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A Review on Phytochemicals and Pharmacological effects reported in *Glycyrrhiza glabra* (Mulethi)

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ABSTRACT

One of the most significant sources of medications for humans has been plants. Due to the safety of natural ingredients, customers have been paying considerably greater attention to natural medicines in recent years. Moreover, there is a rise in industrial demand for plants that are used in herbal therapy and that could be added to meals, cosmetics, and medications. The herb *Glycyrrhiza glabra* Linn., which is a member of the Fabaceae family, has been utilized in ayurvedic medicines for centuries. Plant's secondary metabolites are used in many medicinal substances and are significant from a commercial standpoint. These plants' diverse therapeutic properties are probably explained by the presence of these phytochemical compounds. The goal of this work is to summarize the phytochemicals and their pharmacological effects which are reported in *Glycyrrhiza glabra*.

Key words*: Licorice, Glycyrrhiza glabra, Medicinal plant, Phytochemicals, Pharmacological effects.*

Introduction

Herbal medicines are getting popularized in developed and developing countries because of their lesser side effects and natural origin. Very important lifesaving drugs have been provided by medicinal plants in modern medicine. Plants also produce secondary metabolites which play a vital role in plant defense against herbivory, pests, pathogens, and abiotic stress are commercially important and used in pharmaceutical industries. The most commonly used phytochemicals are saponins, tannins, flavonoids, alkaloids, glycosides, steroids. These phytochemicals have been used as traditional medicine (Hill, 1952).

One of the oldest and most popular herbs in Ayurvedic medicine is *Glycyrrhiza glabra* Linn. It is used as a medicine as well as a flavorings ingredient in confections and to mask the unpleasant flavor of other medications (Biondi *et al*., 2005). It is a perennial herbaceous plant also called as licorice, mulethi, yashtimadhu, and sweet wood. It was foundnative to Western Asia, Northern Africa, and Eurasia (Shah *et al*., 2018). The primary chemical component, GLYCYRRHIZIN (Glycyrrhizin acid), a saponin which is fifty times sweeter than sugar, is what gives the substance its medicinal uses (Tang *et al*., 1992).

It is cultivated for its roots, leaves, and rhizomes (underground stem), which are the most important medicinal part of *Glycyrrhiza* as they have antioxidant, antimicrobial, anti-inflammatory, antiulcer properties (Asl and Hosseinzadeh, 2008). Mulethi root have different chemical compounds such as polysaccharides, triterpenoids, and certain polyphenols such as flavones, flavanones, chalcones, glabridin, liquirtin, etc. (Isbrucker*et al*., 2006; Wang *et al*., 2001; Chin *et al*., 2007). Mulethi has been used for generations to cure a variety of conditions, in-

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cluding rheumatism, allergic reactions, coughing, eczema, hepatitis, and sore throats (Aly *et al.,* 2005; Ates *et al.,* 2003). It is responsible for detoxification and protection of the liver. It has influential potential to exterminate inflammation in mouth ulcers and arthritis (Sanjai, 2005).

Table 1. Scientific classification of *Glycyrrhiza glabra*

Sr. No.	Kingdom	Plantae
1	Division	Angiospermae
2	Class	Dicotyledoneae
3	Order	Rosales
4	Family	Fabaceae (Leguminosae)
5	Genus	*Glycyrrhiza S*
6	Species	*glabra Linn.*

Scientific Classification

Phytochemistry and Bioactive Compounds

Phytochemicals are biologically active, natural occurring substances in plants that have protective and disease preventive properties. They are produced by plants in order of their own self defense against herbivory, pests, pathogens, and abiotic stress are commercially important and used in pharmaceutical industries. A very large number of chemical compounds are present in *Glycyrrhiza glabra.* In traditional medicine and folk applications, secondary plant metabolites were crucial in treating a variety of illnesses. In modern medicine, they contributed lead molecules for the creation of drugs to treat a range of illnesses, from cancer to migraine.

In recent years, the chemical compounds of *Glycyrrhiza glabra* were broadly reported by various authors (Hayashi *et al*., 2016; Siracusa*et al*., 2011). However, various studies were executed and found that licorice is a source of polysaccharides, proteins, resins, pectin, amino acids, gums, mineral salts (silicon, potassium, iron, zinc, calcium, copper, magnesium, selenium, manganese, phosphorus, and sodium), simple sugars, sterols, gums, and starches. Tannins, coumarins, estrogens, phytosterols (stigmasterol and sitosterol), glycosides, and vitamins (E, C, B1, B2, B3, B4, and B5) have also been reported (Wang *et al*., 2015).

