CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.14237433

https://www.iajps.com/volumes/volume11-november-2024/65-issue-11-november-24/

Available online at: http://www.iajps.com Review Article

A REVIEW ARTICLE ON LICORICE (GLYCYRRHIZA GLABRA LINN)

Sandhya karumanchi, Dr.A.Pavani

Sri Venkateswara College of Pharmacy,Hi-tech City Road, Madhapur, Hyderabad.T.S.- 500081

Abstract:

In the last years, consumers are paying much more attention to natural medicines and principles, mainly due to the general sense that natural compounds are safe. On the other hand, there is a growing demand by industry for plants used in traditional medicine that could be incorporated in foods, nutraceuticals, cosmetics, or even pharmaceuticals. Glycyrrhiza glabra Linn. belongs to the Fabaceae family and has been recognized since ancient times for its ethnopharmacological values. This plant contains different phytocompounds, such as glycyrrhizin, 18β-glycyrrhetinic acid, glabrin A and B, and isoflavones, that have demonstrated various pharmacological activities. Pharmacological experiments have demonstrated that different extracts and pure compounds from this species exhibit a broad range of biological properties, including antibacterial, anti-inflammatory, antiviral, antioxidant, and antidiabetic activities. A few toxicological studies have reported some concerns. This review addresses all those issues and focuses on the pharmacological activities reported for G. glabra. Therefore, an updated, critical, and extensive overview on the current knowledge of G. glabra composition and biological activities is provided here in order to explore its therapeutic potential and future challenges to be utilized for the formulation of new products that will contribute to human well-being.

Keywords: , Pharmacological action, Glycyrrhiza glabra, Liquorice, Extraction, Phytochemical constituents

Corresponding author:

Sandhya Karumanchi,

Sri Venkateswara college of pharmacy

Hi-tech City Road, Madhapur, Hyderabad.T.S.- 500081

karumanchisandhya02@gmail.com

QR code

*Please cite this article in press Sandhya Karumanchi et al., **A Review Article On Licorice (Glycyrrhiza Glabra Linn).**, Indo Am. J. P. Sci, 2024; 11 (11).*

INTRODUCTION:

"Glycyrrhiza glabra" also known as Licorice and sweet-wood in English, belongs to the family Leguminosae, is a genus of perennial herbs and under shrubs distributed in the subtropical and warm temperate regions of the world. A high number (More than 400) of chemical compounds have been isolated from Glycyrrhiza species, the compound is composed of triterpene saponins, and flavonoids (liquiritoside, isoliquiritoside) are believed to be responsible for the bioactivities of licorice.[1] It is cultivated mostly for its rhizomes (underground stems) that contain the compound glycyrrhizin, which is a triterpenoid saponin and is 50 times more sweetener than sugar. This glycyrrhizin has intensive use in foods, tobacco products and in traditional use and herbal medicine. In the traditional system of medicine, the roots and rhizomes of licorice was an anti-inflammatory agent in the treatment of allergic reactions, antimicrobial, antiulcer, expectorant and anxiolytic activities. It has also been known to relieve rheumatism, osteoarthritis and arthritis, regulate low blood sugar, and was used for Addison's disease. A medicinal use of licorice includes cough suppression, treatment of early Addison disease, treatment of liver disease and dyspepsia also in the prophylaxis and treatment of gastric and duodenal ulcers.[2] Most cough medicines are prepared to treat either dry coughs or "wet" coughs, usually known as productive coughs. Licorice root with glycyrrhizin treats the latter, working as an expectorant to loosen and thin mucus, thus making the productive cough more. The tea form of licorice root is recommended for coughs, but syrup is also available. Its sweetness property has resulted in its use around the world in cough syrups and lozenges as well as candies. Therefore, it has been widely used in folk medicine and is today a highly commercially important target species. The study of any medicinal plants starts with the pre-extraction and the extraction procedures, which is an important step in the processing of the bioactive constituents from plant materials. Traditional methods such as maceration and Soxhlet extraction are commonly used at the small research setting but significant advances have been made in modern extraction methods which are microwave and ultrasound assisted. With such variety of methods present, selection of proper extraction method needs meticulous evaluation.[3] This review describes the principle, strength and limitations of the commonly used methods in recent years to help in the selection of proper methods for easy, feasible and fast extraction of glycyrrhizin from licorice roots.

