Licorice

Glycyrrhiza glabra

Common names

Liquorice, yashtimadhu, glycyrrhiza, sweet root

Family

Fabaceae (legume)

Part used

Root

Background and traditional uses

Licorice is a perennial, herbaceous shrub with oval leaflets, white to purplish flower clusters and flat seed pods, which is native to the Mediterranean and some parts of Asia. The roots of the plant are popular in herbal medicine and are harvested for their use in the traditional Ayurvedic and Chinese medicine systems.[1]

Licorice has been traditionally used as an expectorant and antitussive, applied in catarrh, coughs (especially those associated with colds) and bronchitis.[2,3] It is also frequently applied as an anti-inflammatory digestive tonic to help relieve gastritis, dyspepsia and heartburn.[2,3]

Licorice derives its botanical name from the Greek words *glykós* (sweet) and *ríza* (root).[4] It is a powerful natural sweetener and can be up to 50-times sweeter than sucrose.[5] The plant has been used as a sweetening and flavouring agent traditionally and in food technology.

Actions

Primary:[3,5-19]

- Adrenal tonic
- Antiulcer
- Anti-inflammatory
- Antitussive
- Demulcent
- Expectorant
- Mucoprotective

Secondary:[3,5,11]

- Antiallergic
- Antibacterial
- Anticancer
- Antidepressant
- Antioxidant
- Antiviral
- Hepatoprotective
- Aperient
- Hypolipidaemic
- Cognition enhancing
- Neuroprotective

Applications and indications

- Whilst the pharmacodynamics of the active constituents of licorice are understood, the lack of clinical human trials for this herb means that modern herbal application is based largely on physiological logic and anecdotal/ traditional use.

- The German Commission E monographs only approves the use of licorice root for gastric and duodenal ulcers and upper respiratory tract cattarh.[1]
- The British Herbal Compendium indicates uses for bronchitis, peptic ulcer, chronic gastritis, rheumatism and arthritis.[1]

Active constituents and pharmacodynamics

Licorice root contains a variety of saponins, **oils, polysaccharides**, **phenols**, amines, **flavonoids**, and isoflavonoids.[1,5]

Glycyrrhizin, a **triterpenoid saponin**, is generally considered the main active compound of licorice root. Glycyrrhizin appears to be hydrolysed by beta-glucuronidase in the intestine to its active glycol, glycyrrhetic acid.[5,6] These compounds have many interesting therapeutic properties:[6-18]

Antiulcer

Glycyrrhizinic acid seems to raise the local concentration of prostaglandins that promote mucous secretion and cell proliferation in the stomach, contributing to the healing of ulcers in experimental and animal studies.[6-8] Licorice preparations appear to raise local concentrations of specific prostaglandins that encourage cell proliferation and mucosal repair in the stomach, making it a useful medication for ulcers. It does this by inhibiting 15-hydroxyprostaglandin dehydrogenase and delta-13-PG-reductase.[7]

Anti-inflammatory

Beta-glycyhrritinic acid inhibits the metabolism of glucocorticoids and potentiates their effects.
Since beta-glycyhrritinic acid is a potent inhibitor of 11-beta-hydroxysteroid hydroxygenase, it creates an accumulation of glucocorticoids with anti-inflammatory properties.
Beta-glycyhrritinic acid also inhibits classical complement pathway activation and its inflammatory processes.[5]

Antibacterial

Several constituents in licorice, including isoflavones, licochalcone A and the phenolic compounds glicophenone and glicoisoflavanone have been shown to have antibacterial action against *Staphylococcus aureus* (both methicillin resistant and methicillin sensitive forms), *Mycobacterium tuberculosis, Escherichia coli, Bacillus subtilis, Enterobacter aerogenes* and *Klebsiella pneumoniae.*[5]

Adrenal tonic and mineralocorticoid activity

Glycyrrhetic acid has the ability to convert cortisol into its inactive form, cortisone, by inhibiting the enzyme hydroxysteroid dehydrogenase (11HSD),[16] resulting in prolonged activity and slowed excretion of cortisol.
Both glycyrrhizin and glycyrrhizic acid bind to glucocorticoid and mineralocorticoid receptors and may remove cortisol from transcortin, its carrier molecule.[12]

Glycyrrhizin/glycyrrhetic acid produce a reliable reduction in testosterone and a highly reliable increase in circulating cortisol after consumption. Both of these effects are dose-dependent, not associated with any toxicological effects and reverse on cessation of licorice-based medicines.[17]

The most common side effect of chronic consumption of high amounts of licorice is hypokalaemic hypertension, which is caused by blocking 11HSD type 2 (11HSD2) activity at the kidneys and other organ targets for aldosterone. In these tissues, this enzyme plays a key role in modulating mineralocorticoid effects by inactivating cortisol to cortisone. Glycyrrhetinic acid can bind directly to mineralocorticoid receptors as an agonist when its plasma concentration is high enough to compete with aldosterone and cortisol for mineralocorticoid receptors.[18]

