



## HEPATOPROTECTIVE AND ANTI - PYRETIC ACTIVITY OF GLYCYRRHIZIN EXTRACTED FROM GLYCYRRHIZA GLABRA (LIQUORICE)

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### ABSTRACT

*Glycyrrhizin, a key bioactive component of Glycyrrhiza glabra (Liquorice), is recognized for its significant pharmacological properties, including hepatoprotective and antipyretic effects. This review consolidates historical, traditional, and scientific perspectives on glycyrrhizin, exploring its phytochemistry, therapeutic applications, and formulation potential. The plant has been valued since ancient times for its expectorant, demulcent, and gastrointestinal protective properties, and modern research highlights its broad-spectrum medicinal activities, including anti-inflammatory, antiviral, and antioxidant effects. With a focus on its utility in treating liver disorders and fever, this study examines extraction techniques, formulations, and pharmacological mechanisms. This review underscores the potential of glycyrrhizin as a natural therapeutic agent, paving the way for novel, effective, and economically viable formulations [1,2].*

### INTRODUCTION

Herbal medicines are also in great demand in the developed world for primary health care because of their efficacy, safety and lesser side effects. They also offer therapeutics for age-related disorders like memory loss, osteoporosis, immune disorders, etc. for which no modern medicine is available. India despite its rich traditional knowledge, heritage of herbal medicines and large biodiversity has a dismal share of the world market due to export of crude extracts and drugs. WHO too has not systematically evaluated traditional medicines despite the fact that it is used for primary health care by about 80% of the world population [3]. However, in 1991 WHO developed guidelines for the assessment of herbal medicine. Herbal medicines are in great demand in both developed and developing countries as a source of primary health care owing to their attributes having wide biological and medicinal activities, high safety margins and lesser costs. Traditional use of medicine is recognized as a way to learn about potential future medicines. Researchers have identified number of Compounds used in mainstream medicine which were derived from "ethnomedical" plant sources [4]. Plants are used medicinally in different countries and are a source of many potent and powerful drugs. Glycyrrhiza glabra is one of the most popular medicinal plants belonging to the Leguminosae family (also known as Leguminosae), and its members are now commonly used as feed and food. The genus Glycyrrhiza is derived from the Greek words **glykos (sweet) and rhiza (root)**. This species is a native of Mediterranean areas, but it is now also present in India, Russia, and China. The extracts are currently used in pharmaceutical and food industries, as well as in the manufacture of functional foods and food supplements. In traditional Chinese medicine, for example, The plant is recommended as a common remedy for gastrointestinal problems, cough, and is also known for its hepatoprotective and

antipyretic properties. In particular, it is still widely used to treat gastritis, peptic ulcers, respiratory infections, and tremors in folk medicine. Commonly, G. glabra root is employed to prepare a tea that is an excellent thirst quencher. The dried root has been described as a tooth cleanser.<sup>4</sup> It was also one of the important plants mentioned in Assyrian herbal (2000 BC). Hippocrates (400 BC) mentioned its use as a remedy of ulcers and quenching of thirsts. The drug was also mentioned by Theophrastus and Dioscorides. In traditional Siddha system of medicine, liquorice is used as a demulcent, expectorant, anti-tussive, laxative and sweetener [5].

### Plant Profile

Liquorice (Glycyrrhiza glabra), a member of the Leguminosae family, is a perennial herb native to southern Europe, the Mediterranean, and parts of Asia. Known by various names like liquorice and mulethi (in India), its roots and stolons have been used for centuries in traditional medicine, particularly in Ayurveda, Traditional Chinese Medicine (TCM), and ancient Greek systems [6]. The primary active constituent, **glycyrrhizin**, gives the plant its sweet flavor and medicinal properties. Other compounds like flavonoids, isoflavonoids, and polysaccharides contribute to its wide therapeutic applications. Traditionally, liquorice is employed as a remedy for gastrointestinal issues, including ulcers, gastritis, and indigestion, and is recognized for soothing respiratory problems like coughs and bronchitis due to its expectorant properties. It is also valued for its **hepatoprotective** effects, protecting the liver from damage, and its **antipyretic** properties, helping to reduce fever. Additionally, liquorice has potent **anti-inflammatory** and **antiviral** effects, making it useful in treating conditions like eczema, viral infections, and liver diseases. Its ability to modulate the immune system, act as an antioxidant, and promote respiratory health has made it a versatile medicinal plant in many cultures [7].