Pre-extraction preparation of plant samples

The initial stage in studying any plant extraction method is preparation of plant samples to preserve their biomolecules in their natural condition prior to their extraction. In case of licorice, the roots can be extracted from the fresh or dried plant material. Other pre preparation of plant materials such as grinding and drying also influences the preservation of phytochemicals in the final extracts.

Fresh vs dried samples

Sometimes few drying procedures are carried out to dry the plant extract isolated from the plant samples. The heat processing can have detrimental effects on natural antioxidants in raw plant materials. Intense and/or prolonged thermal treatment can cause significant loss as a result of the heat instability of compounds in the extract. In contrast to high temperature, Sun-drying and low temperature drying like 40°C oven-drying can increase total polyphenol content and phytochemical activity.[4] Fresh samples are fragile and tend to deteriorate faster than dried samples but still a comparison between fresh and dried Moringa oliefera leaves showed no significant effect in total phenolics but with higher flavonoids content in dried sample.[5] In case of licorice, both the fresh and the dried (40°C oven-drying) root powder can be used as the sweetness (glycyrrhizin content) in it remains intact even after drying.

Grinded vs powdered

By lowering the size of the particles, the chances of surface contact of the plant sample with the extraction solvent can be increased. The more surface area is exposed to the solvent, better is the extraction of the target analytes. Conventional mortar and pestle or electric blenders and mills can be commonly used to reduce particle size of sample.[6] In the case of Licorice roots, both the fresh intact roots as well as the dried powdered form can be used for extraction of glycyrrhizin. The composition of this constituent might vary in the dried powder, but its therapeutic application remains unchanged Experimental.

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.

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.[7] 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. T he recovery of active glycyrrhizic acid by analytical method is 7-8% only.

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. T his heat is transferred through conduction promoting solvent penetration into the sample thereby enhancing migration of the active constituents into the extraction solvent.[8] Strength: This technique reduces extraction time and solvent volume as compared to other conventional methods like Maceration, analytical, sonication. Improved recoveries of the active constituent from the sample can be achieved with constant reproducibility. Limitations: However, this method is limited to small molecule phenolic compounds such as phenolic acids (gallic acid and ellagic acid), quercetin, isoflavin and trans-resveratrol as they are stable under microwave heating conditions up to 100°C for 20 minutes. Excessive exposure of microwave radiations results in drastic decrease in the yield of phenolics and flavanones, mainly caused due to oxidation of compounds. Also, tannins and anthocyanins may not be suitable for this extraction method as they are degraded at high temperatures.[9] Due to these strong sets of limitations, microwave assisted method must be avoided for glycyrrhizin extraction.

Ultrasound assisted extraction or Sonication method

This method involves use of ultrasound using a sonicator probe ranging from 20 kHz to 2000 kHz.[10] The vibrational and acousticeffect 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.[11] Strength: This procedure is relatively simple and low-cost technology that can be used in both smaller and larger scale of phytochemical extraction. The main benefit of this is mainly due to reduction of time for extraction as well as in solvent consumption. Limitations: There lies no such vast set of limitations in using this method for glycyrrhizin extraction. Only when an ultrasound of more than 20 kHz is used, it may have some effects on some of the active phytochemicals through the formation of free radicals. Studies: Due to the various benefits of this method, it was employed on Licorice root extract dissloved in extraction solvent containing ethanol and water (30:70 v/v) in two separate batches, (10 gm and 30 gm). Both the mixtures were then sonicated for about 1 min. and the solvent thus obtained contained glycyrrhizic acid which was monitored by TLC. using the extract of analytical method as a standard. It was observed that the yield of glycyrrhizic acid in both the batches was around 48 to 49%.

