



A REVIEW ON LICORICE

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ABSTRACT

Licorice, an extensively used regular Chinese medicine, consists of many bioactive components. Glabridin is a most important Flavonoid extracted from the root of licorice and has an extensive variety of pharmacological homes which includes anti-inflammatory, anti-cancer, anti-bacterial, regulating blood lipids and blood glucose levels, neuroprotection, anti-Osteoporosis, and phytoestrogen effects.[2] Licorice roots (generally *Glycyrrhiza glabra* L., Leguminosae) are main substances of various licorice sweets which are notably liked by customers all over the world due to their candy and regular long-lasting licorice influence.[4] Wound recovery is a public health concern. Licorice gained a great attention for its antioxidant and anti-inflammatory homes which expand its valuable effects as a herbal medicine.[6] Gustatory sense, particularly sweet and bitter taste, plays a key role in food selection. The attractive candy taste promises a carbohydrate-rich food, whereas unsavory bitter taste may motivate a cautionary effect of possible poisonous food.[4] Licorice extract supplementation Accelerated wound restoration by increasing angiogenesis and collagen deposition through up-regulation of bFGF, VEGF and TGF- β gene expression levels in contrast with the control group. UPLC-PDA-MS/MS aided to authenticate the studied *Glycyrrhiza* species and recognized 101 potential elements that may be responsible for Licorice-exhibited potentials. Based on our observations we concluded that licorice enhanced cutaneous wound Healing via its free radical-scavenging potential, powerful antioxidant activities, and anti-inflammatory actions.[6] Ginseng (JRG) and licorice have been broadly used because of their anti-inflammatory and hepatoprotective effects. Hence, this study assessed JRG and licorice extract mixtures' effects on NASH progression.[1] It is usually believed that glabridin regulates blood lipids and Blood glucose metabolism by activating the expression of PPAR γ and C/EBP α [2] The goal of the present study was to understand the Molecular aspects that contribute to bitter, sweet and licorice sensation of licorice roots, and whether individual Compounds elicit greater than one of these sensations.[4]

Keywords: Licorice, Rheumatoid arthritis, COVID licorice extract; Antiviral and antimicrobial, Anti-inflammatory and antioxidant

1. INTRODUCTION

The pores and skin represents a fundamental protection towards exterior pathogen Invasion and environmental extremes.[6] Coronavirus disorder 2019 (COVID-19), is a variety of viral pneumonia caused by means of a novel coronavirus named Severe Acute Respiratory Syndrome. The pathogen that motivates COVID-19 disorder is a SARS-CoV2 or new coronavirus that has comparable genetic constructions with the other.[3] Licorice is an extensively used traditional Chinese medicine that contains Many bioactive components, such as glycyrrhizic acid, glycyrrhetic Acid, liquiritin, isoliquiritigenin, licochalcones, and glabridin.[2] Licorice roots (generally *Glycyrrhiza glabra* L., Leguminosae) are main components of diverse licorice sweets which are highly appreciated by consumers all over the world due to their candy and typical long-lasting licorice impression.[4] A western life-style and an unhealthy diet are closely related With an increasing prevalence of obesity, metabolic disorder, and Cardiovascular disease.[1] Rheumatoid arthritis (RA) is a chronic, systemic autoimmune sickness that mainly involves synovial tissues (Elwakeel and Hazzaa, 2020). About 1–2% of the population has RA, according to facts provided by the World Health Organization.[5]

Natural herbs symbolize safe natural source of several bioactive Constituents with minimal facet effects as new treatment suggestions for Cutaneous wound healing.[6] Recently, an excessive percentage of patients show high activity in natural medicines. This is mainly due to the general feeling that natural medicines is safer than synthetic drugs.[3] Glabridin has a vast Range of pharmacological activities, including improving metabolic Abnormalities to improve obesity, diabetes, and cardiovascular disease.[2] Gustatory sense, particularly sweet and bitter taste, plays a key role in food selection. The attractive candy taste promises a carbohydrate-rich food, whereas unsavory bitter taste may purpose a cautionary effect of possible poisonous food.[4] Many elements and signaling pathways that are attributable to NASH pathogenesis have been Investigated to discover new therapeutic targets.[1] RA has been recognized in traditional Chinese medicine (TCM) as an arthralgia syndrome (Bi Zheng) with complex causes.[5]

