



PHARMACOLOGICAL ACTIVITY OF GLYCYRRHIZA GLABRA

¹Devesh Kishor Chavare, ²Sunayana Ghodgaonkar, ³Akash Nalawade, ⁴Tanmay Chavan, ⁵Ajay Desale

^{*1,4,5} Student of Shivajirao S. Jondhle College of pharmacy asangaon Thane

²Associate Professor, Shivajirao S. Jondhle College of pharmacy asangaon Thane

Assistant professor department of ³Pharmaceutics, Shivajirao S. Jondhle College of Pharmacy, Asangaon, India

Abstract :-

Since ancient times, plants have been a significant source of medicines for both humans and animals. Due to their lower risk of side effects, herbal remedies have gained appeal worldwide as a substitute for synthetic chemicals. Glycyrrhiza Glabra, The herb linn, which is indigenous to the Mediterranean and some parts of Asia, is a member of the Leguminosae family and is sometimes referred to as liquorice and sweetwood. In the past, the Egyptian, Chinese, Greek, Indian, and Roman civilizations used the plant's dried rhizome and root as a carminative and expectorant. It is frequently used as a herb for many ailments and in ayurvedic preparations. The current review article discusses the pharmacological properties and chemical components found in different portions of Glycyrrhiza glabra. The goal of this page is to provide all the most recent data on its pharmacological and phytochemical actions, which were carried out using a variety of techniques. Antibacterial, antioxidant, antimalarial, antispasmodic, anti-inflammatory, and anti-hyperglycemic qualities are all possessed by Glycyrrhiza glabra Linn. Numerous additional effects, such as antifungal, antiviral, and antiulcer properties, have also been proposed. Triterpene saponins, flavonoids, isoflavonoids, and chalcones are among the many components that have been extracted from liquorice; glycyrrhizic acid is typically thought to be the primary biologically active ingredient. In addition to generating interest in licorice, this could assist design novel formulations that are more cost-effective and therapeutic.

Index terms: Glycyrrhiza glabra, pharmacological effect, antibacterial, and liquorice.

INTRODUCTION :-

Herbal medicines are also in great demand in the developed world for primary health care because of their efficacy, safety and lesser side effect. Additionally, they provide therapies for age-related conditions for which there is now no available modern medication, such as immunological problems, cognitive loss, and osteoporosis.^[1] One of the most well-known medicinal plants in the Fabaceae (sometimes called Leguminosae) family is Glycyrrhiza glabra, and its members are now frequently used as food and feed. The genus Glycyrrhiza comes from the Greek words glykos (sweet) and rhiza (root). Originally from the Mediterranean region, this species is now found in China, Russia, and India. Currently, the extracts are employed in the food and pharmaceutical industries, as well as in the production of dietary supplements and functional foods.⁽²⁾ For instance, the plant is frequently used as a treatment for bronchitis, arthritis, coughing, and gastrointestinal issues in traditional Chinese medicine. In folk medicine, it is still frequently used to treat tremors, respiratory infections, peptic ulcers, and gastritis. The root of G. glabra is frequently used to make a tea that works wonders for quenching thirst. It has been said that the dried root cleanses teeth.⁽³⁾ Additionally, it was one of the significant plants included in the 2000 BC Assyrian herbal. According to Hippocrates (c. 400 BC), it can be used to treat ulcers and quench thirst. Theophrastus and Dioscorides also referenced the medication. Liquice is used as a laxative, expectorant, demulcent, anti-tussive, and sweetener in the traditional Siddha medical system.^[4] In China, licorice has also been shown to alleviate fatigue and weakness. Furthermore, licorice has anti-inflammatory properties that lessen allergic reactions and shield the liver from harm. The World Health Organization states that licorice is used as an expectorant for coughs and bronchial catarrh and as a demulcent for sore throats.^[5]