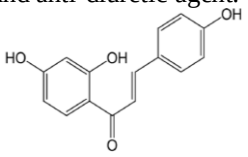
Dipping (Maceration) method

Maceration or dipping method involves soaking plant materials (coarse or powdered) in a stoppered container with a desired solvent and allowed to stand in the room temperature for a period of time. This process intends to break the cell wall of plant cells to release the desired phytochemicals in the extraction solvent being used. The choice of solvent used will determine the type of compound extracted from the samples, basically playing the most critical role. In case of licorice roots, the solvent used was ethanol and water (30:70 v/v) for 10 gm of licorice root extract. The root extract was dipped in this extraction solvent for about 60 mins. so that the glycyrrhizic acid gets dissolved in the solvent . Strength: Though being the most traditional and conventional method of extraction, this technique is the easiest and simple. Alteration in the temperature and the choice of extraction solvents can enhance the extraction process. Thus, it also proves to be a flexible method as per our convenience. Limitations: Being the simplest form of extraction method, there persists no major limitations in this method. But the limitation lies in the choice of

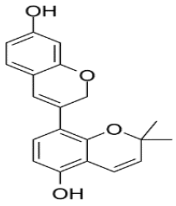
the use of organic extraction solvent. The more complex the extraction solvent is, the more purification techniques needs to be employed to obtain the pure form of the active constituent. Studies: Under the optimum extraction condition, 2.39 mg/g of glycyrrhizic acid was extracted from 10 gm of Chinese licorice root extract using ethanol and water (30:70 v/v). Thus, the maximum recovery was found to be 89.7%.

Traditional Uses

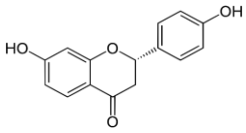
Traditional Uses of *G. glabra* Traditionally licorice has been reported to treat many diseases such as asthma, tonsillitis, sore throat, hyperdipsia, flatulence, epilepsy, fever, sexual debility, paralysis, coughs, stomach ulcers, heartburn, colic, swellings, rheumatism, skin diseases, acidity, leucorrhea, bleeding, hemorrhagic diseases and jaundice.[12-20] 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 anti-diuretic agent.[21]



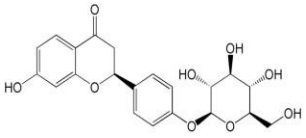
ISOLIQUIRITIGENIN



GLABRENE



LIQUIRITEGENIN



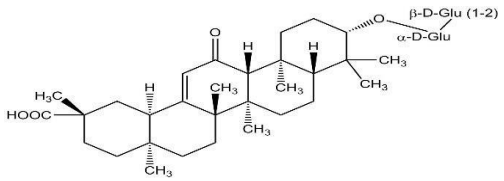
LIQUIRITIN

Chemical Constituents

Glycyrrhiza glabra roots contain several active compounds including flavonoids, such as liquirtin, rhamnoliquirilin, liquiritigenin, prenyllicoflavone A, glucoliquiritin apioside, 1-metho-xyphaseolin, shinpterocarpin, shinflavanone, 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 volatilecomponents (pentanol, tetramethyl pyrazine, hexanol, terpinen-4-ol, linalool oxide A and B, geraniol, and α- 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



GLYCYRRHIZIN

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. 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-O-methylglabridin, are the responsible compounds.[27] Reported a huge antioxidant activity of the dihydrostilbenederivates present in G. glabra leaves. Also, licochalcones Band 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 againstoxidative 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 semisynthetic 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 preventthe 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, werediminished 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 edemaalthough 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 anti-ulcerogenic 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) extractpromotes the healing of ulcers of the stomach and mouthand this fact was known for over 2000 years. According to studies, glycyrrhizic acid inhibits all factors responsible forinflammation. It inhibits cyclooxygenase activity andprostaglandin formation and also responsible for indirectlyinhibiting 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 hemoglobincontent 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 significantimprovement 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 memory-enhancing 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 Herpes simplex.[41] Triterpenoid saponins from *G. glabra* roots have been shown to have antiviral activity. Thus, these saponin inhibitthe 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 of500 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. Thetreatment 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 PPARγ (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 diabeticmice.[44]

