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A COMPREHENSIVE REVIEW ON ANTI-LIPIDEMIC ACTIVITY OF GLYCYRRHIZA GLABRA

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ABSTRACT:
Hyperlipidemic is a significant risk factor for cardiovascular diseases, including atherosclerosis, stroke, and coronary artery disease. Conventional lipid lowering drugs such as statins and fibrates are effective but may cause adverse effects. Promoting the search for natural alternatives to synthetic lipid-lowering drugs. Indigenous plants have been traditionally used in various cultures for their medicinal properties, including lipid lowering effects. This study reviews and evaluates the antilipidemic potential of selected indigenous plants, focusing on their bioactive compounds, mechanism of action and efficacy in preclinical and clinical studies. Key phytochemicals such as flavonoids, polyphenols, saponins, and alkaloids have shown a promising lipid lowering effect by modulating lipid metabolism, reducing cholesterol absorption, and enhancing antioxidant activity. Experimental and clinical studies indicates that plant extract from species like Terminalia arjuna, Allium sativum, Trigonella foenum-graecum, Camelia sinensis and Glycyrrhiza glabra (Licorice) significantly lower total cholesterol, LDL, and triglyceride levels while increasing HDL levels. This study examines the lipid-lowering activity of Glycyrrhiza glabra by analyzing its bioactive constituents and their mechanism of action. Key phytochemicals such glycyrrhizin, flavonoids, and saponins contribute to lipid metabolism regulation by cholesterol synthesis, enhancing bile acid secretion and exerting antioxidant and anti-inflammatory effects. Experimental and clinical studies indicates that the licorice extract significantly reduces low-density lipoprotein (LDL), and triglycerides while increasing high-density lipoprotein (HDL) levels. This finding suggests that glycyrrhiza glabra could serves as a natural alternative for managing hyperlipidemia. However, further clinical studies are required to establish standardized dosage and evaluate long-term safety and efficacy.

KEYWORDS:
Cholesterol, Lipids, Hyperlipidemia, Glycyrrhiza glabra, Phytochemicals

INTRODUCTION:
Atherosclerotic cardiovascular disease is thought to be caused by lipid problems linked to hyperlipidemia. When treating patients with hyperlipidemia, the primary goal is to lower the risk of causes of ischemic heart attack or other cardiovascular disease.[1] In simple words hyperlipidemia can caused by the raised serum TC, TG, VLDL, LDL and IDL which causes various complications such as atherosclerosis, premature coronary artery disease, stroke, heart attack, myocardial infarction and pancreatitis.[2] Even though variety of synthetic medications are utilized in treatment, research is currently being done to find better medications, particularly from the plant kingdom. In this context, numerous therapeutic plants have been investigated.[3] Because of their safe and effective therapeutic effects, medicinal plants have long been regarded as a healthy source of treatment. Several medicinal plants remedies were used to treat hyperlipidemia; these reduced blood lipids through a variety of mechanism, such as blocking fatty acids synthase expression, reducing the release of free fatty acids, blocking HMG-CoA reductase, increasing the excretion of fat and cholesterol in the faces, blocking pancreatic lipase activity, and blocking the absorption of cholesterol. [4-6] Current method for reducing blood cholesterol levels include food control, weight exercise, behavior modifications, and medication therapy.[7]There are pharmaceutical products on the market that effectively lower cholesterol levels; these may be helpful in treating high cholesterol, but they are quite costly and have serious adverse effects.[8] According to epidemiological research, there is a strong positive correlation between coronary artery disease(CAD) and obesity, sex, smoking, hypertension, and plasma cholesterol levels.[9] One of the most significant contributing elements to the atherosclerosis is diet. Vegetarian diets are known to decrease the progression of atherosclerosis, while high-cholesterol diets accelerate it. Atherosclerosis is characterized by thickening and hardness of the arteries as well as loss of flexibility of the inner artery wall. This disorder is gradual, beginning in childhood and manifesting clinically in middle and old life. Atherosclerosis is caused by three main biological process: 1) The aggregation of smooth muscles cells, macrophages, and T lymphocytes; 2) The smooth muscle cells' production of connective matrix; and 3) The buildup of lipids in the cells and the connective tissue surrounding the cells, primarily in the form of free cholesterol and cholesterol ester.[10] Plants have been long been used as a plentiful source of safe and efficient

