

Licorice: Glycyrrhiza glabra root, Chinese licorice, kanzo, alcacuz, liquorice

Common Indications:

- Adrenal stress
- Expectorant
- Hormone regulation support
- Infection, including viral, bacterial, fungal, and parasitic

General Comments:

The use of licorice has a long history stemming from Traditional Chinese Medicine but also used by the ancient Greeks and Egyptians. It has served as an agent that soothes and stimulates protective mucous within the gastrointestinal and urinary tracts. It also helps with coughs and sore throats as soothing agent. ^{1,2,3} Traditional Chinese Medicine has also employed licorine in the treatment of diabetes and tuberculosis. ^{4,5}

Benefits & Mechanism of Action:

Adrenal stress

Licorice has an interesting effect on cortisol. It counteracts the effects of cortisol by inhibiting adrenal and thymus atrophy, as well as by reducing cholesterol manufacturing. There are two mechanisms by which this happens. The glycyrrhetinic acid in licorice catalyses the conversion of cortisol to cortisone and licorice also sits on mineralocorticoid and glucocorticoid receptors and displaces cortisol from the carrier molecule. Licorice is claimed to inhibit antibody formation and support the stress response and the inflammatory response. 8,9,10

Expectorant

Licorice reportedly inhibits inflammatory prostaglandin formation and leukotrienes by inhibiting the enzymes responsible for their metabolic activation and manufacture. Licorice was also found to stimulate tracheal mucus secretion. Licorice may also stimulate interferon production in the body, which could support its antiviral activity.

Hormone regulation support

Licorice has phytoestrogenic activity due to its isoflavone content (formononetin). Because of the weak affinity for binding to estrogen receptors, estrogenic side effects are not seen. 14,15,16,17,18,19,20

Infection, including viral, bacterial, fungal, and parasitic

Licorice has been tested both orally and by injection and has shown effective against multiple strains of viruses. Reduction of symptoms and viral activity was seen with hepatitis B and C, herpes simplex, encephalitis, influenza A virus pneumonia, HIV-1, severe acute respiratory syndrome, coronavirus, hand foot and mouth-related enterovirus, and vasicular stamatitis virus. ^{21,22,23,24,25,26,27,28,29,30,31,32}

The components responsible for antibacterial activity are the phenolic compounds, licochalcone A, and isoflavones. They were found to be active against methicillin-resistant and sensitive *Staphylococcus aureus*. ^{33,34} The component, glabridin, has shown activity against *Mycobacterium tuberculosis*, gram-positive and gram-negative bacteria, including *E. coli*, *B. subtilis*, *E. aerogenes*, *K. pneumonaiae*, and *S. aureus*. ^{35,36}

The licochalcone A and glabridin in licorice had antifungal activity against *Candida* albicans.³⁷

Licorice has also shown activity against the parasites *Plasmodium berghei* and *Plasmodium falciparum*. ^{38,39}

Peptic Ulcer

The deglycyrrhizinised (DGL) form of licorice has been shown effective in treating peptic ulcers. This occurs due to the inhibition of the enzyme that converts prostaglandins to their inactive form. The increase in prostaglandins promote mucus secretion and cell proliferation, allowing ulcers to heal⁴⁰.

Dose:

- Root 5 to 15g per day, equivalent to 200-600mg of glycyrrhizinic acid, 3 times a day
- Fluid extract (1:1)
 - 15-30 drops of liquid extract, 3 times a day in juice or other beverage
 - 2-4mL three times daily
 - 15-40mL per week (Australian manufacturer recommedations)
- Tea pour 150mL boiling water over 2-4 g licorice, steep for 5 minutes and filter through a tea strainer after cooling
- Chronic gastritis one cup of licorice tea after each meal
- Chronic duodenal ulcers 3800 mg per day of DGL in five divided doses before meals and at bedtime (according to clinical studies)

Standardization: Licorice should be standardized to contain 20% glycyrrhizinic acid or contain greater than 30 mg/ml glycyrrhizinic acid.

