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HerbClip™

FILE: ▪ Licorice (*Glycyrrhiza glabra, G. uralensis*)
▪ Glycyrrhizic Acid
▪Herpes
▪ Chemoprevention

HC 040251-280

Date: May 13, 2005

RE: Glycyrrhizic Acid from Licorice Prevents Karposi's Sarcoma-associated Herpes Virus Development

Curreli F, Friedman-Kien AE, Flore O. Glycyrrhizic acid alters Kaposi sarcoma-associated herpesvirus latency, triggering p53-mediated apoptosis in transformed B lymphocytes. *J Clin Invest.* 2005;115(3):642–652.

Cohen JI. Licking latency with licorice. *J Clin Invest.* 2005;115(3):591–593.

Licorice (*Glycyrrhiza glabra*) is commonly used as a food additive for flavoring. Medicinally, it has been used for many years "for the treatment of gastric and duodenal ulcers, sore throat, bronchitis, cough, arthritis, adrenal insufficiency, and allergic diseases," according to the authors of the first article. Previous research showed that glycerrhizic acid (GA), derived from licorice, is effective against herpes simplex, varicella zoster (chicken pox), human cytomegalovirus (CMV), and EBV. The in vitro study described in the first article analyzed the potential of licorice for the prevention of kaposi sarcoma-associated herpesvirus (KSHV), while the accompanying commentary by Cohen elaborates on licorice's chemopreventive potential.

Kaposi sarcoma is a cancer most often seen in men older than 60 years and human immunodeficiency virus (HIV) patients. It is associated with herpes virus infection, which can lie dormant for many years, modifies genetic expression in host cells and can lead to malignancy. The viral DNA modifies the expression of the host's DNA, so that when replication does occur the virus has the potential to cause unrestricted cellular division, a requirement for the development of cancer. The herpesvirus-family of viruses also includes Epstein Barr Virus (EBV), which causes mononucleosis. In some cases, EBV can cause lymphoma after a long latency period after the symptoms from the primary infection have already resolved.

Curreli et al. treated 12 human cell types with 7 different concentrations of glycyrrhizic acid (GA), derived from licorice. GA inhibited the growth of the KSHV-infected cells in a dose-dependent manner, and "within 8–9 days, all KSHV-infected cells died" when treated with 2, 3, or 4 millimol (mM) GA. Cells infected with EBV were killed within 15 days of treatment.

GA's toxic effects resulted from its ability to alter protein expression in these cells. Specifically, GA decreased the expression of latency-associated nuclear antigen (LANA) and increased viral cyclin. LANA inhibits apoptosis (cellular fragmentation or programmed cell death) by binding to and inhibiting p53 (protein responsible for initiating cellular repair and apoptosis). By decreasing LANA expression, GA enables cell death to occur. Viral cyclin may also encourage apoptosis, as shown in previous studies.

Whether GA can effect KSHV cell death and prevent the development of kaposi sarcoma in vivo remains to be determined. As Cohen points out, there are several barriers to GA's efficacy in vivo against KSHV. First, "the levels of GA required for efficacy in vitro might not be achievable in vivo," i.e., in a living organism. Second, "continuous and/or prolonged courses of therapy with GA might be needed." And third, the therapeutic dose might be close to the toxic dose, leading to negative side effects. (This problem is often encountered with herbal extracts that show promise in in vitro research; the quantities sufficient to show an effective result in animals and/or humans are frequently too high to allow the herbal preparation to become a reasonable treatment option.) The dose that is effective at killing 50% of the viral load (ED_{50}) is 2–3 mM; however, 5–6 mM GA was toxic to uninfected cells. Cohen also notes that GA may only be effective when administered intravenously. When GA is taken orally, it is hydrolyzed by gut bacteria to glycyrrhetic acid before it can be absorbed. In Asia GA is given intravenously to obtain therapeutic levels in the treatment chronic hepatitis B and C infections.

—John Neustadt, ND4

The American Botanical Council has chosen not to reprint the original articles.