A s I wrote in last month’s column, licorice was used for medicinal and dietary purposes in ancient Egypt, Greece, and Rome. In China and other parts of Asia, it has been used since the Han Dynasty (circa 200 B.C.) (Yakuwaki Zasahi 2000;120:849-62).

Today, licorice remains one of the most frequently used herbs in traditional Chinese medicine and in its Japanese adaptation, Kampo medicine (Life Sci. 2002;71:1449-63). In fact, several species of licorice have been used in those medical systems and are still in use today.

Glycyrrhiza inflata, the Chinese licorice root, has a wide range of pharmacological and dietary applications, and is related to Glycyrrhiza glabra, which was discussed in part I.

Three of the six Glycyrrhiza species—G. glabra, G. uralensis, and G. inflata—produce glycyrrhizin as a major saponin, while the others—G. cimicifuga, G. maclovinica, and G. pulchra—produce macelisoide C as a major saponin. G. uralensis and G. inflata are closely related (Biol. Pharm. Bull. 2000;23:602-6), but G. inflata is more often used for medical and dietary purposes and is the subject of this discussion.

**Actions of Licochalcone A**


Licochalcone A, also known as 3′,6′,6′-dihydroxy-4′-demethylglycyrrhetinic acid, is derived from the root of G. inflata (Xin-jiang liquorice). This compound has exhibited anti-inflammatory activity against arachidonic acid- and 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced mouse ear edema (Planta Med. 1991;57:221-4).

Licochalcone A has also been reported to exhibit in vivo antitumor properties in mouse skin papilloma initiated by dimethylbenz(a)anthracene and promoted by TPA (Plant Med. 1991;57:221-4). In addition, the compound has shown anticarcinogenic, antibacterial, and antinon-mutagenic properties (Int. Immunopharmacol. 2002;2:549-55; Anticancer Res. 2000;20:2653-8).

In a study assessing the effect of licochalcone A and four other chalcones on human peripheral blood mononuclear cell proliferation and cytotoxic production, researchers found that four of the five tested chalcones inhibited lymphocyte proliferation, and four of five also inhibited the production of pro- and antiinflammatory cytokines from monocytes and T cells. The investigators concluded that licochalcone A and some of its synthetic analogues may have immunomodulatory effects, potentially making them suitable agents for treating microbial and other diseases (Int. Immunopharmacol. 2002:2:345-55).

In a study evaluating the in vitro activities of licochalcone A against some food contaminant microorganisms, the licorice derivative exhibited activity against all gram-positive bacteria tested, particularly all Bacillus species tested, but was ineffective against gram-negative bacteria and eukaryotes at 50 mcg/mL.

This study showed the potential viability of licochalcone A as an integral constituent of antibacterial products designed to preserve food high in salts and proteins (Antimicrob Agents Chemother. 2002:46:1226-30).

Licochalcone A also has shown inhibitory activity in vitro, against human pathogenic bacteria, including Mycobacterium species and Legionella species. Such findings suggest its potential use in the treatment of severe pulmonary infections (Plant Med. 2002;68:416-9). Other applications are suggested by the compound’s broad range of activities.

**Actions of Other Compounds**

Flavonoids extracted from several licorice plant species have exhibited inhibitory activity against Helicobacter pylori growth in vitro. Other licorice plant compounds also have shown the ability to inhibit H. pylori growth, including glabridin and glabrene (components of G. glabra), licochalcone A (G. inflata), and licoricidin and licoisoflavone B (G. uralensis). Anti-H. pylori activity also has been identified against a clarithromycin- and amoxicillin-resistant strain (Life Sci. 2002;71:1449-53).

The phenolic compounds licochalcone A-D and echinatin, retrochalcones isolated from G. inflata roots, have exhibited activity in an array of oxidative stress(es). A study assessing their inhibitory capacity on lipid peroxidation and their radical scavenging activity revealed that licochalcone B and D potently hindered superoxide anion production in the xanthine/xanthine oxidase system, protected red cells from oxidative hemolysis, and had potent scavenging activity (Bioorg. Med. Chem. 1999;6:339-47).

These retrochalcones have also demonstrated antimicrobial activity. Specifically, licochalcones A and C have shown potent activity against some gram-positive bacteria and have hampered oxygen consumption in vulnerably bacterial cells (Phytochemistry 1998;48:125-9).

**Estrogenic and Other Effects**

Noting that the herbal formulation PC-SPES, which contains licorice root, has been shown to possess potent estrogenic activity in vitro, in animals, and in patients with prostate cancer, researchers investigated whether the flavonoid licochalcone A shared these properties. Through a range of assays, they determined that licochalcone A is a phytoestrogen, that it exhibits antihormone activity, enhancing the effects of paclitaxel and vinblastine, and that it affects the apoptotic protein Bel-2 in human cell lines derived from several cancers (Anticancer Res. 2000;20:2653-8).

The licorice derivatives glycyrrhetin and glycyrrhetinic acid occasionally cause edema, hypertension, and hypokalemia in patients treated over a long period and with higher doses. Chemical modifications to these compounds have enhanced the anti-inflammatory, antiallergic, and antinociceptive activities in animal experiments.

For the past 60 years, a glycyrrhizin formulation called Stronger Neo-Minophagen C has been used in the clinical setting in Japan as an antilagistic and antihypertensive treatment (Yakuwaki Zasahi. 2000;120:849-62).

Pursuing the anti-inflammatory angle, Bielersdorf AG commissioned a study of a proprietary rosacea regimen featuring licochalcone A in each product. Sixty-two adults, 12 with mild to moderate rosacea and 30 with erythematous facial skin not ascribed to rosacea, used four test products—a cleanser, an SPF-15 day lotion containing green concealer, a spot concealer, and a night moisturizing cream—during an 8-week study.

In a poster presentation, the researchers reported a statistically significant decline in weeks 4 and 8 in erythema clinical grading scores relative to baseline for this series of well-tolerated products containing the primary active ingredient in Chinese licorice root. This study was also supported by additional proprietary research funding given to several of the same investigators who established that licochalcone A reduced proinflammatory mediators in vitro.

**Conclusions**

Several medical applications have been derived from a variety of licorice species.

The evidence supporting the medical use of G. inflata is slightly less extensive than that of the related species G. glabra, but it is similar in terms of the broad range of potential applications. Licorice species have a long history of traditional uses that are being expanded into the cosmetic and medical realms.

Because we are likely to see the inclusion of licorice species, particularly G. inflata and G. glabra, in an increasingly expansive array of products, I would like to see a corresponding increase in randomized, controlled, double-blind trials of products with these ingredients. Overall, there appears to be ample room for optimism on this front.

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