



Liquorice

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Liquorice (*Glycyrrhiza glabra*) is a herb cultivated throughout Europe, Asia and the Middle East. Sweet aromatic compounds are extracted from the liquorice root, and used as a flavouring in foods, confectionaries, beverages, and tobacco products. Medicinally, liquorice root has been used for a variety of ailments including lung, liver, kidney and circulatory conditions. It is purported to reduce inflammation, thin mucus secretions, suppress cough, aid ulcer healing, and treat infections, sore throat and atopic dermatitis. More recently, the negative effects of liquorice on health were emphasised when a death was reported as result of excessive consumption.

COMMON NAMES: licorice (American English), sweet root, gan cao/zao, glycyrrhiza extract, Chinese liquorice

PREPARATIONS: Available as tea, confectionary, gum, lozenges, capsules, tablets, chewable tablets, powder, liquid extracts, syrups, mouthwashes, toothpaste, and topically as creams, gels, serum,

shampoo, and more. Many products claiming to be liquorice contain anise oil, which has the characteristic smell and taste of black liquorice.

ACTIVE CONSTITUENTS: Glycyrrhizin, or glycyrrhizic acid (GZA), is the main active constituent of liquorice and contributes to the sweetness and yellow colour. The content of GZA in liquorice root varies from 2–25%, and is between 2–3 mg/g (0.2–0.3% w/w) in liquorice products, however this has been shown to vary from 0.026–98 mg/g. With processing, this compound can be removed resulting in deglycyrrhizinated liquorice. Other compounds include coumarins and flavonoids such as the phytoestrogens, glabrene and glabridin.

MEDICAL CLAIMS: Traditionally, liquorice has been used for a myriad of conditions including asthma, cough, lung diseases, mouth ulcers, arrhythmias, angina, skin and eye diseases, and more. Claims have been made that it supports the adrenal glands, liver and digestive health by aiding in the production of bile and digestive juices, and

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Summary message

Ingesting liquorice in large amounts, or in smaller amounts regularly over several months/years, can result in hypertension and other serious adverse effects. Due to differences in response to liquorice, glycyrrhizin content in preparations, and purity of liquorice, there is wide variation in how much liquorice is needed to produce these effects. Patients should be advised to avoid consuming liquorice regularly and in large quantities, especially if they have poor dietary habits or pre-existing cardiovascular or renal conditions. Liquorice is not safe during pregnancy. Insufficient evidence is available for use during lactation. No major drug interactions are known, although caution is advised with digoxin, corticosteroids, and diuretics. Liquorice should be stopped 2 weeks before surgery to minimise effects on blood pressure.

Herbal medicines are a popular health care choice, but few have been tested to contemporary standards. **POTION OR POISON?** summarises the evidence for the potential benefits and possible harms of well-known herbal medicines.

maintains healthy blood glucose levels and lymphatic energy. Topically, liquorice is used for atopic dermatitis, psoriasis, and as a gargle or lozenge for endotracheal intubation-related adverse effects. It has also been administered intravenously in the treatment of hepatitis B and C. Many of these claims remain unsupported by research.

SAFETY AND TOXICITY: If eaten in excessive quantities, or smaller amounts regularly over several weeks or months, GZA can result in pseudohyperaldosteronism. This occurs when glycyrrhetic acid, a metabolite of GZA, prevents the conversion of cortisol to inactive cortisone by inhibiting 11- β -HSD. Cortisol and aldosterone have equal affinity for mineralocorticoid receptors, causing excessive mineralocorticoid stimulation, and resulting in hypokalaemia, metabolic alkalosis, hypertension, arrhythmias, muscle weakness, rhabdomyolysis, paralysis, and encephalopathy. More than 400 mg GZA (20–30 g of liquorice products/200 g of candy) daily may result in hypokalaemia and hypertensive crisis, potentially leading to cardiac arrest and death. In patients with a poor diet, hypertension, high salt intake, and pre-existing cardiovascular or renal disease, the dose required to produce serious adverse effects may be as low as 100 mg GZA/day (5 g of liquorice product). The increase in blood pressure is proportional to the amount of GZA ingested and can take up to several months to normalise. Hypokalaemia may take 1 to 2 weeks to resolve.

Liquorice has abortifacient properties and heavy consumption (500 mg GZA/week) during pregnancy increases the risk of miscarriage or premature birth before 38 weeks gestation. Furthermore, high consumption in pregnancy increases the HPA-axis activity in the offspring. Insufficient data remains for use during breastfeeding.

Short-term, and in small amounts, liquorice is likely to be safe and well tolerated. Rarely, nausea, vomiting and headaches may occur. Safety has also been shown with a 2-week 2% topical preparation, but may cause rash in sensitive individuals.

Deglycyrrhizinated liquorice has been used safely in doses of up to 4.5 g daily for up to 4 months.

DRUG INTERACTIONS: There are no known major interactions, however caution is advised with antihypertensive drugs, warfarin, oestrogen, paclitaxel and cisplatin as liquorice may reduce their effectiveness. Concomitant use with corticosteroids may potentiate potassium depletion and increase levels and duration of activity of corticosteroids. Animal and *in vitro* studies have found liquorice to inhibit CYP2B6, CYP2C19 and CYP2C8, induce CYP3A4, and produce inhibitory and inducing effects on CYP2C9 isoenzymes. Liquorice overuse may increase cardiac toxicity with digoxin and potentiate potassium loss with non-potassium sparing diuretics. Theoretically ethacrynic acid may enhance the mineralocorticoid effects of liquorice.

Key references

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