Anticarcinogenic and antimutagenic activity

Different studies suggest that the extract of *G. glabra* maybe 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 cellwith 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, 18β glycyrrhetinic acid & Liquiritigenin) have antiallergic activity which can relive Ig E- induced allergic diseases such as dermatitis and asthma.[51]

CONCLUSION:

This review has presented a comprehensive view about the phytochemistry composition and pharmacology activities of *G. glabra*. This plant has been broadly used as a traditional medicine and food industry ingredient, particularly as a flavour and sweetening agent. The roots are used in the prevention and treatment of several complications, especially microbial/viral infection, cancer, and skin inflammation. Among the bioactive compounds, flavonoids are the most important, being responsible for most of the biological activities. Different phytochemicals, including glycyrrhizin, 18β-glycyrrhetinic acid, glabrin A and B, or isoflavones, have been identified and associated with the biological activities reported, namely, antioxidant, antiviral, antimicrobial, anticancer, or anti-inflammatory activities as well as hepatoprotection. These activities generally agree with traditional knowledge and folk medicine. Indeed, the side effects and toxicity associated with liquorice are few and are mainly linked with hypertension and fluid retention. Regarding this particular thematic, to date, few studies have been conducted, aside from some isolated ones. Thus, side effects remain an area of potential future study. lthough evidence has grown in the past decade, there is still a need to conduct further robust double-blind randomized controlled trial about *G. glabra*. There is also an immense scope to explore different combinations of liquorice preparations in a wide range of disorders.

REFERENCES:

1. Grace MS, Dubuis E, Birrell MA, Belvisi MG (2013) Pre-clinical studies in cough research: Role of Transient Receptor Potential (TRP) channels. Pulm Pharmacol Ther 26: 498-507.
2. Badkhane Y, Yadav AS, Bajaj A, Sharma AK, Raghuwanshi DK (2014) Glycyrrhiza glabra L. A Miracle Medicinal Herb. Indo American J Pharm Res 4: 5808-5813.
3. Azwanida NN (2015) A Review on the Extraction Methods Use in Medicinal Plants, Principle, Strength and Limitation. Med Aromat Plants 4: 196.
4. Yi W, Wetzstein HY (2011) Effects of drying and extraction conditions on the biochemical activity of selected herbs. Hort Sci 46: 70-73.
5. San AMM, Thongpraditchote S, Sithisarn P, Gritsanapan W (2013) Total Phenolics and Total Flavonoids Contents and Hypnotic Effect in Mice of Ziziphus mauritiana Lam. Seed Extract. Evidence-Based Complement Alternat Med 2013: 1-4.
6. T hermo Scientific (2013) Methods Optimization in Accelerated Solvent Extraction. Tech Note 208: 1–4
7. Mukhopadhyay M, Panja P (2008) A novel process for extraction of natural sweetener from licorice (Glycyrrhiza glabra) roots. Sep Purif Technol 63: 539-545.
8. Kaufmann B, Christen P (2002) Recent extraction techniques for natural products: microwave-assisted extraction and pressurised solvent extraction. Phytochem Anal 13: 105-113.
9. Trusheva B, Trunkova D, Bankova V (2007) Different extraction methods of biologically active components from propolis: a preliminary study. Chem Cent J 1: 13
10. Dalgleish T, Williams JMG, Golden AMJ, Perkins N, Barrett LF, et al. (2007) Reduced specificity of autobiographical memory and depression. J Exp Psychol Gen 136: 23-42.
11. Dhanani T, Shah S, Gajbhiye NA, Kumar S (2017) Effect of extraction methods on yield, phytochemical constituents and antioxidant activity of Withania somnifera. Arab J Chem 10: 1193-1199
12. Mukherjee P K, Wahile A, Integrated approaches

towards drug development from Ayurveda and other Indian system of medicines, J Ethnopharm 2006; 103, 25-35. https://doi.org/10.1016/j.jep.2005.09.024