**Fig. Plant & Root of Glycyrrhiza Glabra**

#### Scientific Classification of Glycyrrhiza Glabra [8]

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

#### Common Names and Botanical Classification of Liquorice [9]

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

### Geographical Source [10,11]

Liquorice (*Glycyrrhiza glabra*) is native to parts of Eurasia, particularly the **Mediterranean** and **southwestern Asia**. The main geographical sources include:

1. **India:** Particularly in northern states, such as Punjab and Uttar Pradesh, liquorice is cultivated for both domestic use and export[8].
2. **Southern Europe:** Particularly Spain, Italy, and Greece, where liquorice has a long history of cultivation and use.
3. **Southwest and Central Asia:** Countries like Turkey, Iran, and Iraq are major producers, providing ideal dry and warm climates for the plant.

### Microscopical Characteristics[12]

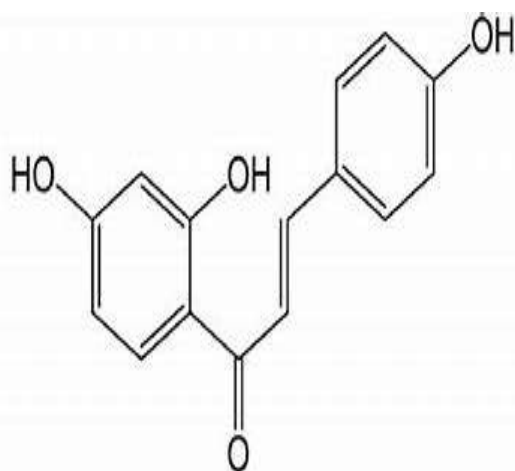
The root of *Glycyrrhiza glabra* exhibits distinct microscopic features. The **epidermis**, being the outermost layer, consists of

flattened cells, sometimes retaining a cuticular layer. Beneath it lies the **cortex**, made up of polygonal, thin-walled parenchymatous cells that often contain clusters of calcium oxalate crystals. The **vascular bundles** show prominent xylem vessels with bordered pitting, thick-walled lignified xylem fibers (sometimes containing crystal inclusions), and slightly thinner lignified phloem fibers interspersed among the xylem. **Medullary rays**, composed of thin-walled parenchymatous cells, are arranged in uniseriate or biseriate rows. **Calcium oxalate crystals**, in prismatic or rosette forms, are scattered throughout the cortex and pith, aiding in distinguishing liquorice from other roots. Additionally, **starch grains**, rounded or oval and abundant in cortical cells, contribute to the powdery texture of the root. The presence of **secretory ducts** in the cortex, which secrete glycyrrhizin, imparts the characteristic sweetness to liquorice.

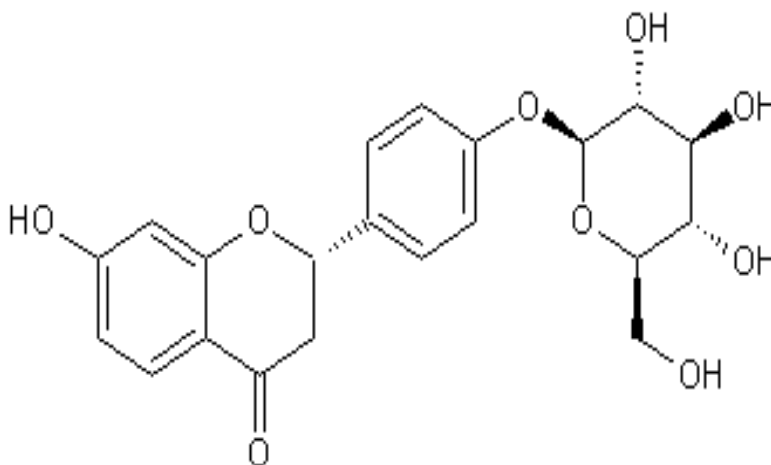
### Chemical constituents [13,14,24]

