

Johe RS, Jenden DJ. Dimethylaminoethanol (deanol) metabolism in rat brain and its effect on acetylcholine synthesis. *J Pharmacol Exp Ther.* 1979; 211:472-479.

Millington WR, Mc Call AL, Wurtman RJ. Deanol acetamidobenzoate inhibits the blood-brain barrier transport of choline. *Ann Neurol.* 1978; 4:302-306.

Penovich P, Morgan JP, Kerzner B, et al. Double-blind evaluation of deanol in tardive dyskinesia. *JAMA.* 1978; 239:1997-1998.

Sergio W. Use of DMAE (dimethylaminoethanol) in the induction of lucid dreams. *Med Hypotheses.* 1988; 26:255-257.

Soares KV, McGrath JJ. The treatment of tardive dyskinesia—a systematic review and meta-analysis. *Schizophr Res.* 1999; 39:1-16.

Zahniser NR, Chou D, Hanin I. Is 2-dimethylaminoethanol (deanol) indeed a precursor of brain acetylcholine? A gas chromatographic evaluation. *J Pharmacol Exp Ther.* 1977; 200:545-549.

Deglycyrrhizinated Licorice (DGL)

DESCRIPTION

Deglycyrrhizinated licorice, commonly abbreviated DGL, is an extract of the root of true licorice, *Glycyrrhiza glabra*, which has significantly reduced mineralocorticoid activity. Licorice has a number of medicinal properties, including peptic ulcer healing, anti-inflammatory, antimicrobial and antioxidant activities. Glycyrrhizinic acid and its metabolite, glycyrrhetic acid, have mineralocorticoid-like, as well as testosterone-reducing, activities. The use of licorice for the management of peptic ulcer disease is associated with hypertension, water retention and hypokalemia. The removal of most of the glycyrrhizinic and glycyrrhetic acids yields a product without these undesirable effects.

ACTIONS AND PHARMACOLOGY

ACTIONS

DGL may have peptic ulcer-healing activity.

MECHANISM OF ACTION

The mechanism of action of the peptic ulcer-healing activity of DGL is not entirely understood. DGL was found to stimulate and/or accelerate the differentiation of glandular cells in the forestomach of the rat, as well as stimulate mucus formation and secretion. The stimulation of mucus secretion in the stomach is believed to account, at least in part, for the activity of DGL. DGL contains some flavonoids that have antimicrobial activity, including activity against the ulcer-causing bacterium *Helicobacter pylori*. This too could account, at least in part, for DGL's activity. New substances

are continually being discovered in licorice, and it is possible that some of these may also play a role in DGL's activity.

PHARMACOKINETICS

There is very little known about the pharmacokinetics of DGL.

INDICATIONS AND USAGE

DGL has been shown to be useful in the management of gastric and duodenal ulcers.

RESEARCH SUMMARY

Several studies in animals and humans have demonstrated positive effects from the use of DGL in gastric and duodenal ulcer conditions. DGL, administered in chewable doses of 760 milligrams a day for one month, was significantly superior to placebo in reducing peptic ulcer size and in hastening healing in human subjects, compared with the placebo control subjects. DGL produced complete healing in 44% of those receiving it, compared with complete healing in 6% of controls.

Subsequent studies have shown that DGL is about as effective as cimetidine and ranitidine for both treatment and maintenance therapy of gastric ulcers. Comparison studies have not been made with DGL and famotidine, lansoprazole, omeprazole and other more recent anti-ulcer drugs.

DGL appears to confer significant protection against the gastric mucosal damage caused by aspirin and other nonsteroidal anti-inflammatory drugs. Gastric bleeding induced by aspirin intake can also be reduced with DGL supplementation.

DGL has also demonstrated significant efficacy in the treatment of duodenal ulcers. In one study, 40 patients who had suffered from severe duodenal ulcers for four to 12 years (and who had experienced more than six relapses in the previous year) were treated with either 3 grams of DGL daily for eight weeks or with 4.5 grams daily for 16 weeks. All showed significant improvement, but more improvement was seen with the higher-dose regimen. None of the patients required surgery during a one-year follow-up period. In other research, DGL had a therapeutic effect in duodenal ulcers equal to that of cimetidine.

DGL's protective activity is attributed by some to its ability to stimulate the formation and secretion of mucus. It has been shown, in rats, to stimulate epithelial proliferation in the forestomach. More recently, it has been demonstrated that several flavonoids that are present in DGL can inhibit *Helicobacter pylori* growth.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to a DGL-containing product.

PRECAUTIONS

Because of lack of long-term safety studies, DGL should be avoided by children, pregnant women and nursing mothers.

