Dr. Bassam Ali Abu Shanab,
BPharm, RPh

Balsam Pharmacy, Tulkarm,
West Bank, Palestine

Glycyrrhiza glabra (Licorice root)

Source

Glycyrrhiza glabra is one of the saponin glycosides. It is the dried rhizome and roots of Glycyrrhiza glabra, and belongs to the Family Fabaceae. It contains a saponin-like glycoside, glycyrrhizin (glycyrrhizic acid, GA), which is 50 times as sweet as sugar. Glycyrrhizin (GL) is responsible for most of the beneficial effects of licorice. Supplements containing therapeutic amounts of licorice come in two forms: either with glycyrrhizin, or without glycyrrhizin, a form known as deglycyrrhizinated licorice, or DGL. Other constituents include flavonoid glycosides, (liquiritin, isoliquiritin, liquiritoside, isoliquiritoside, rhamnoliquiritin, and rhamnoisoliquiritin), coumarin derivatives (herniarin and umbelliferone), asparagine, 22,23-dihydrostigmasterol, various plant estrogens (phytoestrogens), glucose, mannitol, and about 20% starch.

Mode of action for antiulcer effects

This appears to involve the ability of GL and GA to inhibit the enzymes 15-hydroxyprostaglandin dehydrogenase and D-13-prostaglandin reductase, which inactivate the protective prostaglandins (PG) in the gastric mucosa, particularly the PGE series (Endogenous PGs). The gastric mucosas of ulcer patients have been shown to be deficient in PGs, which is believed to play a role in the pathogenesis of peptic ulcers. By elevating the local concentration of selective PGs, licorice provides a protective effect against mucosal damage.

Potential uses

Main use (well documented):

- Oral Uses (DGL form): Ulcers, Heartburn (Esophageal Reflux), Mouth Sores.
- Topical Uses (whole herb): Eczema, Psoriasis, Herpes.
- Oral Uses (whole herb): Cough, Asthma, Chronic Fatigue Syndrome (CFS).

Other possible uses (less well documented):

- Internal: Allergies, arthritis, adrenocortical insufficiency, bronchitis, chronic gastritis, hepatitis, hypoglycemia, hypotension, rheumatism, steroid drug withdrawal.
- External: Dental caries, aphthous stomatitis, and herpes simplex lesions.

Supporting evidence

In a clinical study in 70 patients, 70% healing of gastric and duodenal ulcers by carbenoxolone (a GA derivative) vs. 36% in the placebo group[1]. Carbenoxolone-treated patients with reflux oesophagitis had an 82% improvement in 8 weeks and improved 50% faster than controls, who showed a 63% improvement. Side effects were minimized by small frequent doses (5 x 20 mg daily)[2]. Gastric ulcer responded better to 4-6 weeks of carbenoxolone (glycyrrhetinic acid derivative) than to placebo in a trial with 40 patients[3]. Endoscopic examination in 32 cases of chronic duodenal ulceration treated with deglycyrrhizinized licorice tablets showed that healing of the ulceration had occurred[4].

Herpes healing time and pain associated with these lesions were reduced by carbenoxolone[5].

Whilst aphthous ulcers were improved 50-75% in one day in 15 out of 20 patients followed by complete healing of the ulcers by third day with deglycyrrhizinized licorice[6].

Precautions

Side effects

Long-term use or ingestion of excessive amount of licorice (when taken at dosages exceeding 3 g daily for more than 6 weeks) can produce headache, lethargy, sodium and water retention, excessive loss of potassium, high blood pressure, stiffness, shortness of breath and upper abdominal pain. These effects can be especially dangerous in patients taking digitalis, or those with high blood pressure, heart disease, diabetes, or kidney disease.

Men with impotence, infertility, or decreased libido may wish to avoid this herb because licorice may reduce testosterone levels in men. Licorice may also increase both the positive and negative effects of corticosteroids, such as prednisone and hydrocortisone cream. DGL is believed to be safe, although extensive safety studies have not been performed. Side effects are rare.

Drug interactions

Licorice may interfere with digitalis drugs (digitoxin and digoxin) and neutralize the the effects of antihypertensives. Hazardously low potassium levels may result when licorice is combined with a regimen of thiazide or other diuretics, such as furosemide, indapamide or spironolactone.

Taking licorice with steroid medications, such as prednisone, may increase both their medicinal effects and their often undesirable side effects.

