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REVIEW ON GLYCYRRHIZA GLABRA (LIQUORICE)

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ABSTRACT

Liquorice is a plant of ancient origin in history. Liquorice extracts and its principle component, glycyrrhizin, have extensive use in foods, tobacco and in both traditional and herbal medicine. As a result, there is a high level of use of Liquorice and glycyrrhizin approved for use in foods and treatments of various diseases such as including anti-ulcer, anti-viral, anti-inflammatory and hepatoprotective responses etc. Traditional applications across diverse cultures include as both a demulcent and an anti-inflammatory, often used to soothe respiratory or gastrointestinal (GI) symptoms. Modern botanical applications of the herb continue this tradition with recommendations including the treatment of gastric ulcers, bronchitis, cough, and dyspepsia. While Liquorice is indispensable in these and many other herbal applications, it comes with a slight but measurable risk of side effects when used as a whole-root extract. **KEYWORDS:** Liquorice, Glycyrrhizin, toxicity, Traditional & Pharmacological uses.

INTRODUCTION

Glycyrrhiza glabra, also known as Liquorice and sweet wood, belonging to family Leguminaceae is native to the Mediterranean and certain areas of Asia. Liquorice has been used in medicine for more than 4000 years. The earliest record of its use in medicine is found in 'code Humnubari' (2100 BC). It was also one of the important plants mentioned Assyrian herbal (2000BC). Hippocrates (400BC) in mentioned its use as a remedy of ulcers and quenching of thirds. 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. Historically, the dried rhizome and root of this plant were employed medicinally by the Egyptian, Chinese, Greek, Indian, and Roman civilizations as an expectorant and carminative. In modern medicine, Liquorice extracts are often used as a flavoring agent to mask bitter taste in preparations and as an expectorant in cough and cold preparations. Liquorice extracts have been used for more than 60 years in Japan to treat chronic hepatitis, and also have therapeutic benefit against other viruses, including human immunodeficiency virus (HIV), cytomegalovirus (CMV) and Herpes simplex. Deglycyrrhizinated Liquorice (DGL) preparations are useful in treating various types of ulcers, while topical Liquorice preparations have been used to sooth and heal skin eruptions, such as psoriasis and herpetic lesions.

CLASSIFICATION Kingdom: Plantae Division: Angiospermae Class: Dicotyledonae Order: Rosales Family: Leguminosae Genus: Glycyrrhiza Species: glabra Linn VERNACULAR NAMES Sanskrit: Yashti-madhuh. Madhuka Kannada: Yastimadhuka, atimaddhura Bengali: Jashtimadhu, Jaishbomodhu Gujarat: Jethimadhu Hindi: Jothi-madh, Mulhatti Malayalam: Iratimadhuram Marathi: Jeshtamadha Oriya: Jatimadhu Tamil: Atimaduram Telugu: Atimadhuranu, Yashtimadhukam English: Licorice, Liquorice, Sweet wood Arab: Aslussiesa Persia: Ausareha mahaka France: Boisdoux Germany: Sussholz HABITAT

Glycyrrhiza glabra is a hard herb or under shrub attaining a height up to 6ft. leaves multifoliate, imparipinnate, flowers in axillary spikes, papilionaceous, lavender to violet in colour, pods compressed, and containing reniform seeds. The dried, peeled or unpeeled underground stems and roots constitute the drug, known in the trade as Liquorice. Flowers in March and fruits in August.

PART USED- Root and Rhizomes



ACTIVE CONSTITUENTS

A number of components have been isolated from licorice. including a water-soluble, biologically active complex that accounts for 40-50 percent of total dry material weight. This complex is composed of triterpene saponins, flavonoids, polysaccharides, pectins, simple sugars, amino acids, mineral salts, and various other substances. Glycyrrhizin a triterpenoid compound, accounts for the sweet taste of Liquorice root. This compound represents a mixture of potassium-calcium-magnesium salts of glycyrrhizic acid that varies within a 2-25 percent range. Among the natural saponins, glycyrrhizic acid is a molecule composed of a hydrophilic part, two molecules of glucuronic acid, and a hydrophobic fragment, glycyrrhetic acid. The yellow color of Liquorice is due to the flavonoid content of the plant, which includes liquiritin, isoliquiritin (a chalcone), and other compounds. The isoflavones glabridin and hispaglabridins A and B have significant antioxidant activity and both glabridin and glabrene possess estrogen-like activity.