medications. Up to 80% of people worldwide still rely on traditional medications today, according to the WHO. Herbal medicines are completed, branded pharmaceuticals product that include aerial or subterranean plant parts, other plant elements, or a combination of these, either in their raw form or as plant preparations.[11] Many components, including flavonoids, sesquiterpenes lactone, terpenoids, alkaloids, alkenyl phenols, provide certain plants their beneficial therapeutic qualities.[12] Numerous indigenous systems, including siddha(600), Ayurveda(700), Unani(700), and Allopathy(30) plant species for various illness, list therapeutic plants. Approximately 3,000 of the 17,000 species of medicinal plants that have been identified are utilized in the medicinal industry, according to another estimate. The extensive use of herbal products and aqueous extracts of various plants for the treatment of various illness is also described in the Indian Vedas.[13] Compared to other plant component, like more than 30% of a medicinal plants root portion is utilized in various procedures. India's medicinal plant-based pharmaceutical industry is expanding quickly, but it faces several challenges. Presently utilized hypolipidemic medications have a number of negative side effects, and discontinuation is linked to rebound symptoms, which herbal medicines do not exhibit.[14]

- **Lipids:** The limited solubility of lipids in water and their great solubility in nonpolar (organic) solvents set them apart as a diverse class of compounds. They are essential as energy storage and respiratory substrate, as structural components of cells, as vitamins, as hormones, for the protection of internal organs, for heat conservation, for digestion, and for lactation.[15]

The major lipids found in the blood stream are

- Cholesterol.
- Cholesterol esters,
- Triglycerides
- Phospholipids

- **Cholesterol**

Cholesterol is a lipid that helps your body perform many important jobs. The total cholesterol range is less than 200 mg/dL. The cholesterol is a waxy, fat-like substance essential for good health, produced by the liver and found in all cells, as well as in certain foods, that's needed for building healthy cells, making hormones, and digesting food. But high levels can be dangerous.[16] Over twenty enzymes-catalyzed processes are involved in the multistep processes of cholesterol production, which mostly occurs in the liver and the intestine for the producing cholesterol from acetate. In the production of a cholesterol the rate limiting process is 3-hydroxy-3-metylglutaryl-CoA is the catalyzing agent. One such enzymatic process is (HMG-CoA) reductase. It has been employed as a statin medicinal target therapy. The body uses cholesterol as a starting point for the mending process. This explains why cholesterol and a number of other substances, including calcium and collagen, are present in the damaged artery regions (as in atherosclerosis). Transporters, or lipoproteins, such as LDL and HDL, help carry cholesterol through the blood. Cholesterol is carried out by low density lipoprotein carrier from liver to the cells, tissues, and glands in order to carry out its numerous vital bodily activities. High density lipoprotein carriers are responsible for the reverse transfer of cholesterol from cells and tissue to the liver.[17]

- **Low Density Lipoprotein**

This lipoprotein keeps its cholesterol levels high. Low Density Lipoprotein also refers to bad cholesterol and the range of bad cholesterol is less than 100 mg/Dl is optimal, with 100-129 mg/dL considered near-optimal. This contact is made possibly the protein layer, which enables the tissues to the employ the cholesterol and LDL receptors. Low density lipoproteins are converted to cholesterol in organs like the liver and the inner layer of the artery wall. Low-density lipoprotein cholesterol (LDL) is regarded as bad cholesterol because free radicals, which are highly reactive and oxidative substances, can oxidize LDL and aid in the formation of atherosclerotic plaque in the arteries.[18]

- **High Density Lipoprotein**

High density lipoprotein is regarded as good cholesterol because it circulates throughout the body, gathers excess cholesterol from tissues, mature, and returns to the liver, where it is recognized by its lipoprotein. The range of good cholesterol is 60 mg/dL or higher is desirable. The liver also produces another type of lipoprotein called high density lipoprotein, which collects excess cholesterol that cells metabolized cholesterol cannot use. The enzyme lecithin-cholesterol acyltransferase (LCAT) is in charge of transferring excess cholesterol back to the HDL molecule. HDL cholesterol absorbs unused cholesterol from arteries, the liver, and the other tissues.[19]

Types of cholesterol and their ranges :-

Sr. No.	Types of Cholesterol	Range of Cholesterol
1.	Total Cholesterol	Less than 200 mg/dL
2.	Low density lipoprotein cholesterol	Less than 100 mg /dL
3.	High density lipoprotein cholesterol	Greater than 60 mg/dL
4.	Triglycerides	Less than 150 mg/dL

- **Types of Hyperlipidemias**

Hyperlipidemia can be broadly classified into two types that are as follows:

- Primary Hyperlipidemia

  Primary hyperlipidemia is also seen as familial due to genetic abnormality. It may be polygenic, meaning it has a several gene deficiencies, or monogenic meaning it has just one gene flow. Fredrickson's classification, which summarizes the aberrant lipoproteins patterns, can be used to categorize primary hyperlipidemia.