Those with hypertension, congestive heart failure, arrhythmias, water retention and low potassium and/or magnesium levels should discuss the use of DGL with their physicians and should be certain that any DGL they use is free of glycyrrhizinic acid.

ADVERSE REACTIONS

There are significant adverse effects with licorice extracts containing glycyrrhizinic and glycyrrhetic acid when used for the management of peptic ulcer disease, including hypokalemia, hypomagnesemia, hypertension, headache, cardiac arrhythmias, water retention and congestive heart failure. DGL, however, should be free of these side effects. There are occasional reports of gastrointestinal side effects, such as diarrhea and nausea.

INTERACTIONS

The excretion rate of nitrofurantoin was found to be significantly higher in patients receiving the drug along with DGL. No interactions with drugs used in the treatment of peptic ulcer disease are known.

OVERDOSAGE

There are no reports of overdosage with DGL.

DOSAGE AND ADMINISTRATION

In Europe, Canada and South Africa, DGL is available as a medicinal preparation called Caved-S. In the U.S., DGL is available as a nutritional supplement in the form of chewable tablets. Typically, those who use DGL for management of peptic ulcer disorders chew from one to four 380-milligram tablets or the equivalent before each meal.

LITERATURE

Armanini D, Bonanni G, Palermo M. Reduction of serum testosterone in men by licorice. *N Engl J Med.* 1999; 341:1158.

Balackrishnan V, Pillai MV, Raveendran PM, Nair CS. Deglycyrrhizinated liquorice in the treatment of chronic duodenal ulcer. *J Assoc Physicians India.* 1978; 26:811-814.

Bardham KD, Cumberland DC, Dixon RA, Holdsworth CD. Proceedings: deglycyrrhizinated liquorice in gastric ulcer: a double-blind controlled study. *Gut.* 1976; 17:397

Beil W, Birkholz C, Sewing KF. Effects of flavonoids on parietal cell acid secretion, gastric mucosal prostaglandin production and *Helicobacter pylori* growth. *Arzneimittelforschung.* 1995; 45:697-700.

Bennett A, Clark-Wibberley T, Stamford IF, Wright JE. Aspirin-induced gastric mucosal damage in rats: cimetidine and deglycyrrhizinated liquorice together give greater protection than

low doses of either drug alone. *J Pharm Pharmacol.* 1980; 32:151.

Dalta R, Rao SR, Murthy KJ. Excretion studies of nitrofurantoin and nitrofurantoin with deglycyrrhizinated liquorice. *Indian J Physiol Pharmacol.* 1981; 25:59-63.

Farese Jr RV, Biglieri EJ, Shackleton CHL, et al. Licorice-induced hypermineralocorticoidism. *N Engl J Med.* 1991; 325:1223-1227.

Glick L. Deglycyrrhizinated liquorice for peptic ulcer. *Lancet* 1982; 2:817.

Li W, Asada Y, Yoshikawa T. Antimicrobial compounds from *Glycyrrhiza glabra* hairy root cultures. *Planta Med.* 1998; 64:746-747.

Morgan AG, McAdam WA, Pascoe C, Darnborough A. Comparison between cimetidine and Caved-S in the treatment of gastric ulceration and subsequent maintenance therapy. *Gut.* 1982; 23:545-551.

Morgan AG, Pascoe C, McAdam WA. Comparison between ranitidine and ranitidine plus Caved-S in the treatment of gastric ulceration. *Gut.* 1985; 26:1377-1379.

Morgan AG, Pascoe 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.

Rees WD, Rhodes J, Wright JE, et al. Effect of deglycyrrhizinated liquorice on gastric mucosal damage by aspirin. *Scand J Gastroenterol.* 1979; 14:605-607.

Stewart PM, Wallace AM, Vallentino R, et al. Mineralocorticoid activity of liquorice: 11-beta-hydroxysteroid dehydrogenase deficiency comes of age. *Lancet.* 1987; 2:821-824.

van Marle J, Aarsen PN, Lind A, van Weeren-Kramer, J. Deglycyrrhizinated liquorice (DGL) and the renewal of rat stomach epithelium. *Eur J Pharmacol.* 1981; 72:219-225.

DHEA (Dehydroepiandrosterone)

DESCRIPTION

Dehydroepiandrosterone, commonly abbreviated as DHEA, is a natural substance produced in the adrenal glands, gonads and in the brain. DHEA is a steroid prohormone and a precursor for both androgens and estrogens. DHEA and its metabolite dehydroepiandrosterone-3-sulfate, or DHEAS, are the major secretory steroidal products of the adrenal gland and the most abundant circulating steroids in the human adult. The ratio of DHEAS to DHEA in serum is approximately 300:1 to 500:1, and the concentration of DHEAS in the serum is approximately 20 times higher than that of any other steroid hormone. It is noteworthy that the