Cautions & Side Effects:

Licorice has been reported to be safe in recommended doses.

Symptoms that may indicate acute toxicity include:

- Hypercortisolism and pseudohyperaldosteronism
- Hypokalemia
- Rhabdomyolysis
- Visual disturbance
- Contact dermatitis
- Thrombocytopenia
- Increased sodium retention

Medication interactions

Medications with increased effects while taking licorice include:

- Anticoagulant medications
- Antiplatelet medications
- Drugs metabolized by P-glycoprotein
- Drugs metabolized by CYP 450 enzymes
- Paclitaxel and vinblastine chemotherapy⁴¹
- H₂ antagonist medications
- Corticosteroids
- Diclofenac sodium
- Digoxin
- Diuretics
- Oral contraceptives

Medications with decreased effects while taking licorice include:

- Cyclosporine^{42,43}
- Potassium
- Drugs metabolized by P-glycoprotein
- Drugs metabolized by CYP 450 enzymes
- Blood pressure medications
- Testosterone^{44,45,46,47,48}

Patients with the following disease states or conditions should not use licorice

- Pseudohyperaldosteronism
- Hypertension^{49,50,51}
- Pregnancy⁵²
- Fluid retention
- 11HSD deficiency or genetic mutation of HSD11B2 gene

Nutrient Interactions:

Potassium: Licorice may reduce the effect of potassium when potassium is given as a

supplement.

References:

General Comments

- 1. Glycyrrhiza glabra. Monograph. Altern Med Rev. 2005;10(3):230-7.
- 2. Armanini D, De Palo CB, Mattarello MJ, et al. Effect of licorice on the reduction of body fat mass in healthy subjects. J Endocrinol Invest 2003;26(7):646-650.
- 3. Isbrucker RA, Burdock GA. Risk and safety assessment on the consumption of Licorice root (Glycyrrhiza sp.), its extract and powder as a food ingredient, with emphasis on the pharmacology and toxicology of glycyrrhizin. Regul Toxicol Pharmacol. 2006;46(3):167-92.
- 4. Olukoga A, Donaldson D. Liquorice and its health implications. J R Soc Health. 2000;120(2):83-9.
- 5. Shibata S. A drug over the millennia: pharmacognosy, chemistry, and pharmacology of licorice. Yakugaku Zasshi. 2000;120(10):849-62.

Adrenal Stress

- 6. Kato H et al. 3-monoglucuronyl-glycyrrhetinic acid is a major metabolite that causes licorice-induced pseudoaldosteronism. J Clin Endocrinol Metab 80.6 (1995): 1929–1933.
- 7. Nissen D (ed). Mosby's drug consult. St Louis, MO: Mosby, 2003.
- 8. Biondi DM, Rocco C, Ruberto G. New dihydrostilbene derivatives from the leaves of Glycyrrhiza glabra and evaluation of their antioxidant activity. J Nat Prod. 2003;66(4):477-80.
- 9. Fiore C, Eisenhut M, Ragazzi E, Zanchin G, Armanini D. A history of the therapeutic use of liquorice in Europe. J Ethnopharmacol. 2005;99(3):317-24.
- 10. Visavadiya NP, Narasimhacharya AV. Hypocholesterolaemic and antioxidant effects of Glycyrrhiza glabra (Linn) in rats. Mol Nutr Food Res. 2006;50(11):1080-6.

Expectorant

- 11. Cinatl J, Morgenstern B, Bauer G, et al. Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. Lancet 2003;361(9374):2045-2046.
- 12. Aly AM, Al-Alousi L, Salem HA. Licorice: a possible anti-inflammatory and anti-ulcer drug. AAPS PharmSciTech. 2005;6(1):E74-82.
- 13. Bradley PR (ed). British herbal compendium, vol 1: A handbook of scientific information on widely used plant drugs. Bournemouth, Dorset, UK: British Herbal Medicine Association (1992).