Sr. no	Plant Part	Chemical Constituents (CC)
1	Root and Rhizome	Glycyrrhizin, Glycyrrhetic acid, Liquiritin, Liquiritigenin, Isoliquiritin, Isoliquiritigenin, Starch, Resins, Polysaccharides, Glabrene
2	Leaves	Flavonoids (Liquiritigenin, Isoliquiritigenin), Coumarins (Herniarin, Umbelliferone), Volatile oils
3	Seeds	Proteins, Amino acids, Starch
4	Flowers	Flavonoids, Essential oils
5	Stem	Polysaccharides, Starch, Trace amounts of Glycyrrhizin

### Chemical Structures [13]



Liquiritegenin

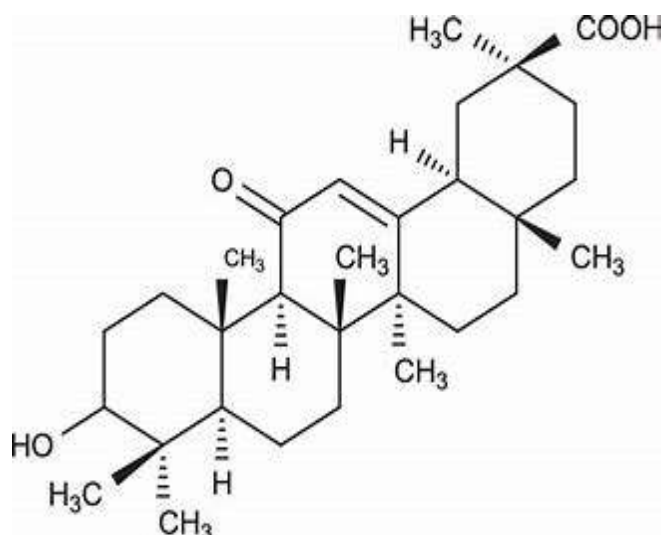


Liquiritin

### Glycyrrhizic Acid

Glycyrrhizic acid, also known as glycyrrhizin, is a naturally occurring compound in liquorice root (*Glycyrrhiza glabra*) with a sweet taste—30 to 50 times sweeter than sucrose. It has a triterpenoid structure with two glucuronic acid units, contributing to its diverse pharmacological actions. Glycyrrhizic acid is renowned for its anti-inflammatory, antiviral, hepatoprotective, and antioxidant properties. It can reduce inflammation by inhibiting pro-inflammatory cytokines and has demonstrated antiviral activity against several viruses, including hepatitis, HIV, and SARS-CoV, by hindering viral replication. The hepatoprotective effects of glycyrrhizic acid are particularly valuable in cases of liver injury or toxicity from drugs like acetaminophen. Mechanistically, glycyrrhizic acid modulates liver enzymes such as CYP2E1 and regulates immune responses by affecting pathways like NF- $\kappa$ B and TLR4. Though used traditionally for digestive, respiratory, and skin ailments, high doses or prolonged use can lead to side effects like hypertension and hypokalemia due to its mineralocorticoid-like activity. Consequently, glycyrrhizic acid is extensively researched for its promising roles in liver protection and anti-inflammatory therapy [15].

Glycyrrhizic acid, traditionally derived from liquorice root, is gaining attention for its multi-faceted therapeutic properties. Alongside its established anti-inflammatory, hepatoprotective, and antiviral effects, glycyrrhizic acid also demonstrates gastroprotective potential by reducing gastric irritation, inhibiting *Helicobacter pylori*, and supporting ulcer healing. Additionally, it shows promise in oncology by impeding the growth and spread of certain cancer cells, notably through its modulation of pathways like NF- $\kappa$ B [16]. Its immune-modulating properties make it useful in managing autoimmune disorders such as lupus and rheumatoid arthritis, where it can balance immune responses without overstimulation. Cardioprotective effects are also evident, as glycyrrhizic acid can help reduce lipid levels, oxidative stress, and arterial plaque buildup, though high doses must be managed due to potential fluid retention and electrolyte imbalances. This versatile compound remains a subject of active research, especially for its promising benefits in chronic inflammatory and liver-related diseases [17].