Additionally, many bioactive substances have been discovered, primarily flavonoids, triterpenes, and saponins (Wang *et al*., 2015; Rizzato *et al.,* 2017). The bioactivity of licorice is thought to be caused by the presence of these chemicals. While the aglycones are present in *Glycyrrhiza glabra* as oleananes, the saponins are present as glucuronides. Geographical origins, harvesting, and processing practices may significantly alter these chemical constituent concentrations, which could have an impact on the medicinal properties of *Glycyrrhiza glabra* (Pastorino *et al.,* 2018).

Licorice's flavonoid content gives it its yellow color. The flavonoids that have been discovered fall under a variety of groups, including flavones, chalcones, flavanones, isoflavones, isoflavenes, flavanonols, and isoflavanones. The main flavonoids are glycosides of liquiritigenin (42,7-dihydroxyflavanone) and isoliquiritigenin (22,4,42-trihydroxychalcone), including liquiritinapioside, licuraside, and liquiritin (Rizzato *et al.,* 2017). Five additional flavonoids, including shinflavanone, prenyllicoflavone, 1-methoxyphaseolin, glucoliquiritinapioside, and shinpterocarpin, have been discovered in dried licorice roots. Licoflavanone and pinocembrin were also isolated from licorice leaves (Fukui *et al.,* 1988). The main isoflavone discovered, glabridin, makes up 0.08% to 0.35% of the dry weight of roots (Simmler *et al.,* 2013).

Isoprenoid-substituted coumarins, benzofurans, chromenes, flavonoids, coumestans, dihydrophenanthrenes, and dihydrostilbenes are among the minor phenolic chemicals. In addition, roots contain a variety of volatile substances that give them their distinctive smell, including pentanol, terpinen-4-ol, geraniol, hexanol, and -terpineol. Additionally abundant in benzoic acid, furfuryl formate, trimethyl pyrazine, maltol, propionic acid, furfuraldehyde, 1-methyl-2-formylpyrrole, and 2,3-butanediol is licorice essential oil (Chouitah *et al*., 2011). According to Tamir *et al*. (2001), glabridin, hispaglabridins A and B, and isoflavones all have estrogen-like action and antioxidant activity (Vaya *et al.,* 1997).

Physico- Chemical Characteristics

Physical properties or solvation properties associated with interactions with various media and characteristics or molecular qualities that define intrinsic chemical reactivity are referred to as physicochemical properties. Physical and chemical analysis of liquorice roots showed that their extractive values were: chloroform (10.56 1.53%), petroleum ether (4.67 0.23%), methanol (13.89 2.42%), and n-butanol (6.54 0.84%); their ash values were total (4.67 0.35%), water-soluble (6.54 0.22%), and acid insoluble (0.56

Table 2. List of Phytochemicals found in Glycyrrhiza Glabra

Sr. No.	Groups	Bioactive compounds	References
1	Triterpenoid	Glycyrrhizin	(Yu *et al*., 2015)
2	Aldehyde	Furfuraldehyde	(El-Saber Batiha *et al*., 2020)
3	Coumarin	Licocoumarin	(Sharma *et al*., 2018; Kinoshita *et al*., 2005)
4	Terpenoid	Glycycoumarin, Licopyranocoumarin,	
6		glabrocoumarone A and B	(Obolentseva *et al*., 1999)
7	Geraniol	Glycyrrhizic acid, 18-â-glycyrrhetinic acid	(El-Saber Batiha *et al*., 2020; G.R. Fenwick *et al*., 1990)
8		Alpha Terpineol	
		Geraniol	
9		Liquiritin, isoliquiritin, liquiritigenin	(Rizzato *et al*., 2017; J. Vaya *et al*., 1997; El-Saber Batiha *et al*., 2020; Zhang and Ye, 2009)
10		Glabrene, Glabridin	
11	Flavonoid	Rhamnoliquiritin	
		Glucoliquiritinapioside, Prenyllicoflavone A, Shrinflavonone, Shrinpterocarpin, 1-Methoxy-Phaseolin	
		Glisoflavone, Kanzonol R	
		Licochalcone A	(Tamir *et al*., 2001; Badr *et al*.,2013)
12		Hispaglabridin A and B, Licuraside, Glyzaglabrin	(Fenwick *et al*., 1990)
13		Hispaglabridin A and B, Licuraside,	(Fenwick *et al*., 1990; G. El-Saber Batiha *et al*., 2020)
14		Glyzaglabrin	
15		Propionic Acid, Benzoic Acid, Ethyl Linoleate	
16		Acetic Acid, Malic acid, Butyric Acid,	
17		Fumaric Acid, Citric Acid	
18		Semilicoisoflavone B,1-Methoxyficifolinol,	
19		Isoangustone A, Licoriphenone	
		Pentanol, Hexanol	
		2,3 Butanediol	

0.34%); their moisture content (0 (Husain *et al.,* 2005).