13. Karahana F, Avsarb C, Ilker I O, Berber I, Antimicrobial and antioxidant activities of medicinal plant Glycyrrhiza glabra var. glandulifera from different habitats, Biotech Biotechnological Equip 2016 ;1-8 https://doi.org/10.1080/13102818.2016.1179590
14. Tene V, Malago O, Finzi P V, Vidari G, An ethnobotanical survey of medicinal plants used in Loja and Zamora chinchipi. Equador, J Ethnopharm 2007; 111: 63-81. https://doi.org/10.1016/j.jep.2006.10.032
15. Kalaiarasi P, Pugalendi K V, Antihyperglycemic effect of 18-beta glycyrrhetinic acid, aglycone of glycyrrhizin on streptozotocin diabetic rats, Europ J Pharm 2009; 1: 269- 73. https://doi.org/10.1016/j.ejphar.2008.12.057
16. Khare, C P, Encyclopaedia of Indian Medicinal Plants, Springer: New York, NY, USA, 2004; pp. 233–235.
17. Ashok S, The Herbs of India, Hi Scan Pvt. Ltd.: Gujrat, India, 2005; Volume 2: p. 566.
18. Damle M, Glycyrrhiza glabra (Liquorice)—A potent medicinal herb, Inter. J. Herb. Medicinal, 2014, 2, 132–136.
19. Kaur R, Dhinds A S, Glycyrrhiza glabra: A phytopharmacological review, IJPSR 2013, 4, 2470–2477.
20. Tewari D, Mocan A, Parvanov E D, Sah A N, Nabavi S M, Huminiecki L, Ma Z F, Lee Y Y, Horba nczuk J O, Atanasov A G, Ethnopharmacological approaches for therapy of jaundice: Part II, Highly used plant species from Acanthaceae, Euphorbiaceae, Asteraceae, Combretaceae, and Fabaceae families, Front. Pharm, 2017, 8, 519.
21. Zadeh J B, Kor Z M, Goftar M K, Licorice (Glycyrrhiza glabra Linn) as a valuable medicinal plant, Inter. J. Advance. Biol. Biomed. Res, 2013, 1: 1281–1288.
22. Biondi D M, Rocco C, Ruberto G, New dihydrostilbene derivatives from the leaves of Glycycrrhiza glabra and evaluation of their antioxidant activity, J. Nat. Prod, 2003, 66: 477–480.
23. Washington D C, Food Chemicals Codex, National Academy Press: USA, 2003; Volume 25.
24. Isbrucker R A, Burdock G A, Risk and safety assessment on the consumption of Licorice root (Glycyrrhiza sp.) its extract and powder as a food ingredient with emphasis on the pharmacology and toxicology of glycyrrhizin, Regul. Toxicol. Pharmacol, 2006, 4: 167–192.
25. Shah, S L, Wahid F, Khan N, Farooq U, Shah A J, Tareen S, Ahmad F, Khan T, Inhibitory effects of Glycyrrhiza glabra and its major constituent Glycyrrhizin on inflammation- associated corneal neovascularization, Evid. Based Complement Alternate Med, 2018, 8.
26. Rackova L, Jancinova V, Petrikova M, Drabikova K, Nosal R, Stefek M, Kovácová M, Mechanism of anti-inflammatory action of liquorice extract and glycyrrhizin. Natural Product Research, 2007, 21(14), 1234–1241.
27. Biondi D M, Rocco C, Ruberto G, New dihydrostilbene derivatives from the leaves of Glycyrrhiza glabra and evaluation of their antioxidant activity. Journal of Natural Products, 2003; 66(4): 477–480.
28. Haraguchi H, Ishikawa H, Mizutani K, Tamura Y, Kinoshita T, Antioxidative and superoxide scavenging activities of retrochalcones in Glycyrrhiza inflata. Bioorganic & Medicinal Chemistry, 1948; 6(3): 339–347.
29. Xuying W, Ming L, Xiao dong L, Ping H, Hepatoprotective and antihepatocarcinogenic effects of glycyrrhizin and matrine, J Chemico Biological Interac, 2009; 181(1): 15-19. https://doi.org/10.1016/j.cbi.2009.04.013
30. Sianne S, Fanie R V H, Antimalarial activity of plant metabolites, Nat Prod Rep, 2002; 19: 675-692. https://doi.org/10.3390/ijms19051382
31. Hojoa H, Satob J, Antifungal Activity of Licorice (Glycyrrhiza glabra) and potential applications in beverage foods Food Ingredients J Japan 2002; 203. https://doi.org/10.1016/j.apsb.2015.05.005
32. Ju HS, Li X J, Zhao B L, Han Z W, Xin W, Effects of Glycyrrhiza Flavonoids on lipid peroxidation and active oxygen radicals, Acta Pharm Sinicia, 1989; 24(11): 807-812.
33. Krausse R, Bielenberg J, Blaschek W, Ullmann U. In anti- Helicobacter pylori activity of Extractum liquiritiae glycyrrhizin and its