*Structure of Glycyrrhizic Acid*

### Pharmacology of Glycyrrhizic Acid

Liquorice (*Glycyrrhiza glabra*) contains active compounds like glycyrrhizin and flavonoids that give it a variety of medicinal properties. It acts as an anti-inflammatory by reducing cytokine production, as an antiviral by inhibiting virus replication, and as a hepatoprotective by stabilizing liver cells. Its antioxidants protect against cellular damage, and it also modulates the immune system by enhancing immune cell activity. Additionally, liquorice soothes the stomach, promoting healing of ulcers, and has antimicrobial effects against certain bacteria, including *H. pylori* [18]. These pharmacological actions make liquorice useful for treating liver disease, respiratory infections, stomach ulcers, and inflammatory conditions. However, prolonged use should be monitored, as high doses of glycyrrhizin can lead to side effects like hypertension [19].

### Pharmacological Activities

#### 1) Hepatoprotective property [20]

Liquorice (*Glycyrrhiza glabra*) is known for its significant hepatoprotective properties, largely attributed to its bioactive compounds, particularly glycyrrhizin and flavonoids. These compounds help protect the liver through multiple mechanisms. One key benefit is its strong antioxidant activity, which neutralizes harmful free radicals that can damage liver cells. Additionally, liquorice has potent anti-inflammatory effects, reducing liver inflammation by inhibiting the release of pro-inflammatory cytokines, making it useful in managing conditions like hepatitis. Glycyrrhizin also exhibits antiviral properties, particularly effective against hepatitis B and C, and is used in certain countries as a treatment for chronic hepatitis. Liquorice further helps safeguard the liver from damage caused by toxins, such as alcohol or drugs, and supports the liver's detoxification processes by enhancing the production of detoxifying enzymes. Furthermore, it may promote liver cell regeneration, aiding in recovery from liver injuries. While these





hepatoprotective effects make liquorice valuable in managing liver health, excessive or prolonged use can lead to side effects, such as hypertension and hypokalemia, due to glycyrrhizin, and should therefore be used with caution.

#### **2) Anti – pyretic property [21] :**

Liquorice (*Glycyrrhiza glabra*) also exhibits antipyretic (fever-reducing) properties, which have been recognized in traditional medicine. The antipyretic effects of liquorice are primarily due to its ability to reduce inflammation and modulate immune responses. The key bioactive compound responsible for this effect is glycyrrhizin, which acts by inhibiting the production of pro-inflammatory cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF- $\alpha$ ). These cytokines play a crucial role in elevating body temperature during fever, particularly in response to infections or inflammatory conditions. By reducing their levels, liquorice helps lower fever and control the body's immune response to inflammation. In addition to glycyrrhizin, other compounds like flavonoids in liquorice also contribute to its antipyretic action by acting as antioxidants and reducing oxidative stress, which often accompanies fever and inflammation. Liquorice has been used traditionally in various herbal formulations for treating fever, especially in combination with other herbs that have similar fever-reducing properties. However, just like with its other medicinal benefits, the antipyretic use of liquorice should be carefully monitored due to the potential side effects of excessive intake, such as fluid retention and increased blood pressure.

#### **3. Antioxidant Property [22]**

Liquorice contains glycyrrhizin and flavonoids that neutralize free radicals, reduce oxidative stress, and protect cells from damage, making it effective in preventing oxidative stress-related disorders.

#### **4. Anti-inflammatory Property [22]**

Liquorice demonstrates anti-inflammatory effects by inhibiting pro-inflammatory cytokines like TNF- $\alpha$  and IL-6 and downregulating pathways like NF- $\kappa$ B, making it useful in managing inflammation-related conditions.

#### **5. Antiviral Property [22]**

Liquorice exhibits antiviral activity, especially against hepatitis B and C, herpes simplex, and HIV. It interferes with viral replication and enhances immune response to fight infections.

#### **6. Anti-ulcer Property [22]**

Liquorice protects the gastric mucosa by promoting mucus secretion and reducing gastric acid levels. It is effective in treating peptic ulcers and gastritis.

#### **7. Antimicrobial Property [23]**

Liquorice has broad-spectrum antimicrobial properties, showing activity against bacteria (e.g., *Helicobacter pylori*), fungi, and viruses, making it valuable in treating infections.

