OVERVIEW
Licorice root is one of the most widely used medicinal herbs worldwide and is the single most used herb in Chinese medicine today. In a recent survey of Western medical herbalists, licorice ranked as the 10th most important herb used in clinical practice. While licorice root is commonly taken in combinations for treatment of catarrhs of the respiratory tract, cough and sore throat, as well as dyspepsia, a few clinical studies have investigated its effects on aphthous, duodenal, and gastric ulcers.

PRIMARY USES
Crude Preparations
• Catarrh of upper respiratory tract

Deglycyrrhized Licorice Extract Preparations
• Aphthous, stomatitis (oral ulcers)
• Gastric ulcers
• Duodenal ulcer

NOTE: The Commission E also approved licorice preparations containing glycyrrhizin for gastric and duodenal ulcers.

OTHER POTENTIAL USES
• Prevention of radiation complications in lungs during radiotherapy
• Chronic hepatitis
• Sore throat
• Cough with viscid expectoration
• Dyspepsia

Purified Licorice Derivatives
• Hepatic failure, subacute
• Reduced risk of liver carcinogenesis in hepatitis C patients

Uses in Traditional Chinese Medicine (TCM)
• Bronchitis, pharyngitis, laryngitis, bronchial asthma, chronic hypocorticoidism

PHARMACOLOGICAL ACTIONS
Anti-inflammatory; expectorant; demulcent; adrenocorticotropic; antioxidant; protection of LDL against lipid peroxidation; accelerates healing of gastric ulcers.

DOSEAGE AND ADMINISTRATION
Licorice should not be ingested for longer than 4 to 6 weeks without medical advice, although licorice root may be used as a flavoring agent up to a maximum daily dosage equivalent to 100 mg glycyrrhizin. A diet rich in potassium (e.g., bananas) is recommended during the period of treatment with licorice.

Crude Preparations
DECOCTION: 1.0–1.5 g licorice root placed in approximately 150–250 ml cold water. Boiled, simmered for 10–15 minutes, then strained; 2–3 times daily.
INFUSION: Approximately 150 ml boiling water poured over 4.5 g licorice root and steeped 10–15 minutes; 2–3 times daily.
FLUID EXTRACT: 2–5 ml, 3 times daily.
POWDERED ROOT: Approximately 5–15 g root daily; equivalent to 200–600 mg glycyrrhizin, 2–4 g single dose.

Deglycyrrhized Licorice (DGL) Preparations
DGL NATIVE DRY EXTRACT: 0.4–1.6 g, 3 times daily.
DGL CHEWABLE TABLETS: For acute cases of gastric or duodenal ulcers; 2–4 tablets chewed before each meal. For chronic cases, 1 to 2 tablets chewed before each meal.

Standardized Preparations
FLUID EXTRACT: 5–15 ml daily, (or 2–5 ml, 3 times daily) corresponding to German Commission E dosage of 5–15 g of root daily.
NATIVE DRY EXTRACT: 0.33–0.8 g, 3 times daily, after meals.

CONTRAINDICATIONS
Patients with cholestatic liver disorders, liver cirrhosis, hypertension, hypokalemia, severe kidney insufficiency, and possibly diabetes (unconfirmed contraindication) should consult a healthcare provider before using licorice.

PREGNANCY AND LACTATION: Not recommended during pregnancy. Heavy exposure to glycyrrhizin (<500 mg/wk) did not affect birth weight, but did double the risk of birth before 38 weeks. No known restrictions during lactation.
ADVERSE EFFECTS
No adverse effects have been associated with licorice when used appropriately. Prolonged use (longer than six weeks) and higher doses (greater than 50 g/day) may lead to sodium and water retention, and to potassium loss accompanied by hypertension, edema, hypokalemia, and, in rare cases, myoglobinuria. Side effects are less likely with aqueous licorice root extract than with isolated glycyrrhizin. In two separate cases, pulmonary edema and life-threatening ventricular tachycardia due to hypokalemia occurred as a result of overdoses of black licorice-flavored candy.

DRUG INTERACTIONS
Licorice may potentiate the side effects of potassium-depleting thiazide diuretics (eg., chlorothiazide, chlorthalidone, hydrochlorothiazide, and metolazone). With potassium loss, sensitivity to digitalis glycosides increases. Licorice should not be combined with corticoid treatment.