Hormone regulation support

14. Armanini D, Bonanni G, Mattarello MJ, Fiore C, Sartorato P, Palermo M. Licorice consumption and serum testosterone in healthy man. Exp Clin Endocrinol Diabetes.

- 2003;111(6):341-3.
- 15. Belhadj-Tahar H, Nassar B, Coulais Y, Montastruc JL, Sadeg N. Acute pseudo-aldosteronism syndrome induced by liquorice. Therapie. 2003;58(4):375-8.
- 16. Fuhrman B, Volkova N, Kaplan M, Presser D, Attias J, Hayek T, Aviram M. Antiatherosclerotic effects of licorice extract supplementation on hypercholesterolemic patients: increased resistance of LDL to atherogenic modifications, reduced plasma lipid levels, and decreased systolic blood pressure. Nutrition. 2002;18(3):268-73.
- 17. Sigurjonsdottir HA, Axelson M, Johannsson G, Manhem K, Nystrom E, Wallerstedt S. Liquorice in moderate doses does not affect sex steroid hormones of biological importance although the effect differs between the genders. Horm Res. 2006;65(2):106-10.
- 18. Tamir S, Eizenberg M, Somjen D, Izrael S, Vaya J. Estrogen-like activity of glabrene and other constituents isolated from licorice root. J Steroid Biochem Mol Biol. 2001;78(3):291-8.
- 19. Wang ZY, Nixon DW. Licorice and cancer. Nutr Cancer. 2001;39(1):1-11.
- 20. Wu YT, Shen C, Yin J, Yu JP, Meng Q. Azathioprine hepatotoxicity and the protective effect of liquorice and glycyrrhizic acid. Phytother Res. 2006;20(8):640-5.

Infection

- 21. Fiore C et al. A history of the therapeutic use of liquorice in Europe. J Ethnopharmacol 99.3 (2005): 317–324.
- 22. Cinatl J et al. Glycyrrhizin, an active component of licorice roots, and replication of SARS-associated coronavirus. (Research letters: possible treatment for severe acute respiratory syndrome.). Lancet 361 (2003): 2045–2046.
- 23. Bradbury J. Liquorice compound beats latent herpesvirus. Lancet Infect Dis 5.4 (2005): 201.
- 24. Cohen JI. Licking latency with licorice. J Clin Invest 115.3 (2005): 591–593.
- 25. Hattori T et al. Preliminary evidence for inhibitory effect of glycyrrhizin on HIV replication in patients with AIDS. Antiviral Res 11 (1989): 255–262.
- 26. Lin JC. Mechanism of action of glycyrrhizic acid in inhibition of Epstein-Barr virus replication in vitro. Antiviral Res 59.1 (2003): 41–47.
- 27. Pompei R et al. Glycyrrhizic acid inhibits virus growth and inactivates virus particles. Nature 281.5733 (1979): 689–690.
- 28. Sasaki H et al. Effect of glycyrrhizin, an active component of licorice roots, on HIV replication in cultures of peripheral blood mononuclear cells from HIV-seropositive patients. Pathobiology 70.4 (2002–2003): 229–236.
- 29. Sekizawa T et al. Glycyrrhizin increases survival of mice with herpes simplex encephalitis. Acta Virol 45.1 (2001): 51–54.
- 30. Utsunomiya T et al. Glycyrrhizin, an active component of licorice roots, reduces morbidity and mortality of mice infected with lethal doses of influenza virus. Antimicrob Agents Chemother 41.3 (1997): 551–556.
- 31. Wang J et al. Glycyrrhizic acid as the antiviral component of Glycyrrhiza uralensis Fisch. against coxsackievirus A16 and enterovirus 71 of hand foot and mouth disease. J Ethnopharmacol 147.1 (2013): 114–121.