#### **8. Immunomodulatory Property [24]**

Liquorice regulates immune activity by stimulating macrophages, natural killer cells, and cytokines. It boosts immunity while controlling excessive immune responses, aiding in autoimmune and infectious diseases.

#### **9. Antidiabetic Property [22]**

Liquorice improves insulin sensitivity, lowers blood glucose levels, and reduces oxidative stress, making it beneficial in managing diabetes and preventing complications.

#### **10. Cardioprotective [25]**

Liquorice reduces oxidative stress and inflammation in the cardiovascular system, lowers lipid peroxidation, and prevents atherosclerosis, contributing to heart health.

#### **11. Neuroprotective [25]**

Liquorice protects the nervous system by reducing neuroinflammation and oxidative damage, with potential benefits in neurodegenerative diseases like Alzheimer's and Parkinson's disease.

### **Mechanism of Action**

#### **1. Hepatoprotective Mechanism [26]**

Glycyrrhizinic acid (GA) exhibits hepatoprotective effects through anti-inflammatory, antioxidant, regenerative, and antiviral mechanisms. It reduces liver inflammation by inhibiting pro-inflammatory cytokines like TNF- $\alpha$  and IL-1 $\beta$  via modulation of the NF- $\kappa$ B pathway, thus preventing inflammation-induced damage. GA's antioxidant properties upregulate enzymes such as superoxide dismutase (SOD) and catalase, neutralizing reactive oxygen species (ROS) and reducing oxidative stress, which protects liver cells. Additionally, GA promotes liver regeneration by inducing growth factors that help repair and rebuild liver tissue. GA also has antiviral effects, particularly against hepatitis B and C viruses, as it disrupts viral replication, reducing the overall viral load and liver infection, further preserving liver function and structure.

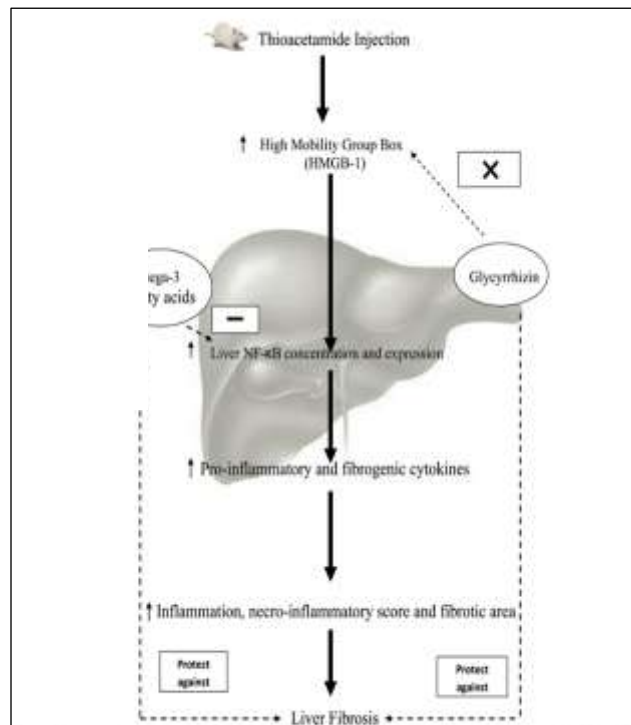


Fig.4 Hepatoprotective Mechanism of Glycyrrhizinic Acid

## 2. Anti – Pyretic Mechanism [27]

Glycyrrhizinic acid (GA) exhibits antipyretic effects primarily through its anti-inflammatory properties. It reduces fever by inhibiting the production of pro-inflammatory cytokines such as  $\text{TNF-}\alpha$ ,  $\text{IL-1}\beta$ , and  $\text{IL-6}$ , which are commonly elevated during fever and contribute to the hypothalamus's temperature-

regulating response. By modulating the  $\text{NF-}\kappa\text{B}$  pathway, GA dampens the body's inflammatory response, reducing cytokine levels and thus indirectly lowering body temperature. This effect on the central pathways of inflammation helps to regulate fever and reduce associated discomfort.