CLINICAL REVIEW
Ten studies that included a total of 2,544 participants had variable research designs and evaluated a wide cross-section of therapeutic uses. Eight showed positive effects for indications including the effects of licorice or its active constituents on pulmonary metabolism, pseudohyperaldosteronism, aphthous ulcer, benign gastric ulcer, chronic duodenal ulceration, LDL cholesterol, subacute hepatic failure, and chemoprevention. Three studies were conducted on licorice root extract, four studies on DGL extract, and two on isolated glycyrrhizin preparations. One study on birth outcome found that licorice did not affect birth weight but did double the risk of birth before 38 weeks.
**Licorice**

*Glycyrrhiza spp.*  
*Glycyrrhiza glabra* L. (syn. *G. glandulifera* Walst. & Kit.), *G. uralensis* Fisch. Ex DC.  
[Fam. Fabaceae]

**OVERVIEW**  
Licorice root is one of the most widely used medicinal herbs worldwide and is the single most used herb in Chinese medicine today. In a recent survey of Western medical herbalists, licorice ranked as the 10th most important herb used in clinical practice. While licorice root is commonly taken in combinations for treatment of catarrhs of the respiratory tract, cough, sore throat, and dyspepsia, a few clinical studies have investigated its effects on aphthous, duodenal, and gastric ulcers.

**PRIMARY USES**  
Catarrh of the upper respiratory tract; oral ulcers; gastric and duodenal ulcers.

**OTHER USES**  
Sore throat; cough with viscid expectoration; dyspepsia; prevention of lung complications during radiation therapy; reduction of risk of liver cancer in hepatitis C; chronic hepatitis.

**TRADITIONAL CHINESE MEDICINE USES**  
Bronchitis; pharyngitis; laryngitis; bronchial asthma; chronic hypocorticoidism.

**DOSAGE**  
Licorice should not be ingested for more than 4 to 6 weeks without medical advice. Licorice root may be used as a flavoring agent up to a maximum daily dosage equal to 100 mg glycyrrhizin. A diet high in potassium-rich foods such as bananas is recommended while being treated with licorice.

**Crude Preparations**  
**DECOCTION:** 1.0–1.5 g licorice root placed in approximately 150–250 ml cold water. Boiled, simmered for 10–15 minutes, then strained; 2–3 times daily.  
**FLUID EXTRACT:** 2–5 ml, 3 times daily.  
**POWDERED ROOT:** Approximately 5–15 g root daily, equivalent to 200–600 mg glycyrrhizin, 2–4 g single dose.

**Deglycyrrhized Licorice (DGL) Preparations**  
**DGL NATIVE DRY EXTRACT:** 0.4–1.6 g, 3 times daily.  
**DGL CHEWABLE TABLETS:** For acute cases of gastric or duodenal ulcers; 2–4 tablets chewed before each meal. For chronic cases, 1 to 2 tablets chewed before each meal.

**Standardized Preparations**  
**FLUID EXTRACT:** 2 to 5 ml, 3 times daily [standardized minimum 7% glycyrrhizin].  
**NATIVE DRY EXTRACT:** 0.33–0.8 g, after meals, 3 times daily [standardized minimum 20% glycyrrhizin].

**CONTRAINDICATIONS**  
Patients with cholestatic liver disorders, liver cirrhosis, high blood pressure, hypokalemia, severe kidney insufficiency, and possibly diabetes (unconfirmed contraindication) should consult a healthcare provider before using licorice.  
**PREGNANCY AND LACTATION:** Not recommended for use during pregnancy. No known restrictions during lactation.

**ADVERSE EFFECTS**  
No adverse effects have been associated with licorice when used appropriately. The prolonged use of licorice in high doses (greater than 50 g/day) and for more than six weeks may lead to sodium and water retention, and to potassium loss accompanied by high blood pressure, water retention, and potential cardiac complications. Aqueous licorice root extracts are less likely than isolated glycyrrhizin to produce side effects.

**DRUG INTERACTIONS**  
Licorice may increase the side effects of potassium-depleting thiazide diuretics, including chlorothiazide, chlorthalidone, hydrochlorothiazide, and metolazone. With the loss of potassium, sensitivity to digitalis glycosides (heart medications) increases. Licorice should not be combined with corticosteroid drug treatment.

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Licorice

**Glycyrrhiza spp.**

*Glycyrrhiza glabra* L. (syn. *G. glandulifera* Walst. & Kit.), *G. uralensis* Fisch. Ex DC.  
[Fam. Fabaceae]

**OVERVIEW**

Licorice root is presently one of the most widely used medicinal herbs, and has been used therapeutically for several thousand years in Western and Eastern medicine (Gibson, 1978; Leung and Foster, 1996; Wang et al., 2000). Licorice ranks as the 10th most important herb for Western medical herbalists and in Unani traditional medicine clinics in Pakistan (Bergner, 1994; American Institute of Unani Medicine, 1999). In Traditional Chinese Medicine (TCM), licorice root is the most commonly-used herb, though it is almost always used in combination with other herbs (Leung, 1999).