- Secondary Hyperlipidemia
  Numerous conditions, including diabetes, chronic alcoholism, hyperthyroidism, nephrotic syndrome, chronic kidney illness, and the use of medications including beta blockers, corticosteroids, and oral contraceptives, are linked to secondary or acquired causes of hyperlipidemia (Stone, 1994). An atherogenic lipoprotein profile with an increased risk of cardiovascular disorders and acute pancreatitis might result from secondary sources.[20]

- **Symptoms of Hyperlipidemia**

Although hyperlipidemia typically doesn't have any overt symptoms, they are typically found during routine exams or when the condition is at risk for a heart attack or stroke. Xanthomas are cholesterol deposits that can grow under the skin, particularly around the eyes, in patients with high blood cholesterols levels or those with family variants of the illness. In addition, individual with high triglycerides levels may get many pimple-like lesions at various body lotion [21]

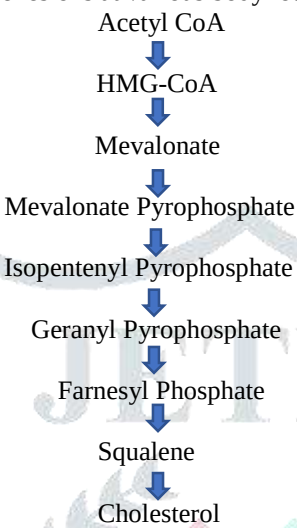

Fig. (1). Cholesterol Synthesis Pathway

- **Drug therapy for hyperlipidemia [22]**

Drugs	Effects on lipids
Levostatin	Decrease Triglycerides
Simvastatin	Decrease Low Density Lipoprotein
Atorvastatin	Increase High Density Lipoprotein
Cholestyramine	Decreases Low Density Lipoprotein
Colestipol	Increase High Density Lipoprotein
Gemfibrozil	Decrease Triglycerides
Bezafibrate	Decrease Low Density Lipoprotein
Fenofibrate	Decrease Triglycerides
Niacin	Decrease Low Density Lipoprotein

- **Pathophysiology of Hyperlipidemia**

According to recent research and reviews, endothelial damage to the blood vessels causes nitric oxides to be lost in the damaged area, which in turn causes an increase in the inflammatory response surrounding the affected area and the accumulation of lipids in the deepest layer of the endothelial wall. Macrophages will then engulf the lipids and form what is known as foam cell with cholesterol. This is how hyperlipidemia begins. Foam cell development will result in mitochondrial malfunction, necrosis and apoptosis. Simultaneously, the smooth muscle cells enclose the foam cell, causing fibrotic plaque and eliminating the foamy cells.

On the other hand, thrombosis and plaque rupture are caused by tissue stimuli that stimulate platelets activity. The development of plaque might happen slowly, causing blood vessels stenosis, or quickly, obstructing the blood vessels. Lipid plaque continues to be the primary causes of CVD development and patient health status declines in both processes.

Patient with hyperlipidemia may experience tendon dysfunction, particularly in the patellar tendon, in addition to CVD. This is due to the fact that over time, hyperlipidemia will increase the amount of macrophages in the tendon, causing collagen fiber destruction and lipids to replace, making the tendon less functional and more vulnerable to damage.[23]

- **Glycyrrhiza Glabra**

For thousands of years, Glycyrrhiza glabra has been recognized in pharmacy. It was regarded as a first-class medication in traditional Chinese pharmacy, and prolonged use was associated with its rejuvenating effects.[24] Licorice was widely utilized in ancient Egypt, Greece, and Rome. It was something Theophrastus mentioned. Code Hammurabi (2100BC) contains the oldest known mention of its

application in medicine.[25] Glycyrrhiza is a diverse genus with approximately 30 species found worldwide.[26] Glycyrrhiza genus plants are widespread in the Mediterranean, Southern and Central Russia, and Asia, with small presence in Iran. Various kinds are grown throughout Europe, Syria, Asia, the United Kingdom, the United State, Italy, France, Germany, Spain, China, the Middle East, Central and Southern Western Asia, the Mediterranean basin of Africa, South Europe, Afghanistan, and Northern India (Punjab and Sub-Himalayan regions). Large-scale commercial growing is possible in Spain, Sicily, and England. [27,28]

In the Unani medical system, Glycyrrhiza Glabra, a perennial plant belonging to family Fabaceae, and is commonly referred to as Asl-Us-Soos. The oldest medicinal plant, Glycyrrhiza Glabra is found across warm, subtropical climates and is utilized in many traditional medicinal systems for its therapeutic benefits. The medication is commonly referred to as licorice roots have many branches that are red or lemon in color on the outside and yellowish or pale yellow on the interior. The wood is wrinkled and fibrous, and glycyrrhizin, which is 50 times sweeter than sugar, gives the root their sweet flavor.[29]