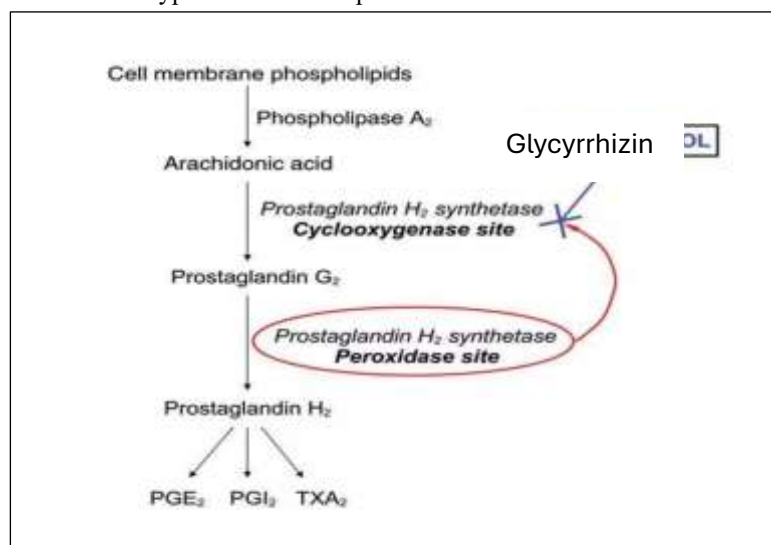


Fig.5 Anti – Pyretic Mechanism Of Glycyrrhizinic Acid

### 2.4.8 Adverse reactions [28]

1. **Hypertension:** Glycyrrhizin can cause sodium retention and potassium loss, leading to increased blood pressure. This is particularly concerning for individuals with pre-existing hypertension.
2. **Hypokalemia:** Prolonged use of liquorice may result in low potassium levels (hypokalemia), which can cause muscle weakness, fatigue, and arrhythmias.
3. **Edema:** Fluid retention due to sodium retention can lead to swelling (edema), particularly in the legs and abdomen.
4. **Hormonal Effects:** Liquorice has estrogenic properties that can lead to hormonal imbalances, potentially causing

menstrual irregularities or exacerbating conditions sensitive to estrogen.

5. **Headaches:** Some individuals may experience headaches as a side effect of liquorice consumption.
6. **Gastrointestinal Issues:** Excessive intake may cause gastrointestinal disturbances, including diarrhea or stomach cramps.
7. **Drug Interactions:** Liquorice can interact with certain medications, including antihypertensives, corticosteroids, and diuretics, potentially reducing their effectiveness or increasing the risk of side effects.
8. **Cortisol Levels:** High doses can affect cortisol metabolism, potentially leading to conditions like pseudoaldosteronism, characterized by symptoms of excess aldosterone.

### Applications of Glycyrrhizinic Acid [29]

1. **Liver Protection :** Used as a hepatoprotective agent, glycyrrhizic acid treats liver disorders, such as hepatitis and liver injury, by reducing inflammation and protecting liver cells from toxins.
2. **Anti-inflammatory and Immune Modulation :** It's applied in managing autoimmune conditions like rheumatoid arthritis and lupus, as it helps balance immune responses and reduce inflammation.
3. **Antiviral Treatments :** Glycyrrhizic acid is incorporated into antiviral therapies for infections like hepatitis, herpes, and HIV, as it can inhibit viral replication and boost immune defenses.
4. **Gastrointestinal Health :** Known for its gastroprotective effects, it helps alleviate gastritis, ulcers, and stomach discomfort by soothing the digestive tract and inhibiting *H. pylori*.
5. **Skin Care and Cosmetics :** In skincare products, glycyrrhizic acid is used for its anti-inflammatory and

depigmenting properties, helping to treat acne, eczema, and hyperpigmentation while soothing sensitive skin.

