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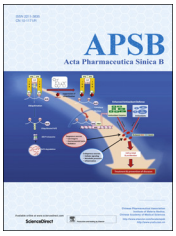

REVIEW

The antiviral and antimicrobial activities of licorice, a widely-used Chinese herb

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KEY WORDS

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Chalcone

Abstract Licorice is a common herb which has been used in traditional Chinese medicine for centuries. More than 20 triterpenoids and nearly 300 flavonoids have been isolated from licorice. Recent studies have shown that these metabolites possess many pharmacological activities, such as antiviral, antimicrobial, anti-inflammatory, antitumor and other activities. This paper provides a summary of the antiviral and antimicrobial activities of licorice. The active components and the possible mechanisms for these activities are summarized in detail. This review will be helpful for the further studies of licorice for its potential therapeutic effects as an antiviral or an antimicrobial agent.

Abbreviations: CCEC, cerebral capillary vessel endothelial; CCL5, chemokine (C-C motif) ligand 5; CVA16, coxsackievirus A16; CVB3, coxsackievirus B3; CXCL10, chemokine, (C-X-C motif) ligand 10; DGC, dehydroglyasperin C; DHV, duck hepatitis virus; EV71, enterovirus 71; GA, 18β-glycyrrhetinic acid; GATS, glycyrrhizic acid trisodium salt; GL, glycyrrhizin; GLD, glabridin; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HMGB1, high-mobility-group box1; HRSV, human respiratory syncytial virus; HSV, herpes simplex virus; HSV1, herpes simplex virus type 1; IFN, interferon; IL-6, interleukin-6; LCA, licochalcone A; LCE, licochalcone E; ISL, isoliquiritigenin; LTG, liquiritigenin; MgIG, magnesium isoglycyrrhizinate; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; PMN, polymorph nuclear; PrV, pseudorabies virus; TCM, traditional Chinese medicine

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1. Introduction

Licorice is a very well known herb in traditional Chinese medicine (TCM). In China, it is called "gancao" (meaning "sweet grass") and has been recorded in the *Shennong's Classic of Materia Medica* around 2100 BC. In this book, licorice was supposed to have life-enhancing properties. During the following thousands of years licorice has been present in most of Chinese traditional prescriptions. It was believed to have the functions of nourishing *qi*, alleviating pain, tonifying spleen and stomach, eliminating phlegm, and relieving coughing[1].

Glycyrrhiza uralensis Fisch., *Glycyrrhiza inflate* Bat. and *Glycyrrhiza glabra* L. were prescribed as licorice in *Chinese pharmacopoeia*[2]. They are widespread in Inner Mongolia, Gansu, Heilongjiang, Ningxia, Qinghai and many other provinces in China[3]. The roots and rhizomes are the main medicinal parts of licorice. Numerous studies have revealed many pharmacological activities of licorice, such as antiviral[4,5], anti-inflammatory[6,7], antitumor[8,9], antimicrobial[10,11] and many other activities[12,13]. Among the pharmacological activities of licorice mentioned above, the antiviral and antimicrobial activities have been most commonly reported. Viral and other microbial infections play a critical role in many highly prevalent diseases, especially in developing countries. The development of safe and effective antiviral or antimicrobial agents is very important, and licorice deserves more attention for its outstanding activities.

Licorice contains more than 20 triterpenoids and nearly 300 flavonoids. Among them, glycyrrhizin (GL), 18β-glycyrrhetinic acid (GA), liquiritigenin (LTG), licochalcone A (LCA), licochalcone E (LCE) and glabridin (GLD) are the main active components which possess antiviral and antimicrobial activities. Their chemical structures are listed in Fig. 1.

2. The antiviral active components and their possible mechanisms

Among the components isolated from licorice, 73 bioactive components and 91 potential targets have been identified to date[14,15]. Many studies have demonstrated that two triterpenoids, GL[16,17] and GA[18], are responsible for the antiviral activity. The possible mechanisms for virus prevention of GL and GA, and the viral types are listed in Table 1.

2.1. GL

GL is one of the major compounds isolated from the roots of licorice. In recent years, many studies have confirmed the antiviral activity of GL. Matsumoto et al.[16] reported that GL targeted the release step in which infectious anti-hepatitis C virus (HCV) particles were infecting cells. These findings indicated possible novel roles for GL to treat patients suffering from chronic hepatitis C. In another study, researchers also found that GL treatment inhibited HCV titer and caused 50% reduction of HCV at the concentration of 14 ± 2 μg/mL by inhibiting HCV full length viral particles and their core gene expression[19].

Previous studies showed that intercellular adhesion molecules played an important role in some viral infections, such as human immunodeficiency virus (HIV)[20]. Huang et al.[5] found that the adhesion force and stress between cerebral capillary vessel endothelial (CCEC) cells and polymorph nuclear (PMN) leukocytes were clearly increased in HSV infection; GL perfusion significantly reduced adhesion force and stress between CCEC and PMN.

Zhang's study[21] reported that GL showed a significant improvement of coxsackievirus B3 (CVB3)–induced myocarditis by improving weight loss profile, reducing serological levels of cardiac enzymes and increasing survival rate. This effect was evidenced by significantly reduced expression of proinflammatory cytokines, such as nuclear factor–κB, interleukin-1β and interleukin-6. The inhibition of CVB3-induced nuclear factor–κB activity blocks the degradation of nuclear factor–κB inhibitor IκB. All these data suggested that GL had an effect on CVB3-induced myocarditis and may present as a new therapeutic approach for the treatment of viral myocarditis.

Soufy et al.[22] found that GL had excellent immunostimulant properties and induced a synergistic effect to duck hepatitis virus (DHV) vaccine by activating T lymphocyte proliferation. Four groups, control, GL treated, vaccinated with live attenuated DHV vaccine and GL treated and vaccinated, were investigated. Among them, treatment with GL alone or with DHV vaccine showed good immune stimulant and antiviral effects against DHV. GL combined with DHV vaccine produced higher antibody titers against DHV than by the use of DHV vaccine alone.

Several studies have demonstrated that GL showed a significant inhibiting effect to influenza virus. At a concentration of 100 μg/mL (a therapeutically achievable concentration), GL weakened

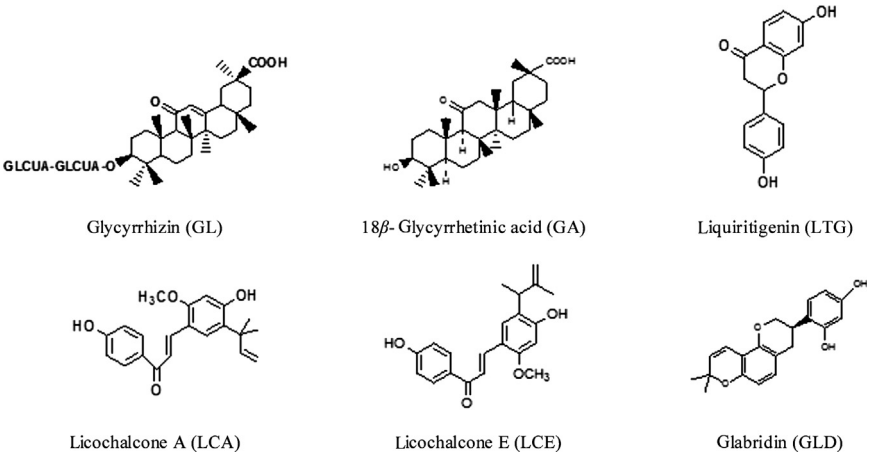

Figure 1 The chemical structures of the antiviral activity or antimicrobial components in licorice.