Licorice, commonly used in respiratory, tremor, gastritis, peptic ulcers, etc. in conventional Persian medications. [30] It is beneficial for improving stomach and upper respiratory tract blockage, as well as ulcer prevention.[31] It improves cognition, acts as an antidepressant, and lowers cholesterol levels.[32] Although it can lessen diabetes symptoms such as frequent urination and polydipsia, it does not alter blood glucose levels. [33]

Fig. No. 2

1]Botanical description

1.1] Classification [34]

Kingdom	plantae
Divisions	Angiosperms
Class	Dicotyledonae
Order	Fabales
Family	Fabaceae
Genus	Glycyrrhiza
Species	G. glabra

1.2] Regional Names [35]

Gujarati	Jethimadhu
Sanskrit	Yashti-madhuh, Madhuka
Hindi	Jothi-madh, Mulhati
Bengali	Jastimadhu, Jaishbomodhu
Malayalam	Iratimadhuran
Oriya	Jatimadhu
Tamil	Antimadhuram
English	Licorice, Liquorice, Sweet, Wood
Marathi	Jeshtamadhu
Telugu	Antimadhuranu,
Kannada	Yastimadhuka, antimaddhura
Persia	Ausareha mahaka
Parts used	Roots and Rhizomes

1.3] Morphology

Licorice is perennial herb or shrub with a rough top and branches from the base. It can reach a height of up to 2.5 meters.[36]

a) Stem

Glycyrrhiza stems are 50-150 cm tall, with white hairs, glandular punctuation, scaly density, and woody base.[37]

b) Leaves

The leaves are alternating, compound pinnately odd, and grow up to 10-20 cm long. 3-8 leaflets with tiny, drooping stipules [38]

Flowers

The blooms are thin, with upright axillary inflorescences around 10-15 cm long. The cultivation period is My-June.[39] They are generally papilionaceous, glandular, lavender to violet in color, and have a short pedicle. Individual flowers measure 1-1.5 cm long. The calyx is small, campanula, with acuminate ends and glandular hairs. [48] Petals: Carina petals are narrow, pointed, and not united.[41]

c) Fruits

The pods are reddish brown and compressed, measuring 1.5-2.5 cm long and 4-6 mm diameter. The cultivation period is July-September. [40] The plant is long, erect, glabrous, flat with thick sutures, glandular, reticulate-pitted, and has 3-5 brown seeds with smooth reniform shapes.[42]

d) Roots

The roots are lengthy, cylindrical, and thick, with several branches. The officinal portion of a plant is its roots and rhizomes, which can be up to 1m long and 50-20mm in diameter. The bark is brownish gray to dark brown and wrinkled longitudinally, with small round or transverse rootlet-scars in roots and dark buds in rhizomes. Liquorice/licorice is a commercial medication made from the dried and cut woody stolon's, which can exceed 8m in length. It can be peeled or unpeeled

The root parts shatter with a fibrous fracture, revealing a yellowish core with a characteristic sweet taste and smell. [43,44]

Fig. No. 3

e) Cultivation

Liquorice grows best in well-drained soils with full light and can be picked after 2-3 years of sowing in autumn. Countries that produce Liquorice include India, Iraq, Uzbekistan, Pakistan, The People's Republic of China, Turkey, Turkmenistan, and Azerbaijan. Licorice thrives in sandy, rich, or clayey soil near a stream or river with enough water supply, or can be irrigated for farming. [45]

2)Chemical Constituents

Numerous chemical constituents, primarily flavonoids, sugar, amino acids, starch, resins, sterols, and essential oils, are found in Glycyrrhiza Glabra, or licorice root. Glycyrrhizin or glycyrrhizic acid, licorice root, and additional triterpenes such as liquiritic acid, glycyrretol, glabrolide, isoglaborlide, and liquirce acid are the primary components of Glycyrrhiza Glabra, which is primarily constituted of triterpenes saponins (4–20%). Liquiritin, liquiritigenin, hamnoliquiritin, neoliquiritin, chelcones isoliquiritin, isoliquiritigenin, neoisoliquiritin, licuraside, glabrolide, licoflavonol, 5,8-dihydroxy-flavone-7-O-beeta-D-glucuronide, and others are among the flavonoids and chalcones that were identified from Glycyrrhiza Glabra. Glycyrrhiza Glabra also contains 4% glucose, 5% sucrose, resins, essential oils, sterols, steroids, amino acids, starches, pectin, mucilage, lipid, and tennin, among other substances. A few heavy metals, such as cadmium, lead, arsenic, and mercury, are also found in Glycyrrhiza Glabra. The trace elements can also be found in licorice root powder. Glycyrrhiza Glabra has the following elements: potassium: 0.66%, calcium: 1.87%, sulfur: 0.06%, iron: 0.14%, aluminum: 0.05%, phosphorous: 0.06%, silicon: 0.12%, magnesium: 0.17%, and sodium: 0.04%.[29]