Pharmacological Activities

Licorice is one of the most popular and oldest plants used as herbal medicine in the world. *Glycyrrhiza glabra* is used both as medicine and also as a flavoring agentto disguise the unpleasant flavor of other medicines (Biondi *et al*., 2005). *Glycyrrhiza* species are described in the literature for their biological activities such as expectorant and anti-inflammatory, it controls coughing and has hormonal effects. Internally, it is used to treat Addison's disease, peptic ulcer, bronchitis, asthma and it is also used in steroid therapy and allergic complaints. It protects and detoxifies the liver (Cooper *et al*., 2007). Externally, it is used to treat eczema, shingles, and herpes. It is helpful in aplastic anemia and it lowers down the serum testosterone level in females. Licorice roots have both estrogenic and anti-estrogenic activity.

Licorice is an important herb for treating hormone-related problems in women. Roots of licorice are being used as a tonic and demulcent laxative emollient. It is also used in Genito-urinary diseases. Licorice is used as an energy- tonic, mainly for the stomach and spleen. Licorice is an important ingredient in medicinal oils for hemorrhagic diseases, rheumatism, epilepsy, paralysis. Licorice roots are also used for their demulcent property. It is also used to treat diarrhea, fever with anuria, and delirium (Kaur *et al*., 2013). It is also useful in asthma, flatulence, gout, sore throat, tonsillitis, epilepsy, fever, cough, hyperdipsia, leucorrhea, bleeding, swellings, skin allergies, hiccough, hoarseness, jaundice. It is also used in the vitiated condition of gastralgia, cephalgia, pharyngodynia, Vatadosha, and ophthalmopathy (Kaur *et al*., 2013).

Since ancient times, plants have been a major source of medicine in all cultures. In the traditional system, several indigenous plants are being used in the prevention, diagnosis, and elimination of acute and chronic diseases (Kamboj, 2000). The demand for herbal medicines is increasing across the globe because these medicines are safe, less expensive, easily accessible, efficacy, culturally acceptable and have lesser side effects. Thousands of plants have been reported to have pharmaceutical activities because of the presence of various bioactive compounds such as steroids, glycosides, alkaloids, flavonoids, terpenes, tannins and saponins, etc. (Beshbishy *et al*., 2019; Batiha *et al*., 2019; Batiha and Adeyemi *et al*., 2019). Medicinal plants are useful for curing human diseases and play an important in healing due to the presence of Phytochemical constituents. Thousands of such plants have been documented which can be used in drug development either pharmacopeial, non-pharmacopeial, or synthetic drug, that can be used to treat several human ailments (Beshbishy *et al*., 2019; Batiha and Alkazmi *et al*., 2020).

Glycyrrhiza glabra Linn. is a well-known medicinal plant used in the medical history of Ayurveda for its ethnopharmacological values to cure serious disorders. *Glycyrrhiza glabra*is used both as medicine and as a flavoring agent to disguise the unpleasant flavor of other medicines. Licorice belongs to the family Fabaceae also known as Leguminosae. It is a perennial herb commonly known as sweet wood, licorice, yashtimadhu, and Mulethi, etc. (Shah *et al*., 2018). The genus *Glycyrrhiza* consists of more than 30 species and is widely distributed throughout the world (Chopra *et al*., 2002).

Licorice has various medicinal uses and health benefits. It controls coughing and has hormonal effects. Internally, it is used to treat Addison's disease, peptic ulcer, bronchitis, asthma and it is also used in steroid therapy and allergic complaints. It protects and detoxifies the liver (Cooper *et al*., 2007). Externally, it is used to treat eczema, shingles, and herpes. It is helpful in aplastic anemia and it lowers down the serum testosterone level in females. Licorice roots have both estrogenic and anti-estrogenic activity. Mulethi extract is used in auto-immune conditions and has various therapeutic benefits in immunodeficiency conditions like AIDS.It is also useful in asthma, flatulence, gout, sore throat, tonsillitis, epilepsy, fever, cough, hyperdipsia, leucorrhea, bleeding, swellings, skin allergies, hiccough, hoarseness, jaundice. It is also used in the vitiated condition of gastralgia, cephalgia, pharyngodynia, Vatadosha, and ophthalmopathy (Kaur *et al*., 2013).