ACTIONS

Tonic, demulcent, expectorant, diuretic, mild laxative, antiarthritic, anti-inflammatory, anti-biotic, anti-viral, anti-ulcer, memory stimulant (being MAO inhibitor), anti-tussive, aphrodisiac, anti-mytotic, estrogenic, anti-oxidant, anti-caries agent, anti-neoplastic, anti-cholinergic, anti diuretic, hypolipidemic activity etc.

TRADITIONAL USES

- A decoction of madhuka or its powder was prescribed with honey in anemia.
- Yashti mixed with cow's milk was prescribed for promoting lactation.
- 10g madhuka powder mixed with 10g sugar, pounded with rice water was prescribed in men-metrorrhagia.
- A confection of rice-milk, prepared with yashtimadhu, was prescribed in hoarseness of voice.
- Charaka prescribed 10g madhuka powder mixed with honey, followed by intake of milk, as an aphrodisiac and as an intellect-promoting tonic.
- Charaka also prescribed a paste of liquorice and Picrorhiza kurroa with sugar-water as a cardiac tonic.
- Charaka datta prescribed yashtimadhu and santalum album, powdered with milk, in haematemisis.
- Sushruta prescribed the paste of yashtimadhu 10g, in intrinsic haemorrhage.
- In oedema, the paste of licorice, sesamum indicum and milk mixed with butter was prescribed.
- Warm clarified butter mixed with licorice, was applied topically on wounds, bruises and burns.
- A decoction of madhuka was applied on erysipelas.
- Yashti is an important ingredient in Narikelanjana (IMCOPS) eye-drops, prescribed in both acute and chronic conjunctivitis, and also in blepharitis.
- A decoction of the root is a good wash for falling and greying of hair.

EXPERIMENTAL PHARMACOLOGY

Glycyrrhiza has the following, experimentally proved activities: Anti-bacterial activity, anti hepato toxic activity, estrogenic activity, anti fungal activity, anti hemorrhoid activity, anti hyper glycemic activity, anti malarial activity, anti oxidant activity, Anti ulcer activity, Immuno stimulatory & anti viral activity.

CLINICAL PHARMACOLOGY

the following. Glvcvrrhiza has clinically proved Pharmacological activities such as anti ulcer activity, anti asthmatic activity, anti diuretic activity, anti hepato toxic activity, eczema, psoriasis and herpes simplex. The beneficial effects of Liquoric can be attributed to a number of mechanisms. Glycyrrhizin and glycyrrhizic acid have been shown to inhibit growth and cytopathology of numerous RNA and DNA viruses, including hepatitis A9 and C, herpes zoster, HIV, Herpes simplex and CMV. Glycyrrhizin and its metabolites inhibit hepatic metabolism of aldosterone and suppress 5-Breductase, properties responsible for the welldocumented pseudoaldosterone syndrome. The similarity in structure of glycyrrhetic acid to the structure of hormones secreted by the adrenal cortex accounts for the mineralocorticoid and glucocorticoid activity of glycyrrhizic acid. Liquorice constituents also exhibit steroid like antiinflammatory activity, similar to the action of hydrocortisone. This is due, in part, to inhibition of phospholipase A2 activity, an enzyme critical to numerous inflammatory processes.

In vitro research has also demonstrated glycyrrhizic acid inhibits cyclooxygenase activity and prostaglandin formation (specifically prostaglandin E2), as well as indirectly inhibiting platelet aggregation, all factors in the inflammatory process. Certain Liquorice constituents possess significant antioxidant and hepatoprotective properties. Glycyrrhizin and glabridin inhibit the generation of reactive oxygen species (ROS) by neutrophils at the site of inflammation. *In vitro* studies have demonstrated Liquorice isoflavones, hispaglabridins A and B, inhibit Fe3+-induced mitochondrial lipid peroxidation in rat liver cells.

Other research indicates glycyrrhizin lowers lipid peroxide values in animal models of liver injury caused by ischemia constituents reperfusion. Liquorice also exhibit hepatoprotective activity by lowering serum. Although the exact mechanisms are still under investigation, research has demonstrated they inhibit liver enzyme levels and improving tissue pathology in hepatitis patients. Glycyrrhizin and other Liquorice components appear to possess anticarcinogenic properties as well. Abnormal cell proliferation, as well as tumor formation and growth in breast, liver and skin cancer. Deglycyrrhizinated licorice formulations used in the treatment of ulcers do not suppress gastric acid release like other anti-ulcer medications rather; they promote healing by increasing mucous production and blood supply to the damaged stomach mucosa, thereby enhancing mucosal healing.