metabolites, J Antimicrob Chemother, 2004; 54(1): 243-246.

34. Ohuchi K, Tsurufuji A, A study of the anti-inflammatory mechanism of glycyrrhizin, Mino Med Rev, 1982; 27: 188- 193.
35. MendesSilva W, Assafim M, Ruta B, Monteiro R Q, Guimaraes J A, Zingali R B, Antithrombotic effect of Glycyrrhizin a plant-derived thrombin inhibitor, ThrombRes 2003; 112: 93-98.

    https://doi.org/10.1016/j.thromres.2003.10.014.
36. Dhingra D, Sharma A, Antidepressant-like activity ofGlycyrrhiza glabra L. in mouse models of immobility tests, Progress in Neuro-Psychopharmacology and Biological Psychiatry, 2006; 30(3): 449–454.
37. Chakravarthi K K, Avadhani R, Beneficial effect of aqueous root extract of Glycyrrhiza glabra on learning and memoryusing different behavioral models an experimental study, Journal of Natural Science, Biology and Medicine, 2013; 4(2): 420–425.
38. Yokota T, Nishio H, Kubota Y, Mizoguchi M, The inhibitory effect of glabridin from licorice extracts on melanogenesis and inflammation, Pigment Cell Research, 1998; 11(6): 355–361.
39. Hasanein P, Glabridin as a major active isoflavan from Glycyrrhiza glabra (licorice) reverses learning and memorydeficits in diabetic rats, Acta Physiological Hungarica, 2011;98(2): 221–230.
40. Plant encyclopaedia, Glycyrrhiza glabra (licorice / liquorice). http:// www. avogel. ch/en/plantencyclopaedia/glycyrrhiza_glabra.php .
41. The Plant list, A working list of all plant species, Glycyrrhiza glabra. http://www. theplantlist.org/tpl1.1/record/ild-7886
42. Pompei R, Pani A, Flore O, Marcialis M A, Loddo B, Antiviral activity of glycyrrhizic acid Experientia 1980; 36: 304. https://doi.org/10.1021/jm0493008
43. Kim Y W, Kang H E, Lee M G, Hwang S J, Kim S C, Lee C, Liquiritigenin a flavonoid aglycone from licorice has a choleretic effect and the ability to induce hepatic transporters and phase-II enzymes, Am J Physiol Gastrointest Liver Physiol, 2009; 296(2): 372-381. https://doi.org/10.1152/ajpgi.90524.2008.
44. Kuroda M, Mimaki Y, Sashida Y, Mae T, Kishida H, Nishiyama H, Tsukagawa M, Konishi E, Takahashi K, Kawada T, Nakagawa K, Kitahara M, Phenolics with PPAR–Ligand-binding activity obtained from Licorice (Glycyrrhiza uralensis roots) and ameliorative effects of Glycyrin on genetically diabetic KK-Ay mice, Bioorg Med Chem Lett, 2004; 55-61. https://doi.org/10.1016/j.bmcl.2003.09.052
45. Lee, C S, Kim Y J, Lee M S, Han E S, Lee S J, 18β- Glycyrrhetinic acid induces apoptotic cell death in SiHa cells and exhibits a synergistic effect against antibiotic anti-cancer drug toxicity. Life Sciences, 2008; 83(13–14): 481– 489.