Licorice extracts have been utilized to treat chronic hepatitis and have therapeutic advantages against viruses in Japan for more than 60 years. Several DNA and RNA viruses have been demonstrated to be inhibited in their proliferation and cytopathology by glycyrrhizic and glycyrrhizin acid (Hattori *et al.,* 1989; Ito *et al.,* 1988). It exhibits higher anti-UV activity (Kato *et al.,* 2012), hepatitis A (Crance *et al*., 1990), and C (Van Rossum *et al*., 1999), as well as cytomegalovirus (CMV), according to an introductory report that discusses the isolation of

licopyranocoumarin and anti-HIV activity of (Numazaki *et al*.,1994).

Licorice is a key herb for treating female hormone-related issues. Licorice roots are employed as a tonic, demulcent, laxative, and emollient. Additionally, it's used for genito-urinary disorders. Licorice is mostly utilized for the stomach and spleen as an energy tonic. Licorice is a key component of oils used to treat hemorrhagic illnesses, rheumatism, epilepsy, and paralysis. Roots of licorice are also

Table 3A. Pharmacological activities reported from Glycyrrhiza glabra

Sl	Therapeutic Activity	Extract	Plant Part Used
1	Antimalarial activity	Alcoholic Extract	Leaves
2	Estrogenic activity	Alcoholic Extract	Whole plant

Table 3B. Pharmacological activities reported from Glycyrrhiza glabra

Sr. No.	Therapeutic Activity	Extract	Plant Part Used
1	Testicular toxicity	Aqueous Extract	Whole plant
2	Antiviral activity	Aqueous Extract	Whole plant
3	Memory enhancing activity	Aqueous Extract	Roots
4	Hepatoprotective activity	Aqueous Extract	Roots
5	Immunomodulatory activity	Aqueous Extract	Whole plant

Table 3C. Pharmacological activities reported from *Glycyrrhiza glabra*

Sr. No.	Therapeutic Activity	Extract	Plant Part Used
1	Antitussive activity	Ethanol Extract	Whole plant
2	Antinociceptive activity	Ethanol Extract	Whole plant
3	Antihyperglycemic activity	Ethanol Extract	Leaves
4	Anticancer activity	Ethanol Extract	Leaves
5	Antidyslipidaemic activity	Ethanol Extract	Roots

Table 3D. Pharmacological activities reported from *Glycyrrhiza glabra*

Sr. No.	Therapeutic Activity	Extract	Plant Part Used
1	Therapeutic Activity	Extract	Plant Part Used
2	Anti-inflammatory activity	Hydroalcoholic Extract	Leaves
3	Chronic fatigue stress	Hydroalcoholic Extract	Root

Table 3E. Pharmacological activities reported from *Glycyrrhiza glabra*

SR. No.	Therapeutic Activity	Extract	Plant Part Used
1	Antioxidant activity	Methanolic Extract	Leaves
2	Enzyme inhibiting activity	Methanolic Extract	Whole plant
3	Antimycobacterial activity	Methanolic Extract	Whole plant

Table 3F. Pharmacological activities reported from *Glycyrrhiza glabra*

SR. No.	Therapeutic Activity	Extract	Plant Part Used
1	Antistress activity	Alcoholic and Aqueous Extract	Whole plant
2	Antimicrobial activity	Ether, chloroform & acetone Extract	Leaves
3	Anticonvulsant activity	Hexane, ethanol & methanol Extract	Leaves
4	Antiulcer activity	Aqueous, acetone & ethanolic Extract	Leaves
5	Cytotoxic activity	CHCL3, methanol & aqueous Extract	Whole plant

employed for their demulcent qualities. Additionally, it is employed to treat delirium, fever with anuria, and diarrhoea (Kaur *et al*., 2013).

It has been discovered after several years of research that glycyrrhizin breaks down in the gut and has anti-inflammatory effects comparable to those of hydrocortisone and other corticosteroid hormones. The result is caused by the kidney and liver breaking down steroids less quickly and the adrenal glands stimulating the production of hormones. Treatment of chronic hepatitis and liver cirrhosis with glycyrrhizin is successful (Khare 2004).