Glycyrrhiza glabra roots have yielded several components, including a water-soluble, physiologically active compound that makes up 40–50% of the dry material weight. The components of this complex include gums, mucilage (rhizome), protein, resins, starches, sterols, volatile oils, tannins, glycosides, triterpene, saponin, flavonoids, polysaccharides, pectins, simple sugars, amino acids, mineral salts, asparagines, bitters, essential oil, fat, female hormone estrogen, and a variety of other substances. [46,47] The triterpenoid component glycyrrhizin (Fig. 3) is responsible for the sweet flavor of licorice root. This substance is a combination of glycyrrhizic acid salts of

potassium, calcium, and magnesium that ranges from 2 to 25%. Glycyrrhizic acid is a naturally occurring saponin that is made up of two glucuronic acid molecules, a hydrophilic portion, and a hydrophobic portion called glycyrrhetic acid. (Fig. 4) [48]
Liquiritin (Fig. 5), isoliquiritin (Fig. 6), a chalcone, and other chemicals are among the flavonoids that give licorice its yellow hue. [49] Significant antioxidant action is exhibited by the isoflavones, glabridin (Fig. 7), and hispaglabridins A and B. [50] Both glabridin and glabrene both have properties similar to those of estrogen. [51]

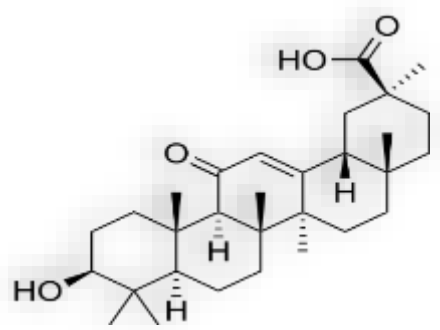

Fig.4- Glycyrrhetic acid

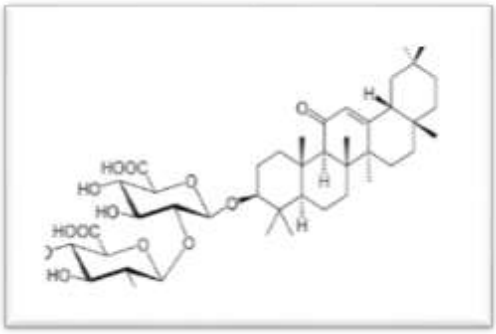

Fig.5- Glycyrrhizin

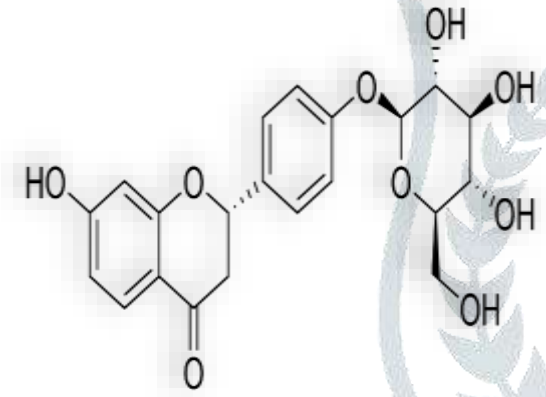

Fig. Liquiritin

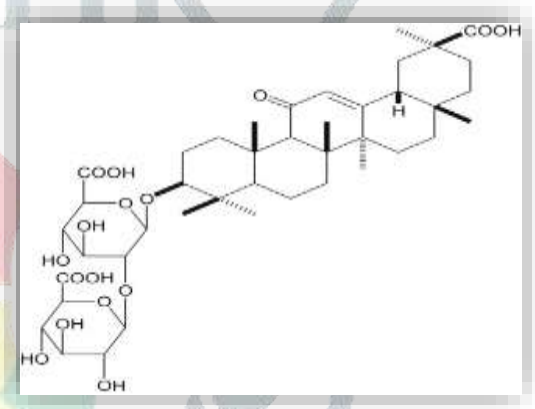

Fig. Isoliquiritin

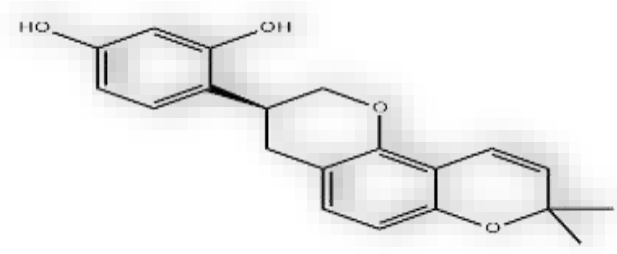

Fig.7.- Glabridin

Table: List of Chemical Constituents of Glycyrrhiza Glabra and their pharmacological actions [29]