**DESCRIPTION**

Licorice root consists of the dried roots and rhizomes of *Glycyrrhiza glabra* L. (syn. *G. glandulifera* Walst. & Kit.) and its varieties or *G. uralensis* (WHO, 1999; McGuffin et al., 2001), or other species of *Glycyrrhiza* (US FDA, 1998), and contains no less than 4% glycyrrhizic acid (syn. glycyrrhizin) (Ph.Eur., 2001). Peeled roots contain no less than 20% water-soluble extractive, and unpeeled roots contain no less than 25% water-soluble extract (Blumenthal et al., 1998), and no less than 25% dilute ethanol-soluble extract (JP XII, 1991; JSHM, 1993).

**PRIMARY USES**

**Crude Preparations**

- Catarrh of the upper respiratory tract (Blumenthal et al., 1998)

**Deglycyrrhized Licorice Extract (DGL) Preparations**

- Aphthous, stomatitis (oral ulcers) (Das et al., 1989)
- Gastric ulcers (Morgan et al., 1985)
- Duodenal ulcer (Kassir, 1985; Larkworthy and Holgate, 1975)

NOTE: The German Commission E also approved licorice preparations containing glycyrrhizin for gastric and duodenal ulcers.

**OTHER POTENTIAL USES**

**Miscellaneous Preparations**

- Prevention of radiation complications in lungs during radiotherapy (Palagina et al., 1999) [extract]
- Chronic hepatitis (Chang and But, 1986; Huang, 1999) [decoction]
- Sore throat, as a demulcent (IP, 1996; WHO, 1999) [form not specified]
- Cough with viscid expectoration (Schilcher, 1997) [extract, tea, or juice]
- Dyspepsia (WHO, 1999) [form not specified]

**Purified Licorice Derivatives**

- Hepatic failure, subacute (Acharya et al., 1993) [NOTE: i.v. preparation]
- Reduced risk of liver carcinogenesis in hepatitis C patients (Arase et al., 1997)

**Uses in TCM**

- Bronchitis, pharyngitis, laryngitis, bronchial asthma, chronic hypoglycemia (PPRC, 1992)

**Combination Preparations**

- Infantile colic—with chamomile flower (*Matricaria* spp.), fennel seed (*Foeniculum vulgare*), vervain herb (*Verbena hastata*), and lemon balm leaf (*Melissa officinalis*) (Weizman et al., 1993; Zand et al., 1994)
- Productive cough in children—with marshmallow root (*Althaea officinalis*), anise seed (*Pimpinella anisum*), and cowslip flower (*Primula veris*) (Schilcher, 1997)

**DOSAGE**

**Internal**

**Crude Preparations**

- Decoction: 1.0–1.5 g licorice root placed in approximately 150–250 ml cold water. Boiled, simmered for 10–15 minutes, then strained, 2–3 times daily (Meyer-Buchtela, 1999; ÖAB, 1991; Wichtl and Bisset, 1994).
- Infusion: Approximately 150 ml boiling water poured over 4.5 g licorice root and steeped 10–15 minutes; 2–3 times daily (Braun et al., 1997).
- Fluid extract BP [1:1 (g/ml), 16–20% ethanol (v/v)]: 2–5 ml, 3 times daily (BP, 1980; Bradley, 1992).
- Powdered root: Approximately 5–15 g root daily, equivalent to 200–600 mg glycyrrhizin (Blumenthal et al., 1998), 2–4 g single dose (API, 1989). **NOTE:** After decocting for 10 minutes, approximately 50% of the available glycyrrhizin, and approximately 45% of the liquiritin are released into the tea. After
30 minutes, approximately 80% of the glycyrrhizin, and 75% of the licoritin are released, respectively (Meyer-Buchtel, 1999).

**Deglycyrrhized Licorice (DGL) Preparations**

**DGL NATIVE DRY EXTRACT BP** [0.5–2.0% total flavonoids, calculated as licoritiginigen]: 0.4–1.6 g, 3 times daily (BP, 1986; Bradley, 1992).

**DGL CHEWABLE TABLETS** [380 mg DGL 4:1]: For acute cases of gastric or duodenal ulcers; 2–4 tablets chewed before each meal. For chronic cases, 1–2 tablets chewed before each meal (Pizzorno and Murray, 1999).

**Standardized Preparations**

**FLUID EXTRACT DAB** [2.0–4.0% glycyrrhizin, 52–65% ethanol (v/v)]: 5–15 ml daily, (or 2–5 ml, 3 times daily) corresponding to Commission E dosage of 5–15 g of root daily (Blumenthal et al., 1998).