Licorice is reported to have antiulcer, antidiabetic, antiviral, anti-malarial, anti-fungal, immunestimulant, anticonvulsant, anticancer, anti-oxidant, anti-thrombin, antithrombotic, anti-bacterial, antiallergenic, and expectorant activities (Zore, 2005; Sahu and Vaghela, 2011). Roots of licorice were also found to have hypotensive, hepatoprotective, memory-strengthening, anti-depressant, and spasmolytic activity (Kaur *et al*., 2013). Licorice is also used in the management of dementia, neurodegenerative disorders, impaired learning, and Alzheimer's disease (Chakravarthi *et al*., 2012).

Pharmacological Effects

Conclusion

Due to the fact that allopathic medications have greater adverse effects than phytopharmaceuticals, their demand has increased globally. The choice of plant for additional phytochemical and pharmacological research can be made on the strength of this information. *Glycyrrhiza glabra* plant has been widely utilised in traditional medicine and as an ingredient in food products, especially as a flavouring and sweetening agent. In particular, microbial/viral infection, cancer, and skin irritation are treated and prevented with the help of the plant. Flavonoids are the most significant bioactive substances and are in charge of the majority of biological processes. Nu-

Table 4. Chemical compounds responsible for Glycyrrhiza Glabra Efficacy

Sr. No.	Activities	Chemical Component	Category	References
1	Estrogenic activity	Glabrene, liquiritigenin	Isoflavan, flavanone	(Kaur *et al*., 2013)
2	Antioxidant	Glabridin, licochalcone, isoliquiritigenin, licocoumarin	Flavonoid, chalcone	(Karahan *et al*., 2016; Sharma *et al*., 2013)
3	Antiulcer	Glycyrrhizic acid, glabridin	Flavonoid and triterpenoid saponin	(Massomeh *et al*., 2007)
4	Immunostimulating activity	Glycyrrhizin	Triterpenoid saponin	(Dhingra *et al*.,2004)
5	Antiallergic	Glycyrrhizin	Triterpenoid saponin	(Shin *et al*.,2007)
6	Hepatocellular carcinoma	Glycyrrhizin	Triterpenoid saponin glycoside	(Kaur *et al*.,2013)
7	Chronic hepatitis C	Glycyrrhizin	Triterpenoid saponin glycoside	(Kaur *et al*., 2013)
8	Anti-inflammatory	Glycyrrhizin and glycyrrhetic A	Flavonoid	(Harwansh *et al*., 2011; Sheela 2006)
9	Antithrombin activity	Glycyrrhizin, isoliquiritigenin	Triterpenoid saponin glycoside	(Kaur *et al*., 2013)
10	Antimalarial	Glycyrrhizin, licochalcone, glycyrrhetinic acid	Flavonoid and triterpenoid	(Mi-Ichi *et al*., 2005)
11	Analgesic & uterine relaxant	isoliquiritigenin	Flavonoid	(Kaur *et al*., 2013)
12	Anticancer	Licochalcone A	Flavonoid	(Yoon *et al*., 2005)
13	Uterine relaxant and analgesic	Licocoumarin, licochalcone, isoliquiritigenin, and glabridin	Coumarin and flavonoids	(Awate *et al*., 2012)
14	Antimicrobial	Liquiritigenin and glabrene	Flavonoid	(Wang *et al*., 2015;
15	Corticosteroidal activity	Liquiritigenin, glycyrrhizin, and 18β-glycyrrhetinic acid	Flavonoid and triterpenoid saponin	(Yang *et al*., 2012)
16	Spasmolytic	liquiritin	Flavonoid	(Kaur *et al*., 2013)

merous phytochemicals, such as glycyrrhizin, 18-glycyrrhetinic acid, glabrin A and B, or isoflavones, have been discovered and linked to the biological activities mentioned, such as antioxidant, antiviral, antimicrobial, anticancer, or antiinflammatory activities as well as immunostimulating activity. In general, these practises are consistent with folk medicine and traditional knowledge. It is true that licorice has minimal toxicities and side effects, most of them are related to fluid retention and hypertension. One could draw the conclusion that the existence of diverse bioactive chemicals explains why traditional healers use the entire plant as a treatment for a variety of diseases. As a result, it is suggested as a plant with potential in medicine. Compared to chemically produced drugs, using *Glycyrrhiza glabra* as a herbal treatment has greater advantages.

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