Sr no.	Active Chemical constituents Glycyrrhiza Glabra	Therapeutic uses
1	Glycyrrhizic acid, Glabridin, glabrene	Gastroprotective activity or Acid blocker
2	Glabridin	Antimycotic and TB
3	Isoliquiritigenin, coumarin, Licochalcone, glabridin,	Antioxidant activity, sedative, Reduce swelling & uterotonic activity
4	Glabridin	Mental stimulation activity or Brain boosting elixir activity
5	18-β- glycyrrhetic acid,	Anti-histaminic activity
6	Glycyrrhizin	Antitumor activity, liver cell carcinoma, Cough Suppressant activity, Anti-retroviral, liver protective activity,
7	liquiritoside, Licochalcone, Glycyrrhetic acid,	Anti-histaminic activity
8	Glycyrrhetic acid,	Anti- Tumor activity
9	Licochalcone A	Malarial parasite inhibition of all type of malaria
10	Glycyrrhetinic acid, licochalcones	Viral suppression activity
11	18-β-glycyrrhetinic acid, glycyrrhizin	Anti-diabetic activity
12	Glycyrrhetinic acid	Immune activation activity
13	Liquiritin	Antispasmodic activity in Menstruation and PCOD Diseases
14	Rhamnoglucoside	Myorelaxant
15	Glabrene, liquiritigenin	Estrogen receptor activity

3) Therapeutic Uses

Numerous medicinal properties of licorice have been discovered by research; a recent review paper outlined the pharmacological properties and explored possible applications of Glycyrrhiza glabra for antitumor, antimicrobial, antiviral, anti-inflammatory, immunoregulatory, and numerous other properties that support the healing and defense of the neurological, gastrointestinal, respiratory, endocrine, and cardiovascular systems.[52]

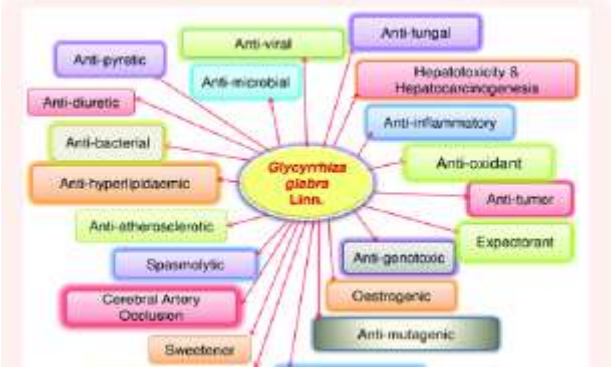

Fig. Potential therapeutic activity and traditional uses of Glycyrrhiza Glabra Linn.

Figure 3 summarizes the traditional applications and known possible therapeutic actions of Glycyrrhiza glabra Linn. By suppressing TNF-α and caspase-3, a crucial cytokine that plays a major role in mediating hepatic apoptosis and necrosis in LPS/D-GalN-induced liver failure, glycyrrhizin, a triterpene glycoside derived from the root of Glycyrrhiza labra, has beneficial effects on the inhibition of hepatic apoptosis and necrosis[53] and matrix metalloproteinase-9 down-regulation in liver damage brought on by lipopolysaccharide/D-galactosamine.[54] Glycyrrhiza glabra hydro-methanolic root extract has strong antibacterial properties since it

contains secondary metabolites such alkaloids, flavonoids, saponins, and others. Aqueous, methanolic, or ethanolic extracts of Glycyrrhiza glabra have been shown in numerous in-vitro investigations to exhibit inhibitory action against a variety of bacterial species. Using the well and disc diffusion method, the in-vitro inhibitory activity of Glycyrrhiza glabra extract against enterotoxigenic E. coli, Shigella sonnei, S. flexneri, Salmonella typhi, and S. paratyphi B was examined. Glycyrrhiza glabra extract was found to inhibit all strains at concentrations greater than 7.5%, indicating that it might be utilized as a substitute herbal antibacterial agent.[55]

The in-vitro anti-bacterial activity of ethanolic extract of Glycyrrhiza glabra against oral microbes such as, Streptococcus mutans, S. sanguis, S. salivarius, S. mitis and Lactobacillus acidophilis using disc diffusion method concluded that ethanolic extract of Glycyrrhiza glabra (500µg/disc) was more effective with high zone of inhibition among various bacterial species in comparison to aqueous extract of Glycyrrhiza glabra. This suggested that Glycyrrhiza glabra extract could be utilized as an herbal remedy for oral infections and dentistry.[56]

Glycyrrhiza glabra root extracts, both aqueous and methanolic, were found to have antibacterial properties against Streptococcus agalactiae and Strephylococcus aureus in vitro.[57]