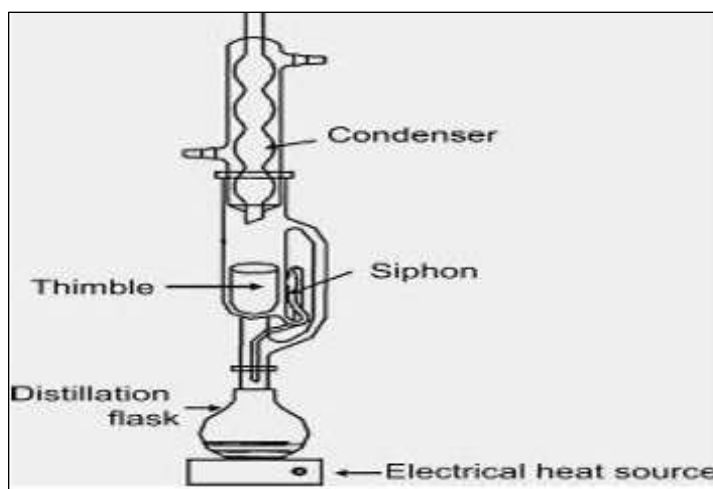
**6. Cancer Research :** Its potential to inhibit cancer cell growth has led to its investigation in cancer treatments, especially for liver, breast, and colon cancers.

**7. Cardiovascular Support :** Glycyrrhizic acid may help reduce cholesterol levels, improve blood vessel health, and lower oxidative stress, though it requires careful use due to possible side effects on blood pressure

### Experimental Studies

#### 1. Extraction [30]

The extraction of glycyrrhizin from *Glycyrrhiza glabra* begins with the collection and preparation of the plant material. The roots are cleaned thoroughly to remove dirt and dried under sunlight to eliminate moisture content. Once dried, the roots are crushed into a coarse or fine powder, which facilitates efficient extraction. For the extraction process, a Soxhlet apparatus is commonly used. The powdered material is placed in the extraction chamber, and a suitable solvent, such as ethanol, methanol, or water, is selected depending on the desired purity and yield of glycyrrhizin. Ethanol, typically in a concentration of 50–95%, is widely preferred for its effectiveness in extracting bioactive compounds. The solvent is heated to evaporate, and the vapors condense to pass through the powdered material repeatedly, allowing glycyrrhizin and other soluble compounds to dissolve into the solvent. This continuous process ensures maximum yield. The extract is then concentrated by evaporating the solvent, resulting in a viscous liquid or dry powder rich in glycyrrhizin, flavonoids, and other bioactive constituents. The composition and quality of the extract depend on factors like solvent type, extraction time, and temperature.



#### 2. Isolation [31]

The separation of glycyrrhizinic acid from liquorice involves a systematic approach to isolate and purify this bioactive compound for medicinal applications. The process begins with Soxhlet extraction, a widely used method to extract glycyrrhizin along with other components such as flavonoids and polysaccharides. Following this, liquid-liquid extraction is employed, where immiscible solvents are used to selectively transfer glycyrrhizinic acid into the phase where it is most

soluble. To further enhance the purity and concentration of the compound, a back-extraction step is carried out, effectively removing impurities and isolating glycyrrhizinic acid in a refined form. This multi-step process ensures the efficient recovery of glycyrrhizinic acid for use in various pharmaceutical and therapeutic formulations.



### 3. Formulation

**a) Syrup [32]** : The formulation of glycyrrhizinic acid syrup is designed to provide hepatoprotective, anti-inflammatory, and antipyretic effects, making it ideal for patients requiring long-term fever treatment. The syrup includes glycyrrhizinic acid (0.5 g per 100 mL) as the active ingredient, complemented by sucrose (15 g per 100 mL) for sweetness and viscosity, and xanthan gum (0.2 g per 100 mL) as a thickening agent to ensure a smooth consistency. Ethanol (95%) and polysorbate 80 are used to dissolve and stabilize the active ingredient, while citric acid adjusts the pH to enhance stability. Flavoring agents like cherry or lemon, along with menthol (0.01 g per 100 mL), improve taste and provide a soothing effect. Sodium benzoate (0.2 g per 100 mL) acts as a preservative, and purified water serves as the primary solvent. The preparation involves dissolving glycyrrhizinic acid in ethanol, creating a syrup base by mixing sucrose and xanthan gum in water, and combining all components to achieve a homogeneous, pH-balanced syrup. Rigorous evaluation ensures proper organoleptic properties, pH, viscosity, microbial safety, and stability under various conditions, resulting in a high-quality therapeutic product.