Summary of clinical evidence

Antiallergic

The results of animal studies suggest that compounds in licorice, namely glycyrrhizic acid, 18-beta-glycyrrhetinic acid and liquiritigenin, inhibit IgE-induced allergic reactions, particularly respiratory and dermatological reactions.[9,10]

Antiviral

In both animal and human studies, glycyrrhizin has been shown to have activity against a number of viruses including Epstein-Barr, herpes simplex, hepatitis A, hepatitis B, hepatitis C, human cytomegalovirus, HIV, influenza, SARS and varicella zoster.[5]

It has been proposed that licorice exerts this activity in several ways, including reducing membrane transport, reducing membrane fluidity and enzyme inhibition.[11]

Respiratory effects

Licorice appears to both stimulate tracheal mucous secretion/facilitate respiratory mucous elimination[12] and exert an antitussive[13] and tracheal relaxant effect.[14] Licorice root also contains significant amounts of mucilage that coats the oral and throat mucosa, soothing irritation and relieving dry cough.[5] These combined effects explain the traditional use of licorice for a wide range of respiratory symptoms.

Endocrinological and mineralocorticoid

The mineralocorticoid effects of licorice are mediated by the inhibitory effects of glycyrrhetinic acid on 11-beta-hydroxysteroid dehydrogenase type 2.[15] One study suggests that glycyrrhetinic acid increases circulating and, thereby, salivary levels of unconjugated deoxycorticosterone and dehydroepiandrosterone by inhibiting their adrenal cortex conjugation. This may contribute to the mineralocorticoid actions of glycyrrhetinic acid and gives substance to claims that licorice root has androgenic properties.[15]

Nine healthy women given 3.5g of licorice root daily, standardised to contain 7.6% glycyrrhizic acid, over two menstrual cycles resulted in reduced testosterone levels in all subjects when tested in the luteal phase, likely due to the blockage of 17-hydroxysteroid dehydrogenase and 17-20 lyase.[18] Although small, the study suggests that licorice may be a useful adjuvant therapy for women experiencing the symptoms of high testosterone, including hirsutism and polycystic ovarian syndrome.[18]

In a four-week intervention study, 36 individuals took 100g of dry licorice root, standardised to 150mg glycyrrhetic acid.[19] Six individuals left the study before completion, with some reporting adverse side effects such as headache and oedema, though all side effects disappeared on cessation of treatment. For those who completed the study, increased blood pressure and cortisol was observed in all, with licorice having more impact on these factors in women relative to men, and in those who had existing hypertension.[19]

Aphthous ulcers

In a double blind clinical trial using an intra-oral slow release patch containing an extract of licorice root on patients with aphthous ulcers, the treatment group showed significantly reduced ulcer sizes and reduced pain when compared to the placebo group and control group.[20] The results of this study indicate that using an adhesive patch containing intra-oral licorice root extract for treatment of aphthous ulcers offers significant benefits in regard to reduction of pain and visual resolution of ulcers.[20]

Dyspepsia and peptic ulcers

In an uncontrolled trial on 32 patients with chronic duodenal ulcers, 3.8g dry herb equivalent daily of deglycyrrhizinised licorice root tablets split into five doses resulted in significant signs of healing in all participants and total membrane restoration in a majority of subjects over a 24-week treatment period. 56% of participants reported improved symptoms by week 12, and 78% by week [16,21] Another four-week trial of 96 patients with chronic duodenal ulceration did not produce clinically significant results,[22] suggesting that longer term treatment results in more positive outcomes.

Lung cancer

A very recent preclinical *in vitro* study on HCC827 (human lung carcinoma) cells showed that treatment with 100μM of glycyrrhizin resulted in a significant inhibition in the expression of osteopontin protein and in the rate of cell proliferation. The treatment also caused cell cycle arrest by preventing the cells from entering into the G2 phase. In addition, glycyrrhizin treatment reduced the expression of MMP-2 and MMP-9 in HCC827 cells significantly after 48 hours. This preclinical data suggests that there are potential benefits for the use of licorice in lung cancer patients.[23]

Dosage summary

Liquid extract (1:1): 15-40mL[24]
Dried herb equivalent: 1-4g three times daily[24]

Safety information

- Contraindicated in pregnancy.[2]
- The safety of internal use in patients under 18 years of age has not been established.[2]
- Patients taking licorice medication should not take other licorice containing products, including confectionary, as serious adverse events may occur such as water retention, hypokalaemia, hypertension and/or cardiac rhythm disorders.[2]
- Licorice is not recommended for patients affected by hypertension, kidney diseases, liver or cardiovascular disorders, or hypokalaemia.[2]
- Concomitant use with diuretics, cardiac glycosides, corticosteroids, stimulant laxatives or other medications which may exacerbate electrolyte imbalance is not recommended.[2]

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