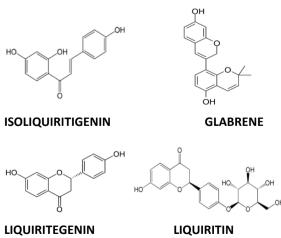
as in soft drinks, sweets and alcohol as well as in the tobacco industry.

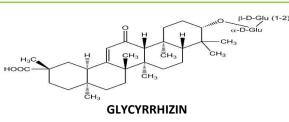
Chemical Constituents

Glycyrrhiza glabra roots contain several active compounds (Table 02) including flavonoids, such as liquirtin, rhamnoliquirilin, liquiritigenin, prenyllicoflavone A, glucoliauiritin apioside. 1-metho-xvphaseolin. shinflavanone, shinpterocarpin, licopyranocoumarin, glisoflavone, licoarylcoumarin, coumarin-GU-12 and saponins namely glycyrrhizin (60 times more sugary than sugarcane). In addition, four isoprenoid-substituted phenolic constituents (isoangustone A, semilicoisoflavone B, licoriphenone, and 1-methoxyficifolinol), kanzonol R (prenylated isoflavan derivative) and several volatile components (pentanol, tetramethyl pyrazine, hexanol, terpinen-4-ol, linalool oxide A and B, geraniol, and $\alpha\text{-}$ terpineol) have also been reported. Whereas propionic acid. 1-methyl-2-formylpyrrole. 2.3-butanediol. benzoic acid, ethyl linoleate, furfuryl formate, trimethylpyrazie, furfuraldehyde, methyl ethyl ketone, and maltol were isolated from the essential oil. Glycyrrhizin a saponin compound as well as its aglycone glycyrrhetinic acid, are the potent components in G. glabra. Glycyrrhizin consists of glycyrrhetic acid, triterpenoid aglycone, glucuronic acid disaccharide and it can be found naturally as calcium and potassium salts in licorice root.²²⁻²⁴ In humans glycyrrhizin can be metabolized and converted to glycyrrhetinic acid. Thus, the pharmacological activities of glycyrrhizin are similar to those of glycyrrhetinic acid.

Raw and tea licorice infusions contain protein, fat, moisture, raw ash, fiber, silica, carbohydrates, minerals (calcium, phosphorus, sodium, potassium, zinc, and copper), and amino acids, including serine, aspartic, glycine, glutamic, threonine, valine, proline alanine, isoleucine, tyrosine, leucine, lysine, phenylalanine, tyrosine, and histidine. Interestingly, HPLC analysis of the methanolic extract of licorice detected the presence of several organic acids, such as acetic, propanoic, fumaric, citric, butyric, malic, and tartaric acids.²⁵

Chemical structures





Pharmacological Activities

Liquorice is one of the oldest and most popular herbal medicines in the world. Many of the liquorice historical uses are still practiced today. Table 02 summarizes the most important pharmacological activities reported for G. glabra as well as the individual compounds related to them.

Antioxidant activity

The antioxidant activity of G. glabra is one of the major reasons for its uses. The phenolic content is probably responsible for the powerful antioxidant activity observed ²⁶ attributed this activity to flavonoids, isoflavones, such as glabridin, hispaglabridin A, and 30-hydroxy-4-Omethylglabridin, are the responsible compounds.²⁷ Reported a huge antioxidant activity of the dihydrostilbene derivates present in G. glabra leaves. Also, licochalcones B and D are present in G. glabra, showing a strong scavenging activity on DPPH radical and the ability to inhibit the microsomal lipid peroxidation. These phenolic compounds are effective in the protection of biological systems against oxidative stress, being able to inhibit the onset of skin damages,²⁸ the topical application of liquorice extract formulations may be of value in innovative dermal and cosmetic products as it counteracts oxidative stress damage, maintaining the skin homeostasis due to its high antioxidant content.

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. 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. 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.²⁹

Anti-malarial activity

Licochalcone A (a chalcone) present in liquorice 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 completely.³⁰

Anti-fungal activity

Glycyrrhiza glabra possess good antifungal 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 Arthrinium sacchari M001 and Chaetomium funicola M002 and its active compound was identified as glabridin.³¹ Thus, liquorice extract has a great potential in formulating cosmetic products with antiseptic activities.