PHARMACOLOGICAL ACTIVITY :-

Expectorant and anti-tussive activity –

A sore throat, cough, and bronchial catarrh were shown to be well treated with licorice powder and extract. Glycyrrhizin may be the cause of its antitussive, demulcent, and expectorant-loosening properties. It also helps to clear congestion in the upper respiratory system by speeding up the release of mucus from the trachea. Recently, it was discovered that the methanolic extract of liquorice contains the active component liquiritin apioside. Capsaicin-induced coughing is inhibited by the chemical.[6,7] Licorice reduces inflammation and relieves sore throats just as well as codeine. Glycyrrhiza glabra is the source of the semisynthetic chemical carbenoxolone, which promotes the release of stomach mucus.[8]

Anti-ulcerogenic activity :

Since the 1070s, glycyrrhiza glabra extract has been utilized as an anti-ulcerogenic agent because it inhibits two enzymes: delta 13-prostaglandin reductase and 15-hydroxyprostaglandin . As an anti-ulcerogenic agent because it inhibits two enzymes: delta 13-prostaglandin reductase and 15-hydroxyprostaglandin . Delta 13-prostaglandin reductase changes prostaglandins into 13, 14-dihydro, 15-ketoprostaglandin, while 15-hydroxy prostaglandin changes prostaglandin E2 and F2 alpha into inactive 15-ketoprostaglandins . The level of prostaglandin rises as a result of these two enzymes being inhibited. Carbazolone is another molecule that may be extracted from glycyrrhiza extract. It may eventually have an anti-ulcerogenic effect by suppressing gastrin secretion.[9] A dosage of 100 mg three times a day is used to treat duodenal and stomach ulcers. Licorice prolongs the life of stomach surface cells by increasing the concentration of prostaglandins in the digestive tract and encouraging the release of mucus from the stomach. Consequently, an anti-pepsin effect is also noted. Because the licorice root fraction FM-100 prevents the secretion of gastrin, licorice has antiulcerogenic properties.[10]

Anti-cancer activity :

Both in vitro and in vivo studies have demonstrated the anti-cancer potential of Glycyrrhiza's bioactive components . This characteristic, which often causes a mitochondrial permeability shift that results in tumor cell apoptosis, is caused by 18-β- glycyrrhetic acid and glycyrrhizic acids found in glycyrrhiza. [11] Glycyrrhizic acid can suppress the growth of breast and endometrial cancer cells by inducing AKT/mTOR signals on these cells. Licorice's antineoplastic properties have also been successfully applied to the treatment of cancer. By interfering with angiogenesis, one of the hallmarks of cancer, glycyrrhiza extracts can also stop the proliferation of cancer cells. This property was demonstrated using an in vivo test.[12] Numerous processes have been linked to colorectal cancer, including oncogene mutations, tumor suppressor inactivation, the presence of multiple signaling pathways, apoptotic dysregulation, and morphological development . In both in vitro and in vivo experiments, the pentacyclic triterpenoid 18-β-glycyrrhetic acid, which is derived from the licorice root, exhibits strong inhibitory effects on the growth of colorectal cancer cells in a dose-dependent and time-dependent manner.[13]

Anti-diabetic activity :

Due to insulin insensitivity and inactivity, type-2 diabetes mellitus, a well-known metabolic disease, causes elevated blood glucose levels. Peroxisome proliferation activated receptors (PPARs) are one of several transcription factors that are involved in the metabolism of fats and carbohydrates. The primary tissues that express these PPAR receptors are the kidney, liver, and muscle. This PPAR falls into one of three categories: delta, gamma, or alpha. This PPAR gamma receptor is the primary target of insulin-sensitizing medications. Glycycomarin, glycyrin, glyasperin D, dehydroglyasperin, glyasperin B, and iso-glycyrol ethyl solution are among the chemicals that were isolated from Glycyrrhiza glabra root and crude extracts. These compounds can bind to PPAR gamma in a considerable way, which lowers blood glucose levels.[14]

Glycyrrhiza yields chalcone and amorfrutin, which improve glucose and lipid metabolism and aid with adipocyte development. Amorfrutin can improve glucose tolerance and insulin sensitivity. Glabridin uses Adenosine Monophosphate Protein Kinase (AMPK) to translocate GLUT-4, preventing glucose intolerance and ensuring optimal glucose utilization.[15]

Anti-asthmatic activity :

Chronic inflammation of the airways is the primary cause of asthma, a common respiratory condition. These airway inflammations are often treated with various corticosteroid medications. But using these corticosteroid medications for an extended period of time can have a number of negative effects. Glycyrrhiza glabra is a far safer alternative to that. This plant's root extract contains licochalcone A, which has anti-asthmatic properties. By preventing IKB kinase complex activity, it prevents TNF-α-induced nuclear factor kappa B (NF-KB) activation.