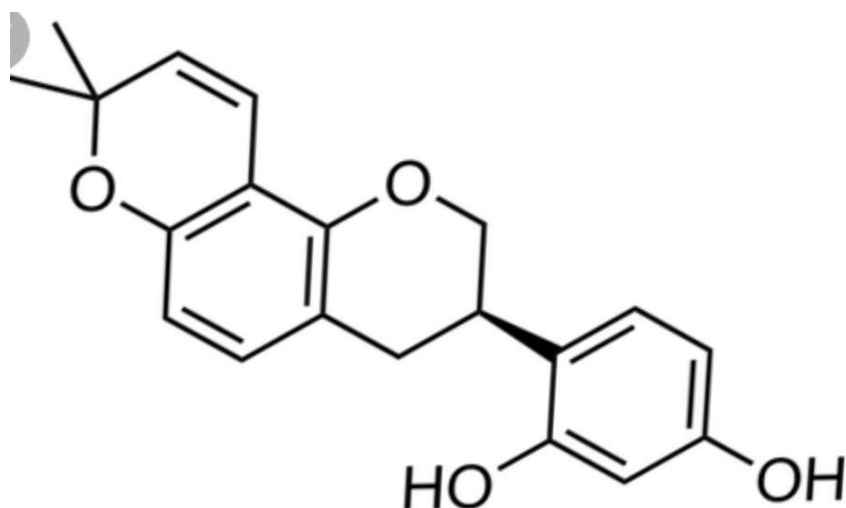


Fig: structure of glabridin

- **LICORICE:**

Synonym: - Jethi madh, Mulethi, Glycyrrhiza



Biological Source: - Licorice consists of peeled and unpeeled roots, stolons, stem of *Glycyrrhiza glabra* linn.

Family: - Leguminosae [8]

2. SCIENTIFIC CLASSIFICATION



Kingdom : plantae

Clade:Tracheophytes

Clade:Angiosperms

Clade:Eudicots

Clade:Rosids

Order: Fabales

Family: fabaceae

Clade:Inverted repeat-lacking clade

Genus:Glycyrrhiza

Species:G. glabra

Binomial name : Glycyrrhiza glabra

Synonyms:

- Glycyrrhiza brachycarpa Boiss.
- Glycyrrhiza glandulifera Waldst. & Kit.
- Glycyrrhiza hirsuta Pall.
- Glycyrrhiza pallida Boiss.
- Glycyrrhiza violacea Boiss.

Microscopy:

Cork consists of various rows of radially arranged thin walled tubular cells. Phelloderm is composed of parenchymatous and sometimes collenchymatous cells. Starch grains and calcium oxalate crystals are seen in phelloderm. Pericyclic fibres are determined in groups. Phloem consists of sieve tissue alternating with thick walled, lignified fibres surrounded by a sheath of parenchymatous cells containing prisms of calcium oxalate. Xylem vessels and xylem parenchyma are present. Medullary rays are radially elongated. Pith is present in rhizomes and absent in root.[7]

- The T.S. exhibits various yellow brown cork layer & a layer of phelloderm that is 1to three phone thick.[8]
- The phloem showcase team of phloem fibers which are surrounded by means of crystal telephone with thick however incompletely lignified walls.[8]

- The vessel are accompanied with the aid of xylem fibers, which are surrounded through crystal mobilephone and through xylem parenchyma cells.[8]
- The parenchyma cells comprise starch grain and regularly incorporate single crystal of Calcium oxalate.[8]