SIDE EFFECTS

The use of liquorice extract in the treatment of peptic ulcer sometimes appeared to invoke oedema and other side effects. Many investigations were carried out and it was shown that glycyrrhizin and glycyrrhetinic acid decreased the output of ACTH, reduced urinary excretion of sodium and chloride, increased potassium excretion, reduced rennin activity and serum aldosterone, elevated blood pressure and induce metabolic alkalosis with severe hypokalaemia and hypernatremia, capable of causing cardiac arrest. Clinical investigations revealed sodium retention to be connected to an aberration in cortisol metabolism in the kidneys, which interferes with 11- β -hydroxy steroid dehydrogenase. Consumption of Liquorice or glycyrrhizin in excessive amounts and over a long period produces pseudo

aldostronism leading to oedema, hypertension, and weight gain.

CAUTION

The intake of higher doses (above50g/day) over an extended period (>6weeks) may cause sodium retention, potassium depletion, hyper tension, cardiac complaints, kidney disease, obesity, disorders associated with pregnancy and hypo kalaemic alkalosis. It should not be taken concurrently with cortico steroid treatment. The drug is contra indicated in patients with a history of hypertension, renal failure and using digitalis preparations. It should not be used for longer than 4-6 weeks without medical advice.

DRUG INTERACTION

Because it increases potassium loss, it should not be administered for prolonged use with thiazide and loop diuretics or cardiac glycosides. Because it reduces sodium and water excretion, the effectiveness of drugs used in the treatment of hypertension may be reduced. It should not be administered in conjunction with spiranolactone or amiloride. **CONCLUSION**

Glycyrrhiza glabra, also known as Liquorice and sweet wood, belonging to family Leguminaceae is native to the Mediterranean and certain areas of Asia. . Glycyrrhizin a triterpenoid compound, accounts for the sweet taste of Liquorice root. This compound represents a mixture of potassium-calcium-magnesium salts of glycyrrhizic acid that varies within a 2-25 percent range. Traditional applications across diverse cultures include as both a demulcent and an anti-inflammatory, often used to soothe respiratory or gastrointestinal (GI) symptoms.

REFERENCES

- 1. Revers FE. The treatment of gastric ulcer and duodenal ulcer with licorice succus. Therapy, *Ned Tijdschr Geneeskd. 1948*:92; 2968-2973.
- Borst JG, Blomhert G, Molhuysen JA, Gerbrandy J, Turner KP, de Vries LA. Excretion of water and electrolytes during a 24-hour period and under influence of licorice extract. *Acta Clin Belg.* 1950; 5(4):405-409.
- 3. Revers FE. Licorice juice without glycyrrhizinic acid in peptic ulcer therapy. *Ned Tijdschr Geneeskd*. 1952; 96(38):2338-2341.
- Krausse R, Bielenberg J, Blaschek W, Ullmann U. In vitro anti-Helicobacter pylori activity of Extractum liquiritiae, glycyrrhizin and its metabolites. J Antimicrob Chemother. 2004; 54(1):243-6.
- Fukai T, Marumo A, Kaitou K, Kanda T, Terada S, Nomura T. Anti-Helicobacter pylori flavonoids from licorice extract. *Life Sci.* 2002; 71(12):1449-1463.
- Rees WD, Rhodes J, Wright JE, Stamford LF, Bennett A. Effect of deglycyrrhizinated liquorice on gastric mucosal damage by aspirin. *Scand J Gastroenterol.* 1979; 14(5):605-607.
- Malhotra SL, Saigal ON, Mody GD. Role of saliva in the aetiology of peptic ulcer. Br Med J. 1965; 1(5444):1220-1222.
- Morgan AG, Pacsoo C, McAdam WA. Maintenance therapy: a two year comparison between Caved-S and cimetidine treatment in the prevention of symptomatic gastric ulcer recurrence. *Gut.* 1985; 26(6):599-602.
- 9. Morgan AG, Pacsoo C, Taylor P, McAdam WAF. Does Caved-S decrease the gastric ulcer relapse rate during maintenance treatment with ranitidine? *Aliment Pharmacol Ther. 1987*:1(6); 633-638.
- Shibata S. A drug over the millennia: pharmacognosy, chemistry, and pharmacology of licorice. *Yakugaku Zasshi*. 2000; 120(10):849-862.
- 11. Blumenthal M. *The ABC Clinical Guide to Herbs*. Austin, TX: American Botanical Council; 2003:282-287.
- MN, Hosseinzadeh H. Review of pharmacological effects of Glycyrrhiza sp. and its bioactive compounds. *Phytother Res. 2008*; (6):709-724.
- 13. Revers FE. Does succus of licorice have a healing effect on the stomach ulcer therapy, *Ned Tijdschr Geneeskd*, 1946; 90:135-137.
- Miething; H. and Speicher- Brinker A., (1989). "A Neolicuroside-A new chalcone glycoside from the roots of *Glycyrrhiza glabra*". Arch. Pharm (Weinheim), 322: 141-143.
- 15. Materia Medica, vol I, 3rd edition, A.K. Nadkarni, Popular Prakashan Pvt. Ltd. Bombay.
- 16. Encyclopedia of Indian medicinal plants, 1st edition, C.P. Khare, Springer-verlag Berlin Heidelberg New York.