Pregnancy and lactation

Safety for either form of licorice in pregnant or nursing women has not been established. According to one report, licorice possesses significant estrogenic activity and, as such, shouldn't be taken by pregnant women or women who have had breast cancer. In addition, an observational study found evidence that heavy licorice use might lead to risk of premature birth.

The safe dosage

- Solid Extract: (4:1) 250-500 mg three times daily.
  (Manufacturer's preparations may vary).
- DGL Capsules: 1-3 caps. Three times daily.
  (Manufacturer's preparations may vary; 300-380 mg/capsule is typical.)
- Tincture: (1:5) 5-15 ml. three times daily.
- Dried root: 1-4 g. three times daily.
  (Daily Maximum 12 g).

Treatment should not be continued longer than 4-6 weeks because of the known common side effects.

References and further reading

1. Loginov AS, et al. The effectiveness of carbenoxolone in the treatment of gastro-duodenal ulcer patients. Scand J Gastroenterol Suppl 1980; 65: 85-91.
2. Young GP, et al. Treatment of reflux oesophagitis with a carbenoxolone/antacid/alginate preparation. A double-blind controlled trial. Scand J Gastroenterol 1986; 21: 1098-104.
3. Schwamberger K, Reissigl H. Carbenoxolone patients with gastric ulcers. A double-blind trial. Scand J Gastroenterol 1980; 65 (suppl): 59-62.
4. Larkworthy W, Holgate PF. Deglycyrrhizinized liquorice in the treatment of chronic duodenal ulcer. A retrospective endoscopic survey of 32 patients. Practitioner 1975; 215: 787-92
5. Partridge M, Poswillo DE. Topical carbenoxolone sodium in the management of herpes simplex infection. Br J Oral Maxillofac Surg 1984; 22:138-45.
6. Das SK.Deglycyrrhizinated liquorice in aphthous ulcers. J Assoc Physicians India 1989; 37:647.
7. Duke, James A. The green pharmacy, Rodale Press, 1997, Emmaus, PA, ISBN: 0875963161.
8. Robbers, James E.; Speedie, Marilyn K.; Tyler, Varro E. Pharmacognosy and pharmacobiotechnology, Williams & Wilkins, 1996, Baltimore, Maryland, ISBN: 068308500X.
9. Baker M. Licorice and enzymes other than 11 beta-hydroxysteroid dehydrogenase: an evolutionary perspective. Steroids 1994; 59:136-141.
10. Konturek S. (1985). Prostaglandins in pathophysiology of peptic ulcer disease. Dig Dis Sci 1985; 30(11):105S-108S.

Birth control patch receives FDA approval

Ortho-McNeil Pharmaceutical has announced US FDA approval for the first birth control patch, Ortho Evra (norelgestromin/ethinyl estradiol transdermal system). Ortho Evra is a thin patch that delivers continuous levels of the hormones norelgestromin and ethinyl estradiol through the skin and into the bloodstream. The patch is worn for one week at a time and is replaced on the same day of the week for three consecutive weeks. The fourth week is 'patch-free.' The patches can be worn on the buttocks, abdomen, upper torso (front or back, excluding the breasts), or upper outer arm and have demonstrated a low rate of detachment even while bathing, swimming, exercising or wearing it in humid conditions.

Allergan and EntreMed alliance for eye diseases

Allergan and EntreMed Inc. have entered into a five-year strategic alliance to develop and commercialise small molecule angiogenic inhibitors for treatment and prevention of eye conditions. Angiogenic inhibitors block the formation of blood vessels associated with over 80 different diseases. EntreMed's Panzem (2-methoxyestradiol) is the first small molecule to be licensed, developed and marketed under this agreement.

Allergan and EntreMed will co-develop Panzem to treat age-related macular degeneration, a leading cause of blindness as the result of bleeding from the rupture of new blood vessels that form under the retina. A key part of this alliance will be the assessment of Oculex Pharmaceuticals' novel drug delivery technology to provide localized administration of Panzem to the back of the eye.

Lilly receives FDA approval for Xigris

Eli Lilly and Company has announced that the US FDA has approved Xigris (drotrecogin alfa (activated)), a recombinant form of human Activated Protein C. Xigris is approved for the reduction of mortality in adult patients with severe sepsis (sepsis associated with acute organ dysfunction), who have a high risk of death. Eli Lilly plans to launch Xigris in the United States in early 2002.

Post-approval trials will include a study of the efficacy of Xigris in adult patients with severe sepsis who have a lower risk of death and a study in pediatric patients with severe sepsis. Eli Lilly and Company has applied for regulatory approval of Xigris in Canada, the EU and Australia for the treatment of severe sepsis.