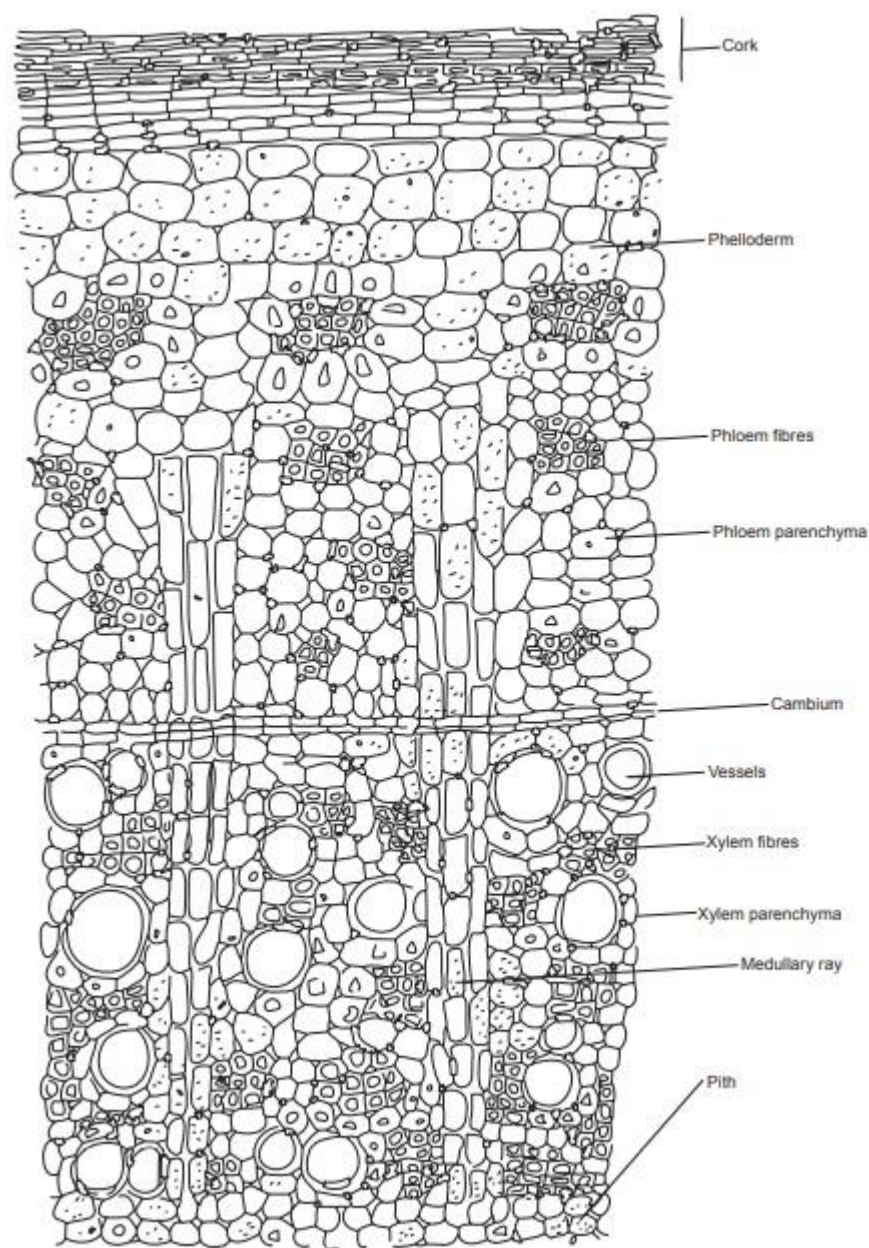


Fig. Transverse section of licorice stolon

3. CHEMICAL CONSTITUENTS

The chief constituent of liquorice root is Glycyrrhizin (6–8%), available in the structure of a sweet, which is 50 instances sweeter than sucrose, white crystalline powder, con-sisting of the calcium and potassium salts of glycyhizic acid. Glycyrrhizic acid on hydrolysis yields glycyrrhetic or glycyrrheticinic acid.[7]