**FLUID EXTRACT PPRC** [minimum 7.0% glycyrrhizin, 20–25% ethanol (v/v)]: 2–5 ml, 3 times daily (PPRC, 1992).

**NATIVE DRY EXTRACT** [4–5:1 (w/w), minimum 20% glycyrrhizin]: 0.33–0.8 g, after meals 3 times daily.

**DURATION OF ADMINISTRATION**

No longer than four to six weeks internally without medical advice. There is no objection to using licorice root as a flavoring agent up to a maximum daily dosage equivalent to 100 mg glycyrrhizin (Blumenthal et al., 1998). A diet rich in potassium (e.g., bananas) is recommended during treatment (Bruneton, 1999).

**CHEMISTRY**

Licorice root contains triterpenoid saponins, mainly glycyrrhizin (glycyrrhizic acid, glycyrrhizinic acid) (Tang and Eisenbrand, 1992; Ph. Eur. minimum 4%) with the sapogenin glycyrrhetic acid (glycyrrhetin, glycyrrhetic acid). Glycyrrhetic acid is a triterpene with an oleanan skeleton (Tang and Eisenbrand, 1992). Licorice also contains approximately 1% flavonoids, mainly flavanones (e.g., liquiritin), chalcones (e.g. isoliquiritin), and isoflavonoids (e.g., formononetin); polysaccharides (arabinogalactans); and sterols (β-sitosterol, stigmasterol) (Bradley, 1992; Tang and Eisenbrand, 1992).

**PHARMACOLOGICAL ACTIONS**

**Human**

**Crude Preparations**

Anti-inflammatory; expectorant; demulcent; adrenocorticotropic (Bradley, 1992); reduces serum testosterone in men (Armanini et al., 1999); antioxidant (Fuhrman et al., 1997).

**Deglycyrrhized Licorice (DGL) Preparations**

Protects LDL against lipid peroxidation (Fuhrman et al., 1997).

**Purified Licorice Derivatives**

Accelerates the healing of gastric ulcers in controlled clinical studies of glycyrrhizic acid and the aglycone of glycyrrhizic acid (Blumenthal et al., 1998).

**Animal**

Secretolytic and expectorant effects in rabbits; antispasmodic action in isolated rabbit ileum has been observed (Blumenthal et al., 1998); antioxidant and oxygen radical-scavenging in rats (Yokozawa et al., 2000); may have cancer chemopreventive effects (Wang et al., 2000); induces liver microsomal cytochrome P450 in mice (Hu et al., 1999); inhibits decline in immune complex (IC) clearance in carrageenan-injected mice (Matsumoto et al., 1996); prevents gastric mucosal damage in rats (Goso et al., 1996); protects mitochondrial function against oxidative stresses (Haraguchi et al., 2000); anti-arrhythmic action of total licorice flavonoids (e.g. liquiritigenin and isoliquiritigenin) in mice and guinea pigs (Hu et al., 1999); protects liver (Nose et al., 1994; Shim et al., 2000); inhibits generation of suppressor T-cells in thermally injured mice (Kobayashi et al., 1993). Phytosterols, beta-sitosterol, and stigmasterol are estrogenic in castrated mice (Van Hulle, 1970).

**In vitro**

Binds estrogen receptors (Zava et al., 1998); antimicrobial (Li et al., 1998; Okada et al., 1989); antioxidant (Okada et al., 1989); decreases arylamine N-acetyltransferase (NAT) activity in Helicobacter pylori cultures from peptic ulcer patients (Chung, 1998); anti-tumor necrosis factor (TNF) activity (Yoshikawa et al., 1997).

**MECHANISM OF ACTION**

- Glycyrrhizin is metabolized to its aglycone 18-β-glycyrrhetinic acid in the intestine by human intestinal bacteria, which is then absorbed into the blood
- Protects liver through 18-β-glycyrrhetinic acid and glycyrrhizin (Shim et al., 2000)
- Relieves gastric inflammation, possibly by inhibiting prostaglandin synthesis and lipoxygenase (Inoue et al., 1986; Tamura et al., 1979)
- Antigastic ulcer activity is due to the FM 100 fraction (licorione), which lowers gastric acidity, reduces pepsin activity, and inhibits gastric secretion (Huang, 1999)
- Inhibits human 11-β-hydroxysteroid dehydrogenase, the enzyme that catalyzes the conversion of cortisol to cortisone, and bacterial 3-alpha, 20-beta-hydroxysteroid dehydrogenase (Duax et al., 2000)
- Inhibits 11-β-hydroxysteroid dehydrogenase, which minimizes the binding of cortisol to mineralocorticoid receptors, creating a mineralocorticoid-like effect (Farese et al., 1991)
- Inhibits peripheral metabolism of cortisol, which binds to mineralocorticoid receptors in the same way as aldosterone (Heikens et al., 1995)
- May also inhibit both 17-β-hydroxysteroid dehydrogenase and 17,20-lyase, which catalyzes conversion of 17-hydroxyprogestosterone to androstenedione (Armanini et al., 1999)
- Modulates the cell-mediated immune system, which may be due to glycyrhrizin stimulating the induction of contrasuppressor cells (Kobayashi et al., 1993)
- Demulcent and expectorant actions due to stimulating tracheal mucous secretion (Hikino, 1985)
- Antioxidant action may be related to absorption and binding of licorice's flavonoids (e.g., glabridin) to the LDL particle, thereby protecting the LDL from oxidation (Fuhrman et al., 1997)