Furthermore, licorice flavonoids can protect against asthma by lowering eosinophilic lung inflammation, Ig levels, IL-3, IL-5, and IL-13 levels, and increasing INF-gamma activity.[16]

Anti-oxidant activity :

Among the main justifications for its applications is *G. glabra*'s antioxidant activity. The strong antioxidant activity that has been linked to flavonoids, isoflavones, and glabridin, hispaglabridin A, and 30-hydroxy-4-O-methylglabridin is likely caused by the phenolic content.[17] Found that the dihydrostilbene derivatives found in *G. glabra* leaves have a significant amount of antioxidant activity. Additionally, *G. glabra* contains licochalcones B and D, which have the capacity to suppress microsomal lipid peroxidation and exhibit potent DPPH radical scavenging action. The topical application of liquorice extract formulations may be useful in innovative dermal and cosmetic products as it counteracts oxidative stress damage and maintains skin homeostasis due to its high antioxidant content. These phenolic compounds are effective in protecting biological systems against oxidative stress and can inhibit the onset of skin damages.[18]

Anti-malarial activity :

One of the most dangerous diseases in Asia, Africa, and Latin America is malaria.[19] According to estimates from the World Health Organization (WHO), there were 219 million cases of malaria worldwide in 2012, and the disease claimed 660,000 lives.[20] One component that may lower the risk of malaria is *Glycyrrhiza glabra*. The *in vivo* study demonstrated that the administration of licorice root extract fractions inhibits 72.2% and 65% growth of *P. berghei* in mice, while the *in vitro* study demonstrated that the 9.95 µg/ml water-methanol and 13 µg/ml ethyl acetate fractions isolated from the root extract of licorice possess good antiparasitic activity against *P. falciparum* strain with low toxicity against HeLa cells. The antimalarial compound licochalcone is found in licorice. Malarial parasites have been completely eradicated in mice given an oral dosage of 1000 mg/kg.[21]

Anti-inflammatory activity :

Glycyrrhiza extracts' anti-inflammatory properties have been investigated *in vitro* and *in vivo*. By lowering the generation of nitric oxide, interleukin-6, and prostaglandin E2 in lipopolysaccharide-induced macrophage cells, five flavonoids that were separated from licorice extract demonstrate anti-inflammatory potential.[22] Treating the macrophage cells with licorice extract at a dosage of (0.2–0.5) mg/ml significantly decreased cytokines including tumor necrosis factor-alpha, interleukin-6, and interleukin-10.[23] An aqueous licorice root extract called glycyrrhizic acid has the ability to suppress cyclooxygenase activity. Like hydrocortisone, it exhibits steroid-like anti-inflammatory properties via blocking the activity of phospholipase A2, which is involved in several inflammatory processes. *Glycyrrhiza* is used to treat inflammatory disorders and allergies.[24]

Skin lightening activity :

According to reports, licorice extract works well as a pigment lightening agent. In cultivated B16 murine melanoma cells, tyrosinase activity is inhibited by glabridin found in the hydrophobic fraction of liquorice extract. [25] Tyrosinase activity is inhibited by a few other active ingredients in liquorice extract, such as glabrene, licochalcone A, and isoliquiritin. Skin lightening is caused by the dispersion of melanin by the liquiritin found in liquorice extract. [26]

Anti-fungal activity :

Good antifungal activity is possessed by *Glycyrrhiza glabra*. Licorice extract with 80% methanol (oil-based extract of licorice, or OEL) was found to have a high fungicidal effect against *Arthrrium sacchari* M001 and *Chaetomium funicola* M002 in a previously published study of screening for antifungal compounds from various plant materials. Glabridin was identified as the active compound in this extract. As a result, licorice extract holds considerable promise for creating antimicrobial cosmetics.[27]

Anticoagulant activity :