Glycyrrhizinic acid is a triterpenoid saponin having α -amyrine structure. It indicates mainly in alkaline solu-tion frothing however it has very vulnerable haemolytic property. The yellow shade of the drug is due to chalcone glycoside isoliquiritin. The drug additionally incorporates sugar, starch (29%), gum, protein, fats (0.8%), resin, asparagin (2–4%), a hint of tannin in the outer bark of the root, yellow colouring matter, and 0.03% of unstable oil.[7]

PHARMACOLOGICAL EFFECTS:

1) Anti-inflammatory effect:

In one of a kind phone lines, it has been discovered that glabridin can inhibit The inflammatory response by way of inhibiting the NF- κ B signaling pathway And the expression of cytokines and chemokines. (1) Macrophages. By Inhibiting factor- κ B degradation and p65 nuclear translocation medi-Ated NF- κ B/Rel DNA binding exercise and NF- κ B/Rel-dependent re-Porter gene activity, glabridin (0.3–10 μ mol/L) inhibited the expression Of iNOS and NO manufacturing in LPS prompted RAW 264.7 cells.[2]In any other find out about Vibha et al. (2009) suggested steroid-like anti-inflammatory exercise of components derived from licorice root, comparable to the motion of hydrocortisone. They defined this discovering due to inhibition of phospholipase A2 activity, an enzyme imperative to severa inflammatory processes.[5]

The species of Glycyrrhiza has additionally been used to deal with allergic reactions and different inflammatory ailments (Matsui et al. 2004). Shin et al. (2008) studied anti-inflammatory results of glycyrol (benzofuran coumarin) remoted from *G. uralensis* and observed that glycyrols have practicable anti-inflammatory impact . In some other learn about Vibha et al.[9]

2) Anti-ulcer:

In formerly work Bennett et al. (1980) validated the anti-ulcer endeavor of deglycyrrhized licorice formulations the usage of a rat mannequin of aspirin-induced gastric mucosal damage.[8]

3) Neuroprotection effects:

Current lookup indicates that glabridin is predicted to be used in the Treatment of neurodegenerative illnesses along with Alzheimer's ailment And amnesia. The simulation consequences of molecular dynamics and prompt Molecular dynamics confirmed that glabridin should inhibit the depoly-Merization of transthyretin dimer. Since one of the primary features of Transthyretin is to act as a neuroprotective agent in Alzheimer's disease, Glabridin is predicted to be used for treating Alzheimer's disease.[2]

4) Anticancer effect:

Antimutagenesis in opposition to N-nitroso compounds make contributions to prevention of human most cancers used to be investigated. It used to be Found that Glycyrrhiza aspera ethanolic extract famous antimutagenic pastime towards N-methyl-N-nitrosourea [MNU].The inhibitory exercise of glabridin and licochalcone A used to be extra tremendous than that of liquiritigenin. Thus, Glycyrrhiza carries antimutagenic elements towards DNA alkylating, direct-acting cancer agents .[screenshot][10]

At present, the effects from mobilephone experiments exhibit that glabridin Induces most cancers cellphone apoptosis by using activating the mitochondrial apoptotic Pathway and the caspase cascade.[2]

