Chapter 12

Medicinal Plants in the Northwestern China and Their Medicinal Uses

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Additional information is available at the end of the chapter

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Abstract

The Northwestern China is a typical arid and semi-arid region of inner Asia, where some important medicinal species such as *Angelica sinensis*, *Radix astragali*, *Radix codonopsis*, *Radix et rhizoma rhei*, *Radix glycyrrhizae*, *Lycium barbarum* L are found and grew in the mountains areas, or desert areas. Among them, *A. sinensis*, *R. astragali* and *R. glycyrrhizae* are frequently used in traditional Chinese medicines and herbal prescriptions, thus encouraged many researchers to investigate and develop them. Our purpose is to provide a review of recent advances about three typical medicinal plants of *A. sinensis, Astragalus membranaceus* and *R. glycyrrhizae* in Northwestern China, mainly referring to botanical identity, chemical constituents, pharmacological studies, application in formulation, safety and cultivation practices. That will provide some valuable information for the further study and development of medicinal plants in Northwestern China.

Keywords: medicinal plants, Northwestern China, *Angelica sinensis*, *Radix astragali*, *Radix glycyrrhizae*

1. Introduction

Approximately 8300 wild plant species of known medicinal species in the Northwestern China, some 400 species are used in traditional Chinese medicines (TCM) or by drug manufacturing units in China. Most of these medicinal plants grow in the arid and semi-arid marginal mountains areas, or desert areas of Northwestern China.

This chapter aims to provide a review of recent advances in the fields of botanical identity, chemical constituents, pharmacological studies, application in formulation, safety and

cultivation practices about three typical medicinal plants of *Angelica sinensis*, *Astragalus membranaceus* and *Radix glycyrrhizae* in Northwestern China.

2. *Angelica sinensis*

当归 (Danggui, *A. sinensis*)

2.1. Botanical identity

A. sinensis is the root of *A. sinensis* (*Oliv.*) *Diels* (Umbelliferae family). The genus Angelica is comprised of over 90 species, a total of 45 angelica species are currently distributed in China, of which 32 are endemic [1]. It is mainly cultivated in the southeastern parts of Gansu Province, occurring in Yunnan, Sichuan, Shaanxi and Hubei and showing strong ecological adaptability at altitudes of 1500–2000 m above sea level in China. Photographs of *A. sinensis* are shown in **Figure 1**. As a perennial herb, *A. sinensis* grows to heights of approximately 0.4–1 m (Flora of China). The whole root is yellowish-brown to brown, about 25 cm long, and irregularly cylindrical with some branch roots stemming from the lower end. The leaves have alternating ovate blades that can range in size between 8 and 18 cm long and 15–20 cm wide. The fruit is elliptical to ovate, and the flowers have 4–7 cm long stems and compound umbels [2].

Figure 1. Photographs of *A. sinensis*.

2.2. Chemical constituents

Studies have shown that *A. sinensis* contains polysaccharides, flavonoids, volatile oils, trace elements, amino acids and vitamins, which account for approximately 0.4–0.7% of the total content. Phthalides, polysaccharides and organic acids are the main chemical components concerned to the bioactivities and pharmacological properties of *A. sinensis* [3]. Phthalides, as one of the characteristic components, have used for the quality control of *A. sinensis*. Ligustilide is also used as an important component for assessing the quality of *A. sinensis*, which can account for 0.5–5.0%, and the concentration of Z-ligustilide in *A. sinensis* varies

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within the range of 1.26–37.7 mg/g [4]. *A. sinensis* is rich in all types of amino acids, containing as many as 17 types and accounting for approximately 6.5% of the total chemical composition of *A. sinensis*. The seven types of non-synthesized amino acids are essential, and content variations can cause great differences among the amino acids extracted [5]. Flavonoids have also been isolated from *A. sinensis*, and total flavonoids have been shown to provide with antibacterial and antioxidant activities [6]. Moreover, phospholipids, adenine, uracil and choline were recently found in *A. sinensis*, a total reported nucleosides content with the range of 1.507–3.119 mg/g [7]. The plant also contains vitamin B12, vitamin A and xanthotoxin, as well as several microelements, including sodium, potassium, calcium, iron, copper, zinc and manganese, among others [8]. In addition, 8,11-dyhydroxyl-ligustilide, 2,7-hydrox-ligustilide and magnolol have been found in *A. sinensis* [9]. The major organic acids in *A. sinensis* are shown in **Figure 2**.