Immunostimulatory activity

A study 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 liquorice root extract was found to prevent the rise in the amount of immune complexes related to autoimmune diseases like systemic lupus erythematosus.³²

Peptic Ulcer Disease

The peptic ulcer activity was reported in systematically study on licorice extract. In an unblended and uncontrolled study 45 patients with confirmed gastric ulcers were administered 10 g/day of powdered licorice extract. The ulcers were reported to disappear in 17 of the cases, were diminished in 22 cases and were unchanged in six of the cases. Patients with duodenal ulcers did not react as favorably. Approximately 20% of the patients were noted to develop edema, some with complications including violent headache, dizziness, upper right quadrant pain, compression in the chest, and hypertension. A reduction of the dosage to 3 g/day reduced the occurrence of edema although not in all cases. Crude fractionation of the licorice extract revealed that glycyrrhizin was the probable agent responsible for the edematous effect and an unknown component was therefore considered to be the active antiulcerogenic agent. The potent in vitro activity of glycyrrhizic acid against H. pylori concludes its beneficial effect on peptic ulcers.³³

Anti-inflammatory activity

It is reported that glycyrrhetinic acid in liquorice extract gives anti-inflammatory effect similar to glucocorticoids and mineralocorticoids Liquorice 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 and also responsible for indirectly inhibiting platelet aggregation.³⁴

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 min 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 antithrombotic agent.³⁵

Neuroprotective activity

The effects of G. glabra on learning and memory were investigated in mice.³⁶ Administered the extract of G. glabra orally to mice during 7 days at different concentrations (75-300 mg/kg). Studied the effects of G. glabra root aqueous extract on the learning and memory of 1- month-old male Wistar albino mice at doses between 75 and 300 mg/kg, orally administered during six successive weeks. Both studies demonstrated a significant improvement of learning and memory in mice, but the exact mechanism behind this action remains unknown.37 These findings suggest a possible neuroprotective role of liquorice in the prevention of diseases such as Alzheimer. The basis of Alzheimer is the chronic inflammation of certain brain regions. Thus, the anti-inflammatory activity of liquorice might contribute to the observed memoryenhancing effects.³⁸ Also oxygen free radicals are implicated in the process of aging and could be responsible for the development of Alzheimer's disease in elderly persons. The protective role of liquorice extract may be attributed to its antioxidant properties resulting in reduced brain damage & improvement of neuronal function and memory. The combination of antiinflammatory and antioxidant activities with neuroprotective role could lead to memory enhancing effects.³⁹

Anti-viral activity

Oral liquorice preparations containing glycyrrhetinic acid are used for the treatment of viral infections-viral hepatitis and common cold. Topical preparations containing glycyrrhetinic acid are used for herpes, eczema, and psoriasis. In Japan a preparation of glycyrrhizin cysteine and glycine is used by injection for the treatment of acute and chronic hepatitis.⁴⁰ Liquorice 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 simplex.41 Herpes Triterpenoid saponins from G. glabra roots have been shown to have antiviral activity. Thus, these saponin inhibit the growth of influenza A virus in hen embryos. Glycyrrhizinic acid inhibits the growth and cytopathology of several unrelated DNA and RNA viruses. It also inactivated Herpes simplex virus particles irreversible. Glycyrrhizin inhibited plaque formation in three different strains of Japanese encephalitis virus at a concentration of 500 mg/ml at 96 hours in connection with its antiviral activity, it should be noted that glycyrrhizin has been shown in Invitro experiments to induce and enhance gamma-interferon in human peripheral lymphocyte macrophage cultures developed by the lactin concanavalin A.42

Anti dysliipidaemic 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 degree.⁴³

Anti-diabetic activity

In a previous study reported that ethyl acetate extract of licorice exhibited a significant PPARy (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 mice.⁴⁴

Anticarcinogenic and antimutagenic activity

Different studies suggest that the extract of *G. glabra* may be a potential supplemental source for different cancer treatments. This activity is due to the 18β-glycyrrhetinic and glycyrrhizic acids that induce mitochondrial permeability transition, leading to the apoptosis of tumour cells demonstrated the toxic effect of G. glabra against the human cervix and uterus tumour cell line SiHa cells.⁴⁵ The in vivo inhibition of Ehrlich ascites tumour cell growth by the aqueous and methanolic extracts of G. glabra with the corresponding reduction in cell number, body weight, and ascites volume. The hydro methanolic root extract of G. glabra also exhibited antimutagenic potential by suppressing micronuclei formation and chromosomal aberration in bone marrow cells of albino mice.46 Glycyrrhizin and glycyrrhezinic acids are effective compounds in gastric cancer treatment whereas

glycyrrhizin suppresses thromboxane A2 in lung cancer cell with low toxicity.⁴⁷

Hair growth stimulation Liquorice 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 liquorice showed good hair growth promoting activity. Comparison between liquorice extract and the standard drug used (Minoxidil 2%) showed that 2% concentration of liquorice extract showed better hair growth stimulatory activity than 2% Minoxidil.⁴⁸

Skin lightening activity

The extract of liquorice is reported to be an effective pigment lightening agent. Glabridin in the hydrophobic fraction of liquorice extract inhibits tyrosinase activity in cultured B16 murine melanoma cells. 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.⁴⁹