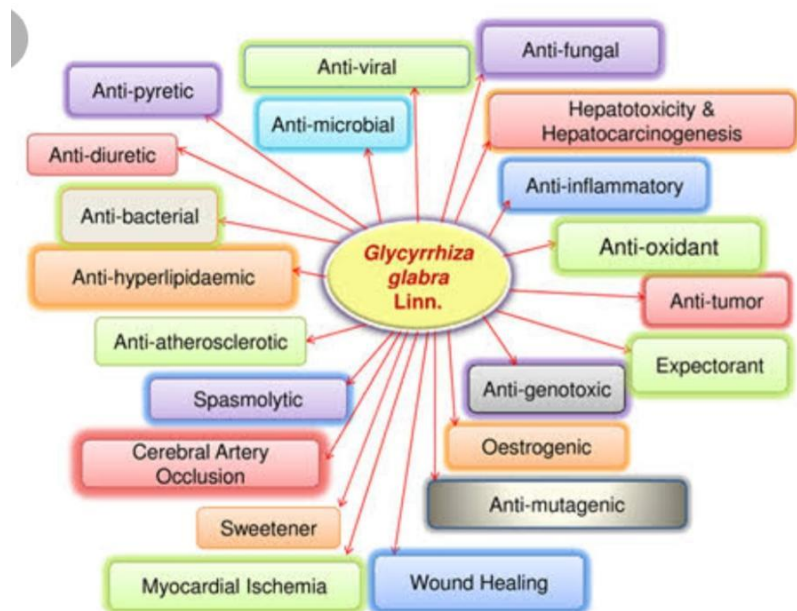


Fig.Pharmacological effect(11)

4. METHODS AND MATERIAL

1. Western blotting:

Synovial tissues and cells have been lysed in ice-cold RIPA buffer, containing a phosphatase inhibitor. Lysates have been centrifuged at 12,000×g For 20 min at 4°C. Protein concentrations have been quantified using the use of the BCA Protein assay, accompanied by using decision of samples (30 µg protein) by means of so-Dium dodecyl sulfate-polyacrylamide gel electrophoresis and electro-Transfer to nitrocellulose membranes. Membranes have been blocked in 5% Skim milk for two h at room temperature, and then incubated in a single day at 4°C with essential antibodies in opposition to TLR4, NLRP3, NF-κB (p 65), and IL-1β (1:500), the use of β-actin as an inner manage(5) Liver tissues or cultured cells have been lysed in a protein extraction reagent (Thermo Fisher Scientific). Protein extracts were obtained by centrifugation at 13,000 g for 15 minutes at 4- C. Protein concentration used to be measured with the Pierce BCA Protein Assay kit (Thermo Fisher Scientific).(1)

2. Chemicals:

The following compounds have been purchased from listed sources given in parenthesis: dimethylformamide, formic acid, and potassium hydroxide (Merck, Darmstadt, Germany), glycyrrhizin ammoniacal (Extrasynthèse, Genay, France), methyl iodide and trifluoroacetic acid (Sigma-Aldrich, Steinheim, Germany). Deuterated solvent (pyridine-d5) for NMR-spectroscopy was once obtained from Euriso-Top (Gif-Sur-Yvette, France). Solvents (acetonitrile and methanol) had been of HPLC grade (Mallinckrodt Baker, Griesheim, Germany). Ultrapure water for HPLC separation was purified by way of means of a Milli-Q® Water Advantage A 10 water machine (18 MΩ; Millipore, Molsheim, France).(4)

3. Statistical analysis:

All information was introduced as means ± preferred deviation (SD). Statistical difference between the corporations was analyzed by using One-way Analysis of variance (ANOVA) using Prism model 8.0.1 (GraphPad Software, CA, USA). Liver histopathological assessment was once per-Formed using the Kruskal-Wallis nonparametric test, accompanied by Dunn's multiple comparisons test. The records was proven as being in The median ± interquartile range. A p-value of 0.05 or less was Regarded to be statistically significant.

- **Antiviral activity and mechanism of action of LICORICE.**Table(3)

Extract	Method of research	Major finding	Mechanism of actions	References
Licorice extract 95% ethanol extract of Glycyrrhiza 'uralensis'	H1N1infected human bronchial epithelial cells (A549).	Inhibition of influenza A virus (H1N1).	Inhibit RANTES secretion.	KO ET AL., 2006.
Licorice extract	Randomized controlled trials	Reduced hepatocellular damage in chronic hepatitis B and C.	Reduced transport to the membrane.	FIORE ET AL., 2008.
Aqueous extract of Glycyrrhiza uralensis.	Human foreskin fibroblast cell line.	Inhibited enterovirus 71.	By preventing viral attachment and penetration.	KUO ET AL., 2009.
Hot water extracts of licorice	Human Respiratory Tract Cell Lines.	Anti-Viral Activity Against Respiratory Syncytial Virus. Aquous ext., are highly effective against HRSV infection on airway	By preventing viral attachment, internalization, and by stimulating IFN secretion.	FENG ET AL., 2013