**CONTRAINDICATIONS**

The German Commission E states that licorice is contraindicated in cholestatic liver disorders, liver cirrhosis, hypertension, hypokalemia, and severe kidney insufficiency (Blumenthal et al., 1998). Licorice is also contraindicated in diabetes by the Belgian Pharmaceutical Association (Van Hellemont, 1986), although this was not confirmed in a subsequent monograph by the World Health Organization (WHO, 1999).
Pregnancy and Lactation: Not recommended during pregnancy (Braun et al., 1997; McGuffin et al., 1997; WHO, 1999). The effect of glycyrrhizin was studied on 1,049 Finnish women and their infants. Heavy exposure to glycyrrhizin (<500 mg/wk) did not affect birth weight, but did double the risk of birth before 38 weeks (Strandberg et al., 2001). No known restrictions during lactation.

Adverse Effects
No adverse effects have been associated with licorice used within proper dosage and treatment period limits (Schulz et al., 1998; WHO, 1999). With prolonged use (longer than six weeks), and higher doses (greater than 50 g/day), sodium and water retention and a loss of potassium may occur, accompanied by hypertension, edema, hypokalemia, and, in rare cases, myoglobinuria (Blumenthal et al., 1998; WHO, 1999). With short-term treatment for cough, these mineralocorticoid effects did not develop (Schilcher, 1997). Within several weeks of discontinuing use, any symptoms of hyperaldosteronism should disappear (Mantero, 1981). Side effects are less likely with aqueous licorice root extract than with isolated glycyrrhizin, due to lower intestinal absorption (approximately 40–70g daily for four months) of a licorice candy (Debeaux), a detoxified preparation used in TCM, the yield of anti-arrhythmic licorice fluid extract containing ~3.6 g glycorrhizic acid in three days) of Hershey Twizzlers® black licorice-flavored candy (Chamberlain and Abolnik, 1997). There is one case report of life-threatening ventricular tachycardia due to hypokalemia induced by overdose (approximately 1,020 g, containing 3.6 g glycyrrhizinic acid in three days) of Hershey Twizzlers® black licorice-flavored candy (Eriksson et al., 1999), though the brand of the candy, and the actual quantity of licorice or licorice derivatives contained in the candy are missing from the report.

Drug Interactions
Licorice may potentiate the side effects of potassium depleting thiazide diuretics (e.g., chlorothiazide, chlorthalidone, hydrochlorothiazide, and metolazone) (Austin et al., 2000; Blumenthal et al., 1998; Shintani et al., 1992). With potassium loss, sensitivity to digitalis glycosides increases (Blumenthal et al., 1998; Van Hellemont, 1986). The 1998 French Explanatory Note warns not to combine with corticoid treatment (Bruneton, 1999). When decocted in combination with toxic herbs such as prepared aconite root (Aconitum carmichaeli Debeaux), a detoxified preparation used in TCM, the yield of anti-arrhythmic licorice flavonoids is significantly higher than when decocted alone. This mitigated the toxic effects (e.g., arrhythmia) induced by aconitine (Hu et al., 1999; Leung, 1999) in mice and guinea pigs.

American Herbal Products Association (AHPA) Safety Rating
Class 2B: Not to be used during pregnancy (McGuffin et al., 1997).

Class 2D: Not for prolonged use or in high doses except under supervision of a qualified health practitioner (McGuffin et al., 1997).

Regulatory Status
Austria: Unpeeled dried root is official in the Austrian Pharmacopoeia (Meyer-Buchtele, 1999; Wichtl, 1997).

Canada: Approved active ingredient in THM products and in Homeopathic products, both requiring pre-marketing authorization with Drug Identification Number (DIN) assigned (Health Canada, 2001). Food if no claim statement is made.

China: Dried root and rhizome, prepared (stir-fried with honey) root and rhizome, alcoholic fluid extract and dry aqueous native extract, containing not less than (NLT) 20.0% glycyrrhizic acid, are official drugs of the Pharmacopoeia of the People’s Republic of China (PPRC, 1997).