Other Activities

liquiritin present in the roots of *Glycyrrhiza glabra* is inactive as an antispasmodic. However, when hydrolysed by heat and converted to isoliquiritigenin it was shown to exhibit strong spasmolytic activity.⁵⁰ *Glycyrrhiza glabra Linn* (Glycyrrhizin, 18 β glycyrrhetinic acid & Liquiritigenin) have antiallergic activity which can relive Ig E- induced allergic diseases such as dermatitis and asthma.⁵¹

 Table 2: Pharmacological Activities Reported From Glycyrrhiza glabra

Sr. No.	Activity	Part/Extract	Animal models & cell lines
1.	Immunomodulatory activity	Aqueous extract	In vivo phagocytosis, determination of cellular immune response haemagglutination antibody titre & plaque forming cell assay using sheep RBCs ³²
2.	Antitussive activity	Ethanol extract	SO ₂ gas induced cough in experimental animals. Mice showed an inhibition of 35.62% in cough on treatment with G.glabra extract ³⁹
3.	Anti-inflammatory activity	Hydroalcoholic extract	Carrageenan induced rat paw oedema at dose levels of 100,200,300 mg/Kg. The extract showed a maximum of 46.86% inhibitory action ³⁴
4.	Chronic fatigue stress	Hydroalcoholic extract	The extract showed the protective effect on mice on exposure to chronic fatigue stress ⁵²
5.	Antinociceptive activity	Ethanol extract	Different pain models in Swiss albino mice. Activity was evaluated at 50-200 mg/Kg ip in mice using various pain models like acetic acid induced abdominal constrictions, formalin induced hyperalgesia & tail flick method ⁵³
6.	Antiulcer activity	Aqueous, acetone, ethanolic extracts of leaves	Micro-organism used: <i>Helicobacter pylori</i> by agar well diffusion method ³³
7.	Hepatoprotective activity	Aqueous extract of roots	PCM induced rats hepatocytes damage <i>in vivo</i> . Rabbit models with acute liver injury induced by CCl ₄ ⁵⁴



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8.	Memory enhancing activity	Aqueous extract of roots	Three months old Wistar albino rats. Elevated -plus maze and Morris water –maze test were conducted ³⁷⁻³⁹
10.	Anticonvulsant activity	Hexane, ethanol, methanol extract of leaves	Fractions were evaluated intraperitoneally in mice using maximal electroshock (MES) & pentylene tetrazol (PTZ) seizure tests ⁵⁵
11.	Antistress activity	Alcoholic & aqueous extract	Reduce stress in <i>Drosophila melanogaster</i> induced by Methotrixate at different conc. ⁵⁶
12.	Antioxidant activity	Methanol extract	The method based on scavenging activity & reduction capability of 1,1-diphenyl-2-picrylhydrazyl radical; also against nitric oxide & superoxide radicals [27,28]
13.	Testicular toxicity	Aqueous extract	Carbendazim induced testicular toxicity in albino rats 57
14.	Cytotoxic activity	CHCl ₃ , methanol & aqueous extract	<i>In vitro</i> cytotoxic activity using two different cell lines MCFT-cancerous & Vero-normal cell line ⁵⁸
15.	Enzyme inhibiting activity	Methanolic extract	<i>In-vitro</i> inhibition of tyrosinase enzyme ⁵⁸
16.	Antihyperglycemic activity		Male albino rats of Wistar strain
17.	Antimalarial activity	Alcoholic extract	Micro-organism used: Plasmodium falciparum. Plasmodium yoelii ³⁰
18.	Antiviral activity	Aqueous extract	Herpes simplex 1 & vesicular stomatitis virus 42
19.	Anticancer activity	Licorice extract	Ames test, Trp-p-1, Trp-p-2 in <i>S.typhimurium</i> TA 98 reverants ^{45,47}
20.	Estrogenic activity	Alcoholic extract	Mouse
21.	Antimycobacterial activity	Methanolic extract	Micro-organisms used: <i>Mycobacteriaum tuberculosis</i> H37Ra & H37Rv strain
22.	Antidyslipidaemic activity	Ethanol extract	Fractions significantly brought down LDL and VLDL in the HFD fed hamsters to various degrees ⁵⁹
23.	Antimicrobial activity	Ether, Chloroform, acetone	Micro-organisms used: E. coli, B. subtilis, P. aerogenosa, S. aureus 60

CONCLUSION

This review examined the medicinal properties and all the phytochemical molecules isolated from *Glycyrrhiza glabra*. Glycyrrhizic acid, 18- β - glycyrrhetinic acid, glycyrrhizin and licochalcones are the main constituents that have been isolated from *G. glabra* extracts. Pharmacologically *G. glabra* and its main constituents possess antimicrobial, antiparasitic, antiviral, antitussive, immuno-enhancing, antioxidant, anti-inflammatory and anticancer effects.

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 good basis for the selection of plant for further phytochemical and pharmacological investigation. The pharmacological and clinical studies reported in the present review confirm the therapeutic value of *Glycyrrhiza glabra*. 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.

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