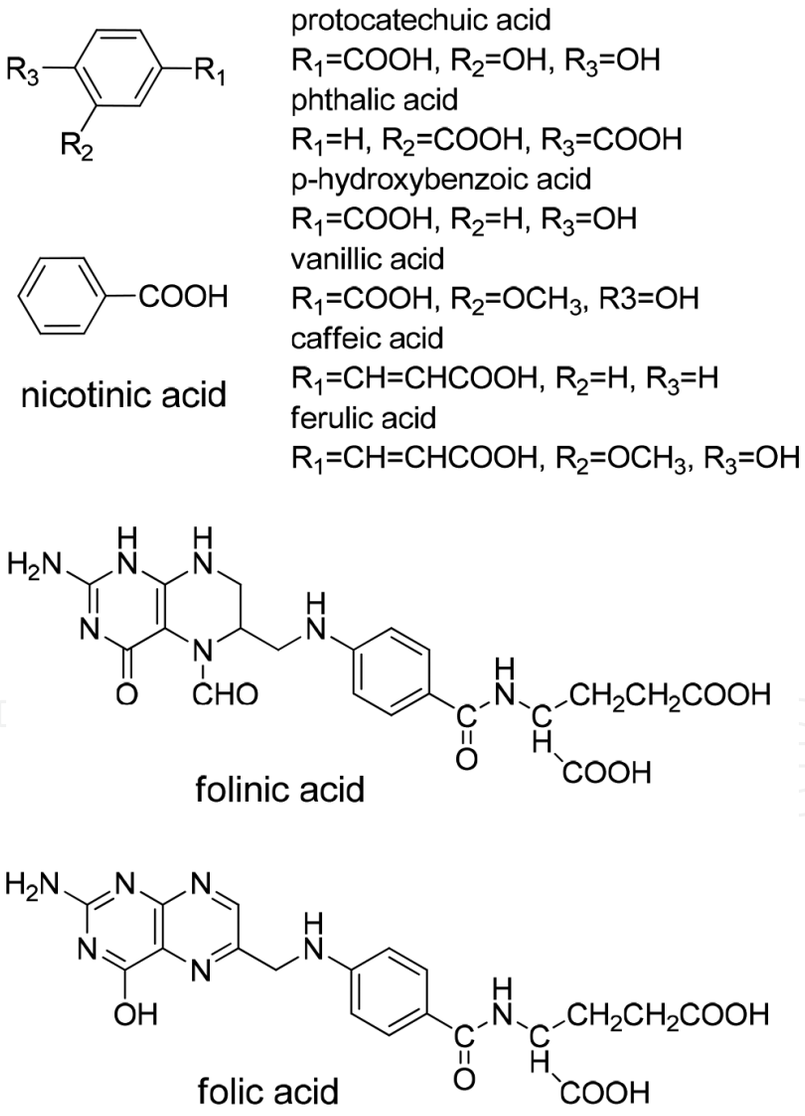

Figure 2. Chemical structures of the major organic acids in *A. sinensis* [10].

2.3. Pharmacological studies

A. sinensis has been used for thousands of years as a health food and drug in Asian countries and also as a dietary supplement in women's care in Europe. In China, the roots of *A. sinensis* have been extensively used in traditional medicine and have been primarily used for treatment of gynecological disease such as dysmenorrhea and amenorrhea and blood disease such as blood deficiency [10]. Modern pharmacological research indicated that *A. sinensis* also exerted pharmacological activities of anticancer, neuroprotective effect [11], antioxidant [12], hepatoprotective effect [13], radioprotection [14], immunoregulation [15], anti-inflammatory [16], antifungal effects and mosquito deterrence [17].