46. Sharma, V, Agrawal R C, Shrivastava V K, Assessment of median lethal dose and anti-mutagenic effects of Glycyrrhiza glabra root extract against chemically induced micronucleus formation in Swiss albino mice, International Journal of Basic & Clinical Pharmacology, 2014; 3(2): 292
47. Deng Q P, Wang M J, Zeng X, Chen G G, Huang R Y, Effects of glycyrrhizin in a mouse model of lung adenocarcinoma, Cellular Physiology and Biochemistry, International Journal of Experimental Cellular Physiology Biochemistry Pharmacology, 2017; 41(4): 1383–1392.
48. Roy S D, Karmakar P R, Dash S, Chakraborty J, Das B, Hair growth stimulating effect and phytochemical evaluation of hydro-alcoholic extract of Glycyrrhiza glabra, Global J Res Med PLants Indigen Med, 2014; 3(2): 40-47.
49. Cronin H, Draelos Z D, Top 10 botanical ingredients in 2010 anti-aging creams, J Cosm Derm, 2010; 9(3): 218-225. https://doi.org/10.1111/j.1473-2165.2010.00516.
50. Mills S Y, Bone K, Principles and Practice of Phytotherapy, Modern Herbal Medicine, Churchill Livingstone, London, 2000.
51. www.banlab.com/healingherbs/yashti madhu.htm[12/09/2009]
52. Trivedi R, Sharma K, Hydroalcoholic extract of Glycyrrhiza glabra attenuates chronic fatigue stress induced behavioral alterations in mice, International Journal of Pharmaceutical & Biological Sciences, 2011; 2: 996-1001.
53. Bhandage A, Shevkar K, Vaishali Undale V, Evaluation of antinociceptive activity of roots of Glycyrrhiza glabra, Journal of Pharmaceutical Research, 2009; 2: 803-7.
54. Ai-Razzuqii R A M, Al-Hussaini J A,

Hepatoprotective effectof Glycyrrhiza glabra in CCl4 induced model in acute liver injury, Journal of Physiology & Pharmacology Advances, 2012; 2: 259-63.

55. Sowmya M, Kumar S, Antistress property of Glycyrrhiza glabra on stress induced Drosophila melanogaster, Journal of Stress Physiology & Biochemistry, 2010; 6: 18-27.
56. Sakr S, Shalaby S Y, Carbendazim induced testicular damage & oxidative stress in albino rats Ameliorative effectof liquorice aqueous extract, Toxicol Ind Health, 2012.
57. Rathi S G, Suthar M, Patel P, In vitro cytotoxic screening ofGlycyrrhiza glabra, Pharmacology, 2009; 1: 239-43.
58. Rastogi R P, Mehrotra B N, Compendium Indian medicinal plants, CDRI Lucknow, National Institute of Science & information resources N D, 1990-94; 6: 395-98
59. Nitalikar M, Munde K C, Dhore B V, Studies of antibacterialactivities of Glycyrrhiza glabra root extract, International Journal of Pharmaceutical Technology & Research, 2010; 2:899-901.