Using the well and disc method, researchers have recently shown that the root and leaf extract of Glycyrrhiza glabra has strong antibacterial activity against E. coli and Pseudomonas aeruginosa, but ineffective against Enterobacter cloacae and Klebsiella sp. Instead, both extracts were ineffective against these bacteria. Consequently, Glycyrrhiza glabra may be helpful in treating rotavirus-induced diarrhea.[58]

The active ingredient in Liquorice extract, glabridin (3-(2',4'-dihydroxyphenyl)-8-dimethylpyrano[8,7-e] chroman), is responsible for the extract's antifungal properties. It also exhibits resistance-modifying properties against drug-resistant mutants of Aspergillus Niger and Candida albicans.[59] It was also discovered that 18-β-glycyrrhetic acid, an active component of Glycyrrhiza glabra, had effective anti-malarial properties both in vitro and in vivo.[60]

The cytotoxicity of a polyphenol compound that is taken from Glycyrrhiza glabra and used to treat prostate and breast cancer has been assessed by researchers.[61] primary mucosal cells that are not malignant and head and neck cancer cell lines,[62] and against several cancer cell lines, including those of liver cancer (HepG2), lung adenocarcinoma (A549), and immortal human keratinocyte (HaCaT).[63] Numerous in-vitro investigations have demonstrated that Glycyrrhiza glabra has immunomodulatory effects at concentrations of 100µg/ml. It promotes the production of TCD69N macrophages and TCD69N lymphocytes from human granulocytes. In-vivo research has shown that Glycyrrhiza glabra maintains the ascent for autoimmune disease-related complexes. Researchers have investigated the antihyperlipidemic and antihyperglycemic properties of Glycyrrhiza glabra ethanolic extract against streptozotocin and high-fat diet-induced diabetic rats. To investigate the antihyperlipidemic effects, a number of physical, biochemical, and histomorphological characteristics were assessed.[64]

In a separate investigation, streptozotocin (40 mg/kg body weight)-induced diabetic rats showed a satisfactory anti-hyperglycemic effect when given an oral dose of 100 mg/kg of 18-β-glycyrrhetic acid, which is equivalent to glibenclamide.[65]

4) Medical Application

Even if a lot of pharmaceutical inspections have been done based on ingredient presence, there is still more that may be looked at, studied, and investigated. Numerous plant species have been studied in the literature for its vital properties, such as anti-inflammatory and anti-expectorant properties, which aid in the management of cough and hormonal impacts. Additionally, it aids in liver detoxification and protection. It is used internally in medications for peptic ulcers, pneumonia, arthritis, allergies, steroid treatments, and Addison's illness [66]. Below is a summary of the different activities:

- **Antitussive and Expectorant Activity**

It was discovered that the licorice extract and powder worked well for treating bronchial catarrh, cough, and sore throat. It has been demonstrated that licorice relieves sore throats just as effectively as codeine. It has expectorant properties and reduces inflammation. Glycyrrhiza is the source of the semi-synthetic chemical carbenoxolone, which promotes the release of stomach mucus. Glycyrrhizin is what gives licorice its calming effects. The active ingredient in licorice's methanolic extract, Liquiritin apioside, prevents coughing brought on by capsaicin.[67]

- **Antioxidant Activity**

Glycyrrhiza glabra has an important free radical scavenging effect. Liquified flavonoids possess potent antioxidant properties that are thought to be more than 100 times more potent than vitamin E's antioxidant activity. Additionally, it can be utilized to prevent oxidant damage in skin and hair cosmetic goods. Glabridin has also been shown to exhibit antioxidant action against low-density oxidative lipoproteins.[68]

- **Anti-inflammatory Activity**

The polyphenolic components found in glycyrrhiza (root) are abundant and may serve as an antioxidant source. Because they prevent microsomal lipid peroxidation, licochalcones B and D show promise. Retrochalcones stop oxidative hemolysis in red blood cells and show signs of mitochondrial lipid peroxidation. It was discovered that certain isoflavones contained in Glycyrrhiza glabra, such as glabridin, hispaglabridin A, and 3′hydroxy-4-O-methylglabridin, may have antioxidant properties. Dehydrostilbene derivatives such as α-dihydro-3,5,4-trihydroxy-4,5-diiodopentenylstilbene have been discovered and found to be free radical scavengers in more recent times. According to research, glycyrrhizin, like hydrocortisone and other corticosteroid hormones, has an anti-inflammatory effect after being broken down in the gut.[69]

- **Antimalarial Activity**

Because of their quick spread and ability to induce long-term infections, bacteria that are multidrug-resistant are a major problem in clinical care today. Glycyrrhiza Linn species are distinguished by their isoprenoid phenols, which possess specific antibacterial properties. Recent studies have demonstrated the antibacterial properties of G. glabra's hydro methanolic extract of root towards a variety of gram-positive and gram-negative pathogens. [70]