Cardiovascular disorders, pulmonary emboli, and deep vein thrombosis are the main causes of death and disability that can result from blood clotting. The use of anticoagulant therapy, such as low molecular weight heparins, unfractionated heparin, and vitamin K antagonists (warfarin), as a treatment approach, can raise the risk of bleeding. Factor Xa (FXa) is a trypsin-like serine protease enzyme that contributes to the coagulation cascade by aiding in the creation of fibrin and clots.[28] FXa inhibitors are new oral anticoagulants (NOACs) that have been utilized recently. *In vitro*, a 250 mg dosage of hydromethanolic licorice extract has FXa inhibitory effects.[29] *Glycyrrhiza glabra*, a plant noted for its ability to inhibit thrombin, contains glycyrrhizin. It can thereby prolong the duration of plasma recalcification, prevent thrombin-induced platelet aggregation, and postpone the thrombin-fibrinogen clotting time. This procedure, however, has no effect on collagen-induced platelet agglutination.[30]

CONCLUSION :-

Glycyrrhiza glabra (licorice) is a powerful medicinal herb with a variety of therapeutic uses. Its uses span from historic remedies for gastrointestinal and respiratory conditions to more recent ones for diabetic control, cancer prevention, and skin care. Glycyrrhizin and licochalcone, two of the bioactive substances found in *G. glabra*, add to its broad pharmacological profile by providing anti-inflammatory, antioxidant, anti-ulcer, anti-diabetic, anti-cancer, and anticoagulant properties. In addition to its therapeutic effectiveness, licorice is still widely acknowledged for its safety and low side effects, which makes it a useful natural substitute for both primary care and specialized therapies. Its significance in medicine may be further cemented by further studies and clinical trials, which could broaden its applications and validate its advantages for a range of medical ailments.