European Union: Dried unpeeled or peeled, root and stolons containing NLT 4.0% glycyrrhizic acid and standardized ethanolic fluid extract containing NLT 3.0% and NMT 5.0% glycyrrhizic acid are official in European Pharmacopoeia (Ph.Eur. 2001).

France: THM permitted for specific indications, internal or locally (mouth and throat). Official in French Pharmacopoeia (Bradley, 1992; Bruneton, 1999; WHO, 1998).

Germany: Dried root or dry extract for infusion, decoction, liquid or solid dosage forms, are approved non-prescription drugs in the German Standard License monographs (Blumenthal et al., 1998). Licorice root tea is approved as an over-the-counter (OTC) drug in the German Standard License monographs (Braun et al., 1997). Peeled dried root containing NLT 4.0% glycyrrhizic acid, and standardized ethanolic fluid extract containing NLT 5.0% and NMT 7.0% glycyrrhizic acid are official in German Drug Codex supplement to German Pharmacopoeia (DAC, 1990 & 1995). Standardized ethanolic fluid extract containing NLT 2.0% and NMT 4.0% glycyrrhizic acid are official in German Pharmacopoeia (DAB, 1999).

India: Dried unpeeled roots and stolons containing NLT 4.0% glycyrrhizinic acid are official in Indian Pharmacopoeia (IP, 1996). Dried unpeeled stolon and root are official in the Government of India Ayurvedic Pharmacopoeia of India (API, 1989). Prepared mature root (min. 4 years) is an official single-drug and/or component of multiple-ingredient drugs dispensed in Unani system of medicine (CCRUM, 1986 & 1997). A monograph for dried root occurs in the Indian Herbal Pharmacopoeia (IHP I, 1998).

Italy: Listed in the Italian Pharmacopoeia (Newall et al., 1996).

Japan: Traditional Kampo medicine. Dried peeled or unpeeled root and stolon are official in the Japanese Pharmacopoeia (JSHP, 1993).

Russian Federation: Official in the State Pharmacopoeia of the Union of Soviet Socialist Republics, Ph.USSR X (Bradley, 1992; Newall et al., 1996).

Sweden: Classified as foodstuff. As of January 2001, no licorice products are listed in the Medical Products Agency (MPA) “Authorised Natural Remedies” (MPA, 2001).

Switzerland: Official in Swiss Pharmacopoeia, Ph.Helv.VII (Bradley, 1992; WHO, 1998; Wichtl, 1997). Licorice is an approved component of multi-ingredient phytomedicines listed in the Swiss Codex 2001/02 available in juice, syrup, tea infusion, and tincture dosage forms (Ruppanner and Schaefer, 2000) with positive classification (List D) by Interkantonale Konzrollstelle für Heilmitel (IKS) and corresponding sales Category D with sale limited to pharmacies and drugstores, without prescription (Morant and Ruppaner, 2001).

U.K.: Herbal medicine on the General Sale List, Schedule 1 (requires full Product License), Table A (internal or external use) (GSL, 1994). Dried unpeeled roots and stolons containing NLT
4.0% glycyrrhizinic acid, ethanolic fluid extract, and DGL dry aqueous extract containing 0.5–2.0% total flavonoids, calculated as liquiritigenin, are official in the British Pharmacopoeia (BP, 1986). U.S.: Dietary supplement or food depending on label claim statement (USC, 1994). Licorice root and derivatives are affirmed as Generally Recognized as Safe (GRAS) for use as a flavoring agent or flavor enhancer in vitamin or mineral dietary supplements, herb and seasoning products and nonalcoholic beverages, including tea (US FDA, 1998). Dried roots, rhizome and stolons, powdered root, and powdered dry extract are subjects of botanical monographs in development for the US National Formulary. Previews of the standards development were published in Pharmaceutical Forum (USP, 2002).

**CLINICAL REVIEW**

Ten studies are outlined in the following table, “Clinical Studies on Licorice,” including a total of 2,544 participants. Eight studies including a total of 1,505 participants. All but one of these studies (Armanini et al., 1999) demonstrated positive effects for indications such as treatment of various types of ulcers, chemoprevention, and use as an antioxidant. Three studies were conducted on licorice root extract (Armanini et al., 1999; Armanini et al., 1996; Palagina et al., 1999), four studies were on DGL extract (Fuhrman et al., 1997; Das et al., 1989; Kassir, 1985; Morgan et al., 1985), and two studies were conducted on isolated glycyrrhizin preparations (Arase et al., 1997; Acharya et al., 1993). These include an open (O) study on the effects of licorice root tablets on gonadal function (Armanini et al., 1999), a comparison (Cm) study on pulmonary metabolism during radiotherapy (Palagina et al., 1999), an O study on pseudohyperaldosteronism (Armanini et al., 1996), a placebo-controlled (PC) study on LDL cholesterol (Fuhrman et al., 1997), an O, uncontrolled study on aphthous ulcer (Das et al., 1989), a Cm, randomized (R) study on chronic duodenal ulceration (Kassir, 1985), and a single-blind, controlled, R study on benign gastric ulcers (Morgan et al., 1985). Isolated glycyrrhizin has been investigated as a chemopreventive in one retrospective Cm (Arase et al., 1997) and one O study on the treatment of subacute hepatic failure (Acharya et al., 1993). One study on birth outcome found that licorice did not affect birth weight but did double the risk of birth before 38 weeks (Strandberg et al., 2001).

