
Abstract
Licorice, the root of Glycyrrhiza spp. (Fabaceae), has been used since ancient Egyptian, Greek, and Roman times in the West and since the Former Han era (the 2nd-3rd century B.C.) in ancient China in the East. In traditional Chinese medicine, licorice is one of the most frequently used drugs. In Japan, the oldest specimen of licorice introduced from China in the middle of the 8th century still exists in Shosoin, the Imperial Storehouse, in Nara. Extracts of licorice were recommended as a remedy for gastric ulcer by Revers of the Netherlands in 1946, which was soon withdrawn owing to its side effects. Carbenoxolon sodium, glycyrrettinic acid (GA) hemisuccinate Na, was prepared from licorice to treat peptic ulcer in the UK. In Japan for the past 60 years, a glycyrrhizin (GL) preparation under the name of Stronger Neo-Minophagen C (SNMC) has been used clinically as an antiallergic and antihepatitis agent. GL and GA sometimes induce edema, hypertension, and hypokalemia in patients treated with higher doses and long-term administration. The mechanism of this side effect, pseudoaldosteronism, has been explained as due to the 11-hydroxy-steroid dehydrogenase inhibitory activity of GL and GA. The excess of endogenous cortisol produced combines with the renal mineral corticoid receptor, which promotes an aldosterone-like action. GL and GA reduce alanine transaminase (ALT) and aspartate transaminase (AST) values in the serum. This hepatoprotective effect has recently been explained as the inhibitory effects of GL and GA on immune-mediated cytotoxicity against hepatocytes and on nuclear factor (NF)-kappa B, which activates genes encoding inflammatory cytokines in the liver. To exclude the side effects and enhance the therapeutic activities, chemical modification of GL and GA has been performed. Deoxoglycyrrhetol (DG), homo- and heteroannular diene homologs of dihemiphthalates, showed a remarkable improvement in antiinflammatory, antiallergic, and antiulcer activities in animal experiments. Immunomodulating effects of GL, GA, and DG derivatives, which induce interferon-gamma and some other cytokines, have been demonstrated in relation with their antiviral activities. Antiinflammatory, antitumorigenic, and antimalarial effects of licorice flavonoids have also been investigated.