- 17. The Wealth of India, Raw materials, IV F-G, 1st edition, Council of Scientific and Industrial Research. New Delhi.
- Indian Herbal Pharmacopoeia, vol. I, 1998, Regional research laboratory & Indian drug manufacture association, Mumbai.
- The useful plants of India, National Institute of science communication, CSIR, 4th reprint 2000, Shri. S.P, Ambasta, New Delhi.
- Indian medicinal plants, A compendium of 500 species, vol.3, Orient Longman P. Ltd, Reprint 2002, P.K.Warrier, V.P.C. Nambiar, C.Ramankutty, Chennai-2.
- 21. Su XS, Chen HM, Wang LH, et al. Clinical and laboratory observation on the effect of glycyrrhizin in acute and chronic viral hepatitis. *J Tradit Chin Med* 1984; 4:127-132.
- 22. Turpie AG, Runcie J, Thomson TJ. Clinical trial of deglycyrrhizinized liquorice in gastric ulcer. *Gut* 1969; 10:299-302.
- Ito M, Sato A, Hirabayashi K, et al. Mechanism of inhibitory effect of glycyrrhizin on replication of human immunodeficiency virus (HIV). *Antiviral Res* 1988; 10:289-298.
- 24. Armanini D, Karbowiak I, Funder JW. Affinity of liquorice derivatives for mineralocorticoid and glucocorticoid receptors. *Clin Endocrinol* (*Oxf*) 1983; 19:609-612.
- 25. Tamir S, Eizenberg M, Somjen D, et al. Estrogen like activity of glabrene and other constituents isolated from licorice root. *J Steroid Biochem Mol Biol* 2001; 78:291-298.
- Vaya J, Belinky PA, Aviram M. Antioxidant constituents from licorice roots: isolation, structure elucidation and antioxidative capacity toward LDL oxidation. *Free Radic Biol Med* 1997; 23:302-313.
- 27. Pompei R, Flore O, Marccialis MA, et al. Glycyrrhizic acid inhibits virus growth and inactivates virus particles. *Nature* 1979; 281:689-690.
- Hattori T, Ikematsu S, Koito A, et al. Preliminary evidence for inhibitory effect of glycyrrhizin on HIV replication in patients with AIDS. *Antiviral Res* 1989; 11:255-261.
- 29. Baba M, Shigeta S. Antiviral activity of glycyrrhizin against Varicellazoster virus in vitro. Antiviral Res 1987; 7:99-107.
- Numazaki K, Umetsu M, Chiba S. Effect of glycyrrhizin in children with liver dysfunction associated with cytomegalovirus infection. *Tohoku J Exp Med* 1994; 172:147-153.
- Akamatsu H, Komura J, Asada Y, Niwa Y. Mechanism of antiinflammatory action of glycyrrhizin: effect on neutrophils functions including reactive oxygen species generation. *Planta Med* 1991; 57:119-121.
- 32. Wang ZY, Nixon DW. Licorice and cancer. Nutr Cancer 2001; 39:1-11.
- Haraguchi H, Yoshida N, Ishikawa H, et al. Protection of mitochondrial functions against oxidative stresses by isoflavans from *Glycyrrhiza glabra. J Pharm Pharmacol* 2000; 52:219-223.
- Nagai T, Egashira T, Yamanaka Y, Kohno M. The protective effect of glycyrrhizin against injury of the liver caused by ischemia-reperfusion. *Arch Environ Contam Toxicol* 1991; 20:432-436.
- Van Rossum TG, Vulto AG, Hop WC, Schalm SW. Glycyrrhizininduced reduction of ALT in European patients with chronic hepatitis C. *Am J Gastroenterol* 2001; 96:2432-2437.
- 36. Tamir S, Eizenberg M, Somjen D, et al. Estrogenic and antiproliferative properties of glabridin from licorice in human breast cancer cells. *Cancer Res* 2000; 60:5704-5709.
- 37. Shiota G, Harada K, Ishida M, et al. Inhibition of hepatocellular carcinoma by glycyrrhizin in diethylnitrosamine-treated mice. *Carcinogenesis* 1999; 20:59-63.
- Nishino H, Kitagawa K, Iwashima A. Antitumor promoting activity of glycyrrhetic acid in mouse skin tumor formation induced by 7,12 dimethylbenz[a]anthracene plus teleocidin. *Carcinogenesis* 1984; 5:1529-1530.
- Goso Y, Ogata Y, Ishihara K, Hotta K. Effects of traditional herbal medicine on gastric mucin against ethanol-induced gastric injury in rats. *Comp Biochem Physiol C Pharmacol Toxicol Endocrinol* 1996; 113:17-21.
- Morgan AG, McAdam WA, Pacsoo C, Darnborough A. Comparison between cimetidine and Caved-S in the treatment of gastric ulceration, and subsequent maintenance therapy. *Gut* 1982; 23:545-551.
- 41. Morgan AG, Pacsoo C, McAdam WA. Maintenance therapy: a two year comparison between Caved- S and cimetidine treatment in the prevention of symptomatic gastric ulcer recurrence. *Gut*1985; 26:599-602.
- 42. Turpie AG, Runcie J, Thomson TJ. Clinical trial of deglycyrrhizinized liquorice in gastric ulcer. *Gut* 1969; 10:299-302.
- Glick L. Deglycyrrhizinated liquorice for peptic ulcer. Lancet 1982; 2:817.
- Peterson WL. *Helicobacter pylori* and peptic ulcer disease. N Engl J Med 1991; 324:1043-1048.