**BRANDED PRODUCTS**

Caved-S®: Tillots Pharma AG / Hauptstrasse 27 / CH–4417 Zeifen / Switzerland / Tel: +41-61-935-2626 / Fax: +41-61-935-2625. Each tablet contains 380 mg deglycyrrhizinated licorice extract. This product is no longer available.


Stronger Neo Minophagen-C (SNMC); Minophagen Pharmaceutical Co. / No. 3 Tomizawa Bldg. / 2-7, Yotsuya 3-chome / Shinjuku, Tokyo 160 / Japan / Tel: +81-3-3355-6565 / Fax: +81-3-3355-6565. Standardized to contain 0.2% glycyrrhizin, 0.1% cysteine, and 2.0% glycyrrhizinic acid. This product is no longer available.

**REFERENCES**


APl. See: Ayurvedic Pharmacopoeia of India.


BP. See: British Pharmacopoeia.


CCRUM. See: Central Council for Research in Unani Medicine.


DAC. See: Deutscher Arzneibuch.

DAC. See: Deutscher Arzneimittel-Codex.


### Clinical Studies on Licorice (Glycyrrhiza spp.)

**Ulcers**

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Subject</th>
<th>Design</th>
<th>Duration</th>
<th>Dosage</th>
<th>Preparation</th>
<th>Results/Conclusion</th>
</tr>
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<tbody>
<tr>
<td>Das et al., 1989</td>
<td>Aphthous ulcer</td>
<td>O, U n=20</td>
<td>2 weeks</td>
<td>Mouthwash with 200 mg DGL extract solution, 4x/day</td>
<td>DGL powdered extract dissolved in 200 ml warm water (brand not stated)</td>
<td>15 of 20 (75%) experienced 50–75% improvement within 1 day followed by complete healing of ulcers by 3rd day.</td>
</tr>
<tr>
<td>Kassir, 1985</td>
<td>Chronic duodenal ulceration</td>
<td>Cm, R n=874 (169 in Caved-S® group)</td>
<td>3 months</td>
<td>380 mg tablet 3x/day</td>
<td>Caved-S® tablet (380 mg DGL extract) vs. antacid (AL-Mg hydroxide equivalent) vs. cimetidine vs. Gefarnate</td>
<td>At 6 weeks a highly significant difference (p&lt;0.01) in favor of antacid, but at 12 weeks no significant difference (p&gt;0.05) among the 4 groups. There were fewer relapses in the DGL group compared to the 3 other treatments.</td>
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<td>Morgan et al., 1985</td>
<td>Benign gastric ulcer</td>
<td>SB, C, R, Cm n=82</td>
<td>3 months</td>
<td>Two, 380 mg DGL extract tablets plus antacid combination chewed between meals 3x/day vs. cimetidine (200 mg 3x daily and 400 mg at bedtime)</td>
<td>Caved-S® containing 380 mg DGL extract per tablet vs. cimetidine</td>
<td>No significant difference between 2 drug regimens. After ulcer healing, drug dosage was reduced. After one year of maintenance therapy, there were 4 ulcer recurrences in each group. After second year, recurrence rate was 29% in Caved-S® group and 25% in cimetidine group. Authors conclude that long-term maintenance therapy is safe and reasonably effective.</td>
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<td>Kassir, 1985</td>
<td>Chronic duodenal ulceration</td>
<td>Cm, R n=874 (169 in Caved-S® group)</td>
<td>3 months</td>
<td>380 mg tablet 3x/day</td>
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**Other**