Extract	Method of research	of	Major finding	Mechanism of actions	References
			epithelial cells.		
Licorice extract	HCV culture system.	cell	It has anti-HCV more than glycyrrhizin.	Unknown	ADIANTI ET AL., 2014
Licorice extract	Cell line		Superiority of alkaline extraction over water extraction as anti-HIV.	Unknown	OHNO ET AL., 2014
Licorice extract rich Oleanane-Type Triterpene Saponins	MDCK cells		Inhibit many virus.	Inhibition of neuraminidase.	WEI ET AL., 2014
Licorice extract rich oleanane-type triterpenoid saponins.	Cell line		In vitro anti-influenza virus activity comparable to and even higher than that of oseltamivir.	Suppression of virus release by GL treatment may be due to its inhibitory effect on PLA2G1B.	SONG ET AL., 2014
Alkanine extract & water extract of licorice root	Cells line		Alkaline extract was highly effective against HIV and more than aqueous extract. While aqueous extract was more effective against HSV-infected cells.	Unknown	FUKUCHI ET AL., 2016
Licorice extract and bioactive ingredients	Molecular Docking and ADMET Study	and	Inhibitor SARS-CoV2 GI better ADMET.	Potential to be strong inhibitors for Main protease of SARS-CoV2.	SRIVASTAVA ET AL., 2020

- **Prevention of COVID-19-induced secondary bacterial infection by glycyrrhizin licorice extract:**

Viral respiratory infections regularly lead to bacterial pneumo-Nia. Therefore, antibacterial agents have grown to be a popular therapy for COVID-19 patients in mixture with antiviral agents (Hendaus et al., 2015). In uncontrolled research that appeared to exhibit the combination of hydroxychloroquine, azithromycin was wonderful in COVID 19. (3) the anticarcinogenic undertaking of the extract of licorice has been nicely documented (Bhadoria et al., 2019). Alcohol licorice extract used to be proven to have an inhibitory impact on Streptococcus mutants most efficient to that of Licorice aqueous extract or Chlorhexidine (Ajagannavar et al., 2014(3))

- **Prevention of COVID-19 induced autoimmune disease by immunomodulatory activity of glycyrrhizin and Licorice extract:**

Licorice includes quite a number bioactive compounds such as polysaccharides, triterpenes, and flavonoids that should decorate immunity through the activation of distinct targets. Early, an expand of interferon- γ manufacturing was once discovered in glycyrrhizin-treated human peripheral lymphocytes in response to the floor antigen of the hepatitis B virus (Shinada et al., 1986). Also, glycyrrhizin cure enhances the lymphocytic proliferation in response to viral contamination after 4 days postinoculation (3)

5. CONCLUSION

In the current review, we conducted a comprehensive review of recent progress in studies of the beneficial therapeutic potential, safety, and mechanism of action of glycyrrhizin and licorice extract against COVID-19. Licorice, as a traditional Chinese medicine, has been widely used clinically. There are many medicines with licorice extract as the main raw material, such as "Compound Licorice Tablets", "Compound Glycyrrhizin Oral Solution" and "Compound Proglumide Chewable Tablets". In addition, there are many medicines that also contain licorice extract, such as "Sijunzi Granule", "Fuzilzhong pills" and "Yinqiao Powder". Although it is rare to use glabridin alone as a medicine, the use of licorice extract as the main raw material of these medicines makes the potential use rate of glabridin high. In terms of food, licorice flavonoid oil has been proved to be a potential functional food by clinical studies, and glabridin is the major component of licorice flavonoid oil. Licorice-processed DGN products displayed better anti-inflammatory effects via the TLR4/NF- κ B/NLRP3 signaling pathway on CIA in rats and LPS-induced RAW264.7 cells and regulation of the metabolic profile in treating RA.

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