- 45. Kassir ZA. Endoscopic controlled trial of four drug regimens in the treatment of chronic duodenal Ulceration. *Ir Med J* 1985; 78:153-156.
- Armanini D, Mattarello MJ, Fiore C, et al. Licorice reduces serum testosterone in healthy women. *Steroids* 2004; 69:763-766.
- Basso A, Dalla Paola L, Erle G, et al. Licorice ameliorates postural hypotension caused by diabetic autonomic neuropathy. *Diabetes Care* 1994; 17:1356.
- Walker BR, Edwards CR. Licorice-induced hypertension and syndromes of apparent mineralocorticoid excess. *Endocrinol Metab Clin North Am* 1994; 23:359-377.
- 49. Stormer FC, Reistad R, Alexander J. Glycyrrhizic acid in liquorice evaluation of health hazard. *Food Chem Toxicol* 1993; 31:303-312.
- Christensen SB, Ming C, Anderson L, et al. An antileishmanial chalcone from Chinese licorice roots. *Planta Med* 1994; 60:121-123.
- 51. Chen M, Theander TG, Christensen SB, et al. Licochalcone A, a new anti-malarial agent, inhibits *in vitro* growth of the human malaria parasite *Plasmodium falciparum* and protects mice from *P. yoelii* infection. *Antimicrob Agents Chemother* 1994; 38:1470-1475.

- Shibata S. A drug over the millennia: pharmacognosy, chemistry, and pharmacology of licorice. *Yakugaku Zasshi* 2000; 120:849-862.
- Loginov AS, Speransky MD, Speranskaya IE, et al. The effectiveness of carbenoxolone in the treatment of gastro-duodenal ulcer patients. *Scand J Gastroenterol Suppl* 1980; 65:85-91.
- Arase Y, Ikeda K, Murashima N, et al. The long term efficacy of glycyrrhizin in chronic hepatitis C patients. *Cancer* 1997; 79:1494-1500.
- Numazaki K. Glycyrrhizin therapy for liver dysfunction associated with cytomegalovirus infection in immunocompetent children. *Antimicrobics Infect Dis Newsl* 1998; 17:70-71.
- Numazaki K, Chiba S. Natural course and trial of treatment for infantile liver dysfunction associated with cytomegalovirus infections. *In Vivo* 1993; 7:477-480.
- 57. Aikawa Y, Yoshiike T, Ogawa H. Effect of glycyrrhizin on pain and HLA-DR antigen expression on CD8-positive cells in peripheral blood of herpes zoster patients in comparison with other antiviral agents. *Skin Pharmacol* 1990; 3:268-271.
- Pompei R, Pani A, Flore O, et al. Antiviral activity of glycyrrhizic acid. Experientia 1980; 36:304.