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</tr>
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<tr>
<td>Strandberg et al., 2001</td>
<td>Birth effects</td>
<td>O n=1,049 questionnaire distributed in the hospital and review of maternity records</td>
<td>9 months</td>
<td>Glycyrrhizin levels from licorice consumption grouped into 3 levels: low (&lt;250 mg/week; n=751), moderate (250–499 mg/week; n=145) and heavy (&gt;500 mg/wk; n=110)</td>
<td>Brand not stated</td>
<td>Heavy exposure to glycyrrhizin (&lt;500 mg/wk) did not affect birth weight, but did double the risk of birth before 38 weeks.</td>
</tr>
<tr>
<td>Armanini et al., 1999</td>
<td>Gonadal function</td>
<td>O n=7 healthy men (ages 22–24 years)</td>
<td>1 week</td>
<td>7 g licorice root extract/day (500 mg glycyrrhizin)</td>
<td>Salla licorice root tablets</td>
<td>Serum testosterone concentrations decreased and serum 17-hydroxy-progesterone concentrations increased during treatment period. Authors concluded that men with decreased libido or other sexual dysfunction should be cautioned about licorice ingestion.</td>
</tr>
<tr>
<td>Palagina et al., 1999</td>
<td>Pulmonary metabolism during radiotherapy in women ages 20–40 years with breast cancer Stage I–II</td>
<td>Cm n=25 women with breast cancer Stage I–II</td>
<td>2 weeks</td>
<td>Not available</td>
<td>Ural licorice extract (brand not stated)</td>
<td>Administration of licorice promoted inactivation of lipid peroxidation and maintenance of most biochemical parameters on baseline level. It is speculated that this effect is due to licorice components with antioxidant and lung surfactant synthesis stimulant actions. Authors conclude that licorice extract is promising for prevention of radiation complications in lungs during radiotherapy in chest area.</td>
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## Clinical Studies on Licorice (Glycyrrhiza spp.) (cont.)

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<tr>
<td>Arase et al., 1997</td>
<td>Chemo-prevention</td>
<td>RS, Cm n=453 patients with hepatitis C (84 in SNMC group)</td>
<td>16 years (median, 10.1 years)</td>
<td>100 ml/day intravenous first 8 weeks, followed by 2–7x/week for 2–16 years</td>
<td>Stronger Neo-Minophagen-C (SNMC) providing 0.2% glycyrrhizin, 0.1% cysteine, and 2.0% glycine in physiologic saline</td>
<td>After 10 years, cumulative incidence of hepatocellular carcinoma (HCC) was 7% in SNMC group and 12% for non-treatment group. After 15 years, cumulative incidences were 12% and 25%, respectively. Statistically significant reduction in serum alanine aminotransferase (ALT) levels was reported in 34 of 84 patients (35.7%) in treatment group. HCC in 30 patients with normal ALT levels was slightly lower than the 54 remaining patients with higher ALT scores (p=0.08). An increase in blood pressure was noted in 3 of 84 patients. Authors concluded that long-term administration of SNMC in patients with chronic HCC is effective in reducing risk of liver carcinogenesis.</td>
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<tr>
<td>Fuhrman et al., 1997</td>
<td>Antioxidant action</td>
<td>PC (ex vivo assay) n=20 healthy male volunteers</td>
<td>2 weeks</td>
<td>100 mg DGL extract/day</td>
<td>DGL extract in softgel capsule (brand not stated)</td>
<td>In licorice group, 44% reduction in lipid peroxides formed per mg of LDL cholesterol after exposure of plasma to copper sulfate ex vivo, and 36% reduction after exposure to water-soluble free radical generator, vs. no significant changes observed in plasma of placebo group.</td>
</tr>
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<td>Armanini et al., 1996</td>
<td>Pseudohyperaldosteronism</td>
<td>O n=6 male volunteers</td>
<td>1 week</td>
<td>7g licorice root extract/day (500 mg glycyrrhizin)</td>
<td>Saila licorice root tablets</td>
<td>Pseudohyperaldosteronism occurred during treatment period. Ratio of tetrahydrocortisol + allo tetrahydrocortisol to tetrahydrocortisone in urine increased in 5 cases after 3 days without increase of plasma mineralocorticoid activity. Authors concluded that pseudohyperaldosteronism is due to decreased activity of 11-ß-hydroxysteroid-dehydrogenase and in some cases a direct effect on mineralocorticoid receptors.</td>
</tr>
<tr>
<td>Acharya et al., 1993</td>
<td>Subacute hepatic failure</td>
<td>O n=18</td>
<td>3 months</td>
<td>40 or 100 ml/day intravenous first 30 days, followed by 3x/week for 8 weeks</td>
<td>Stronger Neo-Minophagen-C (SNMC) providing 0.2% glycyrrhizin, 0.1% cysteine, and 2.0% glycine in physiologic saline</td>
<td>Survival rate was 72.2% compared to reported rate of 31.1% in 98 patients who received supportive therapy (p&lt;0.01). Authors concluded that further studies are necessary to standardize the dose and duration of therapy with SNMC in subacute hepatic failure.</td>
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