- **Antifungal Activity**

Glycyrrhiza glabra develops strong antifungal characteristics. According to a new research report on antimicrobial chemicals, the extract of licorice with 80% methanol has a strong fungicidal effect against Arthrinium sacchari M001 and the bacterium funicola M002, and its active ingredient is thought to be glabridin. [71]

- **Anti-ulcer Activity**

Glycyrrhizic acid, one of the most significant ingredients in licorice, has antiulcer properties by raising prostaglandin concentrations and promoting the growth of stomach and mucous secretions. The in vitro action of glycyrrhizic acid, which combats H. pylori, demonstrates its beneficial impact on peptic ulcers. [72]

- **Anticoagulant and Memory Enhancing Activity**

It has also been discovered that glycyrrhizin, a well-known anti-inflammatory substance, is the first plant-based thrombin inhibitor. It increased the duration of plasma recalcification and the thrombin and fibrinogen clotting times. It was discovered that glycyrrhizin decreased thrombin-induced formation of platelets, but it had no effect on collagen production- or PAF-induced agglutination.[73]

- **Antidiabetic Activity**

Non-insulin dependent type 2 diabetes mellitus is a condition that is becoming more and more of a health problem in the age of modern technologies. The ligand-dependent transcriptional variables known as active receptor (PPARs) of peroxisome proliferation aid in the control of gene group expression and are consequently essential for glucose and lipid metabolism. Licorice has historically been used as an artificial sweetener and to help prevent insulin resistance syndrome.[74]

- **Anti-hyperglycemic Activity**

Glycyrrhiza glabra root extract, when taken in small amounts, has antihyperglycemic and anti-lipidemic properties. In albino mice, the effects of licorice extract on live enzymes and serum with a lipid profile were examined.[75]

- **Hepatoprotective Activity**

persistent hepatitis is seen as a slow-moving liver disease that causes cirrhosis and the increasingly severe liver damage that follows. In Japan, glycyrrhiza has been used for over 60 years as a clinical antihepatitic and antiallergic medication for the treatment of chronic hepatitis with the name stronger Neo-Minophagen C (SNMC).[76]

Anti-Hyperlipidemic Activity of some medicinal plants [77]

Sr.No.	Botanical Name	Family	Parts used
1	Spiny amaranth	Amaranthaceae	Leaves
2	Licorice	Fabaceae	Root
3	Withania Somnifera	Solanaceae	Root
4	Chlorophytum tuberosum	Liliaceae	Root
5	Anoma moringa L.	Moringaceae	Leaves, root
6	Sphaeranthus hirtus	Asteraceae	Flower heads
7	Rhinacanthus communis Nees	Acanthaceae	Whole plant
8	Inga dulcis willd.	Leguminosae	Fresh leaves
9	Hibiscus henriquesii P. Lima	Malvaceae	Fresh leaves
10	Eclipta alba	Asteraceae	Plant juice
11	Agati grandiflora	Fabaceae	Leaves
12	Lycium chinense Mill.	Solanaceae	Fruit
13	Dalbergia oojeinensis Roxb.	Fabaceae	Bark
14	Catunaregam spinosa	Rubiaceae	Fruit
15	Luffa cylindrica	Cuccurbitaceae	Fruit

Conclusion

Hyperlipidemia is one of the serious health issues across the globe and affecting a significantly higher proportion of population worldwide. Moreover, it is a major risk factor for cardiovascular heart disease. Due to adverse side effect of synthetic medicines plant derived medicines are most preferred for treating various diseases. As a result, treating hyperlipidemia with plant-derived molecules that are readily available and need only somewhat difficult pharmaceutical production is critical at this time.

This study revealed a plant that is Glycyrrhiza glabra found in parts of Europe, Asia, and the middle East. Glycyrrhiza glabra (licorice) exhibits significant potential as a natural antilipidemic agent, supported by various preclinical and limited clinical studies. Its bioactive compounds, particularly glycyrrhizin, flavonoids, and saponins, contribute to lipid-lowering effects through mechanisms such as inhibition of lipid absorption, modulation of lipid metabolism enzymes, and antioxidant properties. While current evidence suggests its efficacy in reducing total cholesterol, LDL, and triglycerides, and improving HDL levels, more extensive and standardized clinical trials are needed to validate its safety, efficacy, optimal dosage, and long-term effects. The promising results advocates for further exploration of G. glabra as a complementary or alternative therapy in the management of hyperlipidemia and associated cardiovascular disorders. The present review is mainly focused on the pharmaceutical and therapeutic activities of licorice. The review will be helpful in further studies and researchers for exploring its potential in treating and preventing diseases.

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