- 32. Wolkerstorfer A et al. Glycyrrhizin inhibits influenza A virus uptake into the cell. Antiviral Res 83.2 (2009): 171–178.
- 33. Hatano T et al. Phenolic constituents of licorice. VII: structures of glicophenone and glicoisoflavone, and effects of licorice phenolics on methicillin-resistant Staphylococcus aureus. Tokyo: Chem Pharm Bull 48.9 (2000): 1286–1292.
- 34. Long DR et al. 18β -Glycyrrhetinic acid inhibits methicillin-resistant Staphylococcus aureus survival and attenuates virulence gene expression. Antimicrob Agents Chemother 57.1 (2013): 241–247.
- 35. Gupta VK et al. Antimicrobial potential of Glycyrrhiza glabra roots. J Ethnopharmacol 116.2 (2008): 377–380.
- 36. Onkarappa R et al. Efficacy of four medicinally important plant extracts (crude) against pathogenic bacteria. Asian J Microbiol Biotech Env Sci 7 (2005): 281–284.
- 37. Messier C & Grenier D. Effect of licorice compounds licochalcone A, glabridin and glycyrrhizic acid on growth and virulence properties of Candida albicans. Mycoses 54.6 (2011): e801–e806.
- 38. Kalani K et al. In silico and in vivo anti-malarial studies of 18β glycyrrhetinic acid from Glycyrrhiza glabra. PLoS One 8.9 (2013): e74761.
- 39. Cheema HS et al. Glabridin induces oxidative stress mediated apoptosis like cell death of malaria parasite Plasmodium falciparum. Parasitol Int 63.2 (2014): 349–358.

Peptic Ulcer

40. Braun, Lesley et al. Licorice. Herbs and Natural Supplements: An Evidence Based Guide Volume 2 4th Edition. (2015) Pages 643 – 659.

Cautions & Side Effects

- 41. Rafi MM et al. Modulation of Bcl-2 and cytotoxicity by licochalcone-A, a novel estrogenic flavonoid. Anticancer Res 20.4 (2000): 2653–2658.
- 42. Hou YC, Lin SP, Chao PD. Liquorice reduced cyclosporine bioavailability by activating P-glycoprotein and CYP 3A. Food Chem. 2012;135(4):2307-12.
- 43. Liu L, Xiao J, Peng ZH, et al. In vitro metabolism of glycyrrhetic acid by human cytochrome P450. Yao Xue Xue Bao. 2011;46(1):81-7.
- 44. Armanini D, Bonanni G, Palermo M. Reduction of serum testosterone in men by licorice. N Engl J Med 341.15 (1999): 1158.
- 45. Armanini D et al. Licorice consumption and serum testosterone in healthy man. Exp Clin Endocrinol Diabetes 111.6 (2003a): 341–343.
- 46. Armanini D et al. Licorice reduces serum testosterone in healthy women. Steroids 69.11–12 (2004): 763–766.
- 47. Sakamoto K, Wakabayashi K. Inhibitory effect of glycyrrhetinic acid on testosterone production in rat gonads. Endocrinol Jpn 35 (1988): 333–342.
- 48. Takeuchi T et al. Effect of paeoniflorin, glycyrrhizin and glycyrrhetic acid on ovarian androgen production. Am J Chin Med 19.1 (1991): 73–78.

- 49. Breidthardt T, Namdar M, Hess B. A hypertensive urgency induced by the continuous intake of a herbal remedy containing liquorice. J Hum Hypertens. 2006;20(6):465-6.
- 50. Janse A, van Iersel M, Hoefnagels WH, Olde Rikker MG. The old lady who liked liquorice: hypertension due to chronic intoxication in a memory-impaired patient. Neth J Med. 2005;63(4):149-50.
- 51. Sigurjonsdottir HA, Franzson L, Manhem K, Ragnarsson J, Sigurdsson G, Wallerstedt S. Liquorice- induced rise in blood pressure: a linear dose-response relationship. J Hum Hypertens. 2001;15(8):549-52.
- 52. Strandberg TE, Andersson S, Jarvenpaa AL, et al. Preterm birth and licorice consumption during pregnancy. Am J Epidemiol 2002;156(9):803-805.