REFERENCES :-

- 1) Kamboj V.P, Current Science, Jan 2008; Vol. 78: 1-10 root@cscdri.ren.nic.in
- 2) Herrera M, Herrera A, Arino A, Estimation of dietary intake of ochratoxin A from licorice confectionery. Food and Chemical Toxicology, 2009; 47(8): 2002-2006.
- 3) Armanini D, Fiore C, Mattarello M J, Bielenberg J, Palermo M, Histor of the endocrine effects of licorice, Experimental and Clinical Endocrinology & Diabetes, 2002; 110(06): 257-261.
- 4) Kumar A, Dora J, Review on Glycyrrhiza glabra: licorice, J Pharm Scient Innovation, 2012; 1: 1-4.
- 5) Xiaoying W., Han Z., Yu W. Sustained Energy for Enhanced Human Functions and Activity. Elsevier; Amsterdam, The Netherlands: 2017. Glycyrrhiza glabra (Licorice) pp. 231–250
- 6) Hikino H, Wagner H, Farnsworth NR (eds) (1985) Recent research on oriental medicinal plants. Economic and medicinal plant research, vol 1. Academic, London, pp 53-85
- 7) Kamei J, Nakamura R, Ichiki H, Kubo M (2003) Anti-tussive principles of Glycyrrhiza radix, a main component of Kampo preparations Bakumondo-to. E J Pharm 69:159-163
- 8) Pandey, S. · Verma, B. · Arya, P. A review on pharmacological activities of Glycyrrhiza glabra Univers. J. Pharm. Res. 2017; 2:26-31
- 9) Malek Jafarian, M. · Ghazvini, K. In vitro susceptibility of Helicobacter pylori to licorice extract Iran. J. Pharm. Res. Nov. 2007; 6:69-72
- 10) 10.Aswatha Ram, H.N. · Lachake, P. · Kaushik, U. Formulation and evaluation of floating tablets of liquorice extract Pharmacognosy . Res. 2010; 2:304
- 11) Sharma, V. · Katiyar, A. · Agrawal, R.C.Glycyrrhiza Glabra: Chemistry and Pharmacological Activity Sweeteners, 2018 87-100
- 12) Hamad, G.M. Chemical composition, antioxidant, antimicrobial and anticancer activities of licorice (Glycyrrhiza glabra L.) root, J. Food Nutr. Res. 2020; 8:707-715
- 13) Wang, S. · Shen, Y. · Qiu, R. ,18-β-glycyrrhetic acid exhibits potent antitumor effects against colorectal cancer via inhibition of cell proliferation and migration Int. J. Oncol. Aug. 2017; 51:615-624
- 14) Kgc, D. · Wmtdn, W. · Wprt, P. Root/stem extracts of Glycyrrhiza glabra; as a medicinal plant against disease forming microorganisms Int. J. Sci. Basic Appl. Res. 2020;3 :329-340
- 15) Gaur, R. · Yadav, K.S. · Verma, R.K. In vivo anti-diabetic activity of derivatives of isoliquiritigenin and liquiritigenin Phytomedicine. Mar. 2014; 21:415-422
- 16) Kim, S.-H. · Yang, M. · Xu, J.-G. ...Role of licochalcone A on thymic stromal lymphopoietin expression: implications for asthma Exp. Biol. Med. Jan. 2015; 240:26-33
- 17) Biondi D M, Rocco C, Ruberto G, New dihydrostilbene derivatives from the leaves of Glycyrrhiza glabra and evaluation of their antioxidant activity. Journal of Natural Products, 2003; 66(4): 477-480.
- 18) Haraguchi H, Ishikawa H, Mizutani K, Tamura Y, Kinoshita T, Antioxidative and superoxide scavenging activities of retrochalcones in Glycyrrhiza inflata. Bioorganic & Medicinal Chemistry, 1948; 6(3): 339-347.
- 19) Chen, M. · Theander, T.G. · Christensen, S.B. ... Licochalcone A, a new antimalarial agent, inhibits in vitro growth of the human malaria parasite Plasmodium falciparum and protects mice from P. yoelii infection Antimicrobial Agents Chemother. 1994; 38:1470-1475
- 20) 22.World Health Organization (WHO) World Malaria Report 2011
- 21) Ramazani, A. · Tavakolizadeh, M. · Ramazani, S. ... Antiplasmodial property of Glycyrrhiza glabra traditionally used for malaria in Iran: promising activity with high selectivity index for malaria J. Arthropod. Borne. Dis. Jun. 2018; 12:135-140
- 22) Fu, Y. · Chen, J. · Li, Y.J. ...Antioxidant and anti-inflammatory activities of six flavonoids separated from licorice, Food Chem. Nov. 2013; 141:1063-1071
- 23) Mueller, M. · Hobiger, S. · chemistry, A.J.-F. Anti-inflammatory activity of extracts from fruits, herbs and spices, Undefined 2010Food Chem. 2010; 122:987-996

- 24) Vibha, J. · Choudhary, K. · Singh, M., A study on pharmacokinetics and therapeutic efficacy of Glycyrrhiza glabra: a miracle medicinal herb, Undefined 2009 Bot. Res. Int. 2009; 2:157-163
- 25) Cronin H, Draelos Z D, Top 10 botanical ingredients in 2010 anti-aging creams, J Cosm Derm, 2010; 9(3): 218-225. <https://doi.org/10.1111/j.1473-2165.2010.00516>.
- 26) Mills SY, Bone K, Principles and Practice of Phytotherapy, Modern Herbal Medicine, Churchill Livingstone, London, 2000.
- 27) Hojoa H, Satob J, Antifungal Activity of Licorice (Glycyrrhiza glabra) and potential applications in beverage foods Food Ingredients J Japan 2002; <https://doi.org/10.1016/j.apsb.2015.05.005> 203.
- 28) Ibrahim, R.S. · Mahrous, R.S. · Fathy, H.M., Anticoagulant activity screening of an in-house database of natural compounds for discovering novel selective factor Xa inhibitors; a combined in silico and in vitro approach, Med. Chem. Res. Apr. 2020; 29:707-726
- 29) De Caterina, R. General mechanisms of coagulation and targets of anticoagulants (Section I): position paper of the ESC Working Group on Thrombosis – task Force on anticoagulants in heart disease Thromb. Haemostasis. Feb. 2013; 109:569-579
- 30) Sharma, V. · Katiyar, A. · Agrawal, R.C. Glycyrrhiza Glabra: Chemistry and Pharmacological Activity Sweeteners, 2018 87-100