2.4. Application in formulation

These are ready-made combinations of herbs available to the general public to treat certain conditions without reference to a complete system of medicine. One company alone manufactures 280 of these formulations, designed for specific indications. Of these, 71 contain danggui [10]. Some of the herbs are traditionally put together ("Classic Pairs"), such Danggui and Chuanxiong Rhizoma (Ligusticum chuanxiong) or Danggui and *Radix astragali* or in "Standard Combinations". Danggui Buxue Tang is available in various formulations ranging from the TCM "Drug Pair" *A. sinensis* and *R. astragali* in a ratio of 5:1. Its suggested use for gynecological disorders such as anemia, infertility, has proved to be of potential for the perimenopause and menopause [18]. Moreover, there are also some popular formulations for Women's Health: Si Wu Tang (four substance decoction) formulated with varying ratios of *A. sinensis* (dang gui), *Radix rehmanniae* (shu di huang), *Radix paeoniae alba* (bai shao yao) and *Rhizoma ligustici* (chuan xiong). It is traditionally used as a decoction. Its function is to tonify and activate blood, smooth the liver and regulate menstruation [19].

2.5. Safety

It was reported that no obvious acute toxicity appeared through oral *A. sinensis* polysaccharide iron complexes (APIC) in mice and the maximum tolerated dose (MTD) of APIC in mice was 4800 mg/kg, 1920 times the adult daily dose. Thus, APIC was considered safe for oral use [20]. The toxicity of *A. sinensis* injection in the chick embryo chorioallantoic membrane model was explored. Results indicated that survival of chick embryos was not inhibited by *A. sinensis* injection. Furthermore, there were no differences between the treatment groups and the negative control, indicating that the resulting toxicity was very limited. Acute toxicity studies indicate that administration of *A. sinensis* produces no effects at doses up to 5000 mg/kg; similar results were observed in sub-chronic studies [21]. Therefore, *A. sinensis* is "generally recognized as safe (GRAS)" by the FDA but a number of side effects have been reported.

2.6. Cultivation practices

At present, the market supply of angelica is cultivated varieties. The proper field production altitude is from 2000 to 2500 m above sea level, while the proper seedling field is from

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2500 to 2700 m above sea level. The annual average temperature of 4.5–5.7°C and average rainfall of 570–650 mm are suited for cultivating *A. sinensis*. It is also advisable to choose soil with a rich organic matter content, gray cinnamon soil and a neutral to weak alkaline of pH. The seedling fields should be chosen in uncultivated land, shifting land and especially in fertile uncultivated land with thick soil layer from 2500 to 2700 m above sea level. The most appropriate seedling field is a cool and humid place, short sunshine duration, and north-facing slope at an incline from 5 to 25°. The sowing time begins during the early to mid-June. After sowing, the seedling fields need to be kept humid and covered by grass cover in order to make it grow early, even and strong. The seedlings should be stored with a cellaring or piled storage before the ground freezing. There are two methods for seedlings storage. Crop rotation is a key measure of controlling soil-borne disease in cultivation practices of *A. sinensis*. The crop rotation in previous crop had better grains with a rotation cycle of 3 years. The optimal transplanting period is the middle of April. The reserve density is 9–12 plats/m^2. Combined with tillage, weeding should be carried out timely during growing period. Early bolting stage usually occurs in the middle of June, so it should be timely to remove of the plants of early bolting in case of water and fertilizers waste and affecting normal plants growing. Organic manure (4500–7500 kg/ha) as base fertilizer with timely topdressing the nitrogen, phosphorus and potassium (NPK) fertilizer should be combined. Ditylenchus destructor and root rot disease are the main diseases during the growth period of *A. sinensis*. The strategy of integrated pest management (IPM) is relied mainly on agricultural control while making insecticide chemical control subsidiary for controlling the diseases. The optimal harvest period of *A. sinensis* is during the mid-to-end of October. Fumigating by burning broad bean stalks and branches of poplars and/or willows is a traditional drying method. Introducing a modern drying technology for improving quality and increasing processing efficiency is the direction of future efforts. Dried angelica should be stored in clean, cool, dry, ventilates, moisture-resistant and smelling free storehouse, and a regularly checking store process is very necessary.