**b) Capsule [33]** : The formulation of glycyrrhizinic acid capsules involves incorporating the active ingredient, glycyrrhizinic acid, along with excipients to create a stable, effective, and consistent dosage form. Each capsule typically contains 100 mg of glycyrrhizinic acid as the active ingredient, supported by microcrystalline cellulose (150 mg) as a filler to improve bulk and flowability, hydroxypropyl methylcellulose (HPMC, 10 mg) as a binder for structural integrity, magnesium stearate (3 mg) as a lubricant to prevent sticking during manufacturing, and silica gel (2 mg) to absorb moisture and maintain stability. The capsule shell, made of gelatin or HPMC, encloses these ingredients. The manufacturing process includes sieving all components for uniformity, blending glycyrrhizinic acid with other ingredients, and using a capsule-filling machine to ensure consistent weight and content. Post-manufacturing, the capsules undergo evaluations for appearance, content uniformity, weight variation, disintegration, and dissolution to ensure they meet pharmacopeial standards. Proper storage in airtight containers protects the capsules from moisture and maintains their efficacy.

### 4. Evaluation [34]

The document outlines a detailed evaluation of glycyrrhizinic acid formulations, focusing on syrups and capsules derived from *Glycyrrhiza glabra*. For the syrup, organoleptic properties such as clarity, uniformity of color, and flavor are assessed to ensure consumer acceptability. The pH is measured to optimize stability and palatability, while viscosity and density tests verify the product's consistency and flow properties. Stability testing is conducted under various conditions to observe changes in physical and chemical properties, including glycyrrhizin degradation, ensuring the product remains effective over time. Microbial testing evaluates contamination levels to meet safety standards, and specific gravity is measured to ensure uniform composition. Similarly, the capsules are evaluated for appearance, content uniformity, weight variation, disintegration, and dissolution to confirm consistency and bioavailability. Moisture permeation tests and stability studies

further ensure long-term quality. These evaluations highlight the importance of quality assurance in developing safe, stable, and effective formulations for glycyrrhizinic acid-based products.

### Need of experimental studies

Experimental studies focusing on derivatives of paracetamol that incorporate hepatoprotective and antipyretic agents are crucial for enhancing its therapeutic efficacy and safety profile. Paracetamol, widely used for its antipyretic and analgesic properties, is associated with potential hepatotoxicity at high doses or prolonged use. By integrating compounds like glycyrrhizin—extracted from *Glycyrrhiza glabra*—the formulation can address these limitations. Glycyrrhizin provides hepatoprotective benefits by reducing oxidative stress, inhibiting inflammatory cytokines, and supporting liver regeneration. Its antipyretic properties complement paracetamol's action by modulating the body's inflammatory response and reducing fever more effectively. Experimental evaluations of such formulations ensure the stability of both active ingredients, confirm their synergistic effects, and assess safety through toxicity and bioavailability studies. These studies help establish a novel, dual-action medication that is not only effective in fever management but also protects the liver from potential damage, making it a safer option for long-term or high-dose antipyretic therapy.

### CONCLUSION

Glycyrrhizin, derived from *Glycyrrhiza glabra*, offers a promising natural solution for managing various health conditions, particularly liver-related and inflammatory disorders. Its pharmacological efficacy, rooted in a combination of traditional wisdom and modern scientific validation, positions it as a valuable bioactive compound. However, challenges such as potential side effects and standardization of formulations necessitate further research and careful application. By leveraging advanced extraction techniques and innovative formulation approaches, glycyrrhizin-based products can be optimized for enhanced therapeutic outcomes and safety. This comprehensive understanding of glycyrrhizin's potential supports its integration into modern healthcare systems while maintaining a strong foundation in traditional medicine.

In summary, glycyrrhizinic acid from liquorice (*Glycyrrhiza glabra*) presents a compelling case for further research and application in pharmacology and traditional medicine. Its historical significance, coupled with modern scientific validation, highlights the need for continued exploration of its therapeutic potential while addressing safety considerations. The comprehensive understanding of its properties, uses, and extraction methods will facilitate the development of effective and safe herbal products, thereby enhancing the role of glycyrrhizinic acid in contemporary health care.

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