3. *Radix astragali*

黄芪 (Huangqi, *R. astragali*)

3.1. Botanical identity

R. astragali has a long history of medicinal use in Chinese herbal medicine and is one of the most popular herbal medicines worldwide. It is the dried root of *A. membranaceus* (Fisch.) Bge. (*A. membranaceus*) or *A. membranaceus* (Fisch.) Bge. var. mongholicus (Bge.) Hsiao. *A. membranaceus* and *A. membranaceus* var. mongholicus are mainly grown in Northwest China as well as in Mongolia and Korea, and they have some different botanical characteristics.

A. membranaceus var. mongholicus is a perennial herb, 50–150 cm high, with a straight, long and cylindrical root, measuring 20–50 cm, diameter 1–3.5 cm. Its stems are erect, with branches in

the upper part, and are quilted with pubescence. It has an odd-pinnate, alternate, petiole base with lanceolate stipules, 25–37 leaflets, elliptical small leaves 4–9 mm long, and apex with long white pubescence. It has 10–25 flowers, racemes axillary, bracts linear-lanceolate, calyx tubular, calyx teeth—5, corolla yellow, butterfly, upper petal obovate triangular, glabrous, stamens—10, ovary stalked, ovate pods oblong, apex beaked, and significantly textured. The flowering period is from June to July, whereas fruiting is from August to September. It generally grows on hillsides, beside ditches, or in woodland and is found in Heilongjiang, Jilin, Liaoning, Inner Mongolia, Tibet and other places.

A. membranaceus has lobular 13–31 pieces, elliptic or ovate-lanceolate small leaves, length 7–30 mm, width 4–10 mm, corolla light yellow, ovary puberulous, ovate pod oblong 2–2.5 cm and apex beaked with a black undercoat (**Figure 3**). It grows on sunny hillslopes, sandy riverbanks or shrub edges. This species is found in Heilongjiang, Jilin, Liaoning, Inner Mongolia, Tianjin, Beijing, Shanxi, Gansu and other places [22]. Moreover, both species are cultivated in the Northeast China, and they are gathered in the spring and autumn.

Figure 3. Photographs of *A. membranaceus*.

3.2. Chemical constituents

To date, *A. membranaceus* have been isolated and identified more than 100 compounds. Some of the compounds are shown in **Figure 4** [23]. Its major active constituents include triterpene saponins, flavonoids and polysaccharides. Other components found in the herb include γ-aminobutyric acid, L-canavanine, phytosterols (and other volatile oils) [24], fatty acids, choline, betaine, sterols, 3-hydroxy-2-methylpyridine, (−)-syringaresinol, (+)-lariciresinol, lupenone [25], bifendatatum, coumarin and amino acids [26]. Trace elements including zinc, iron, copper, magnesium, manganese, calcium, sodium, potassium, rubidium, silver, chromium, tin, vanadium and cobalt may also be present in varying quantities [27].

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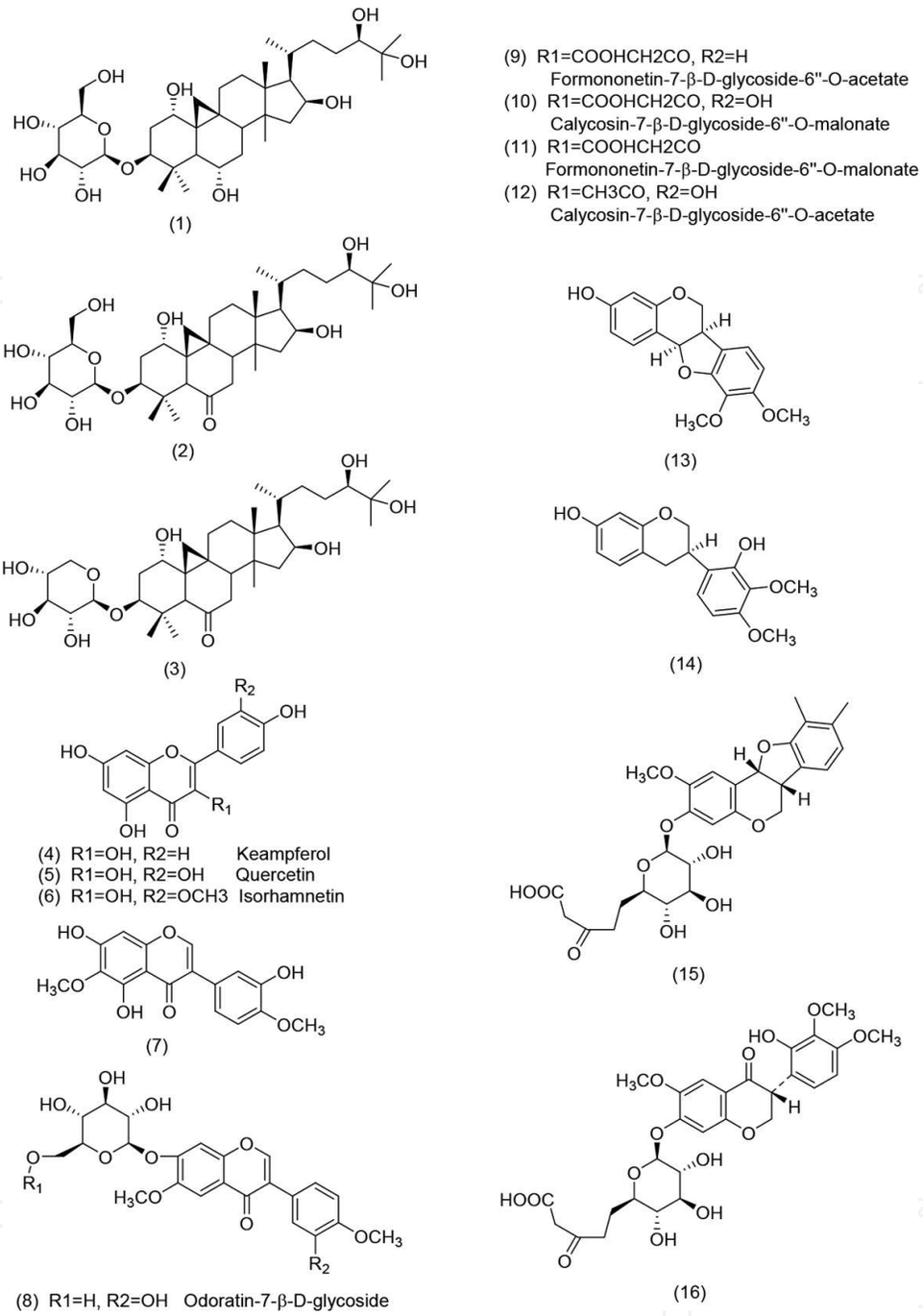

Figure 4. Chemical structures of the major compounds from Astragalus [23].

3.3. Pharmacological studies

The Chinese name Huangqi is the symbol of the "yellow leader" in china, linking to the yellow root and its status as one of the most important tonic herbs in traditional Chinese medicine (TCM). It was recorded in "Shen Nong Ben Cao Jing", the first book of Chinese herbal medicine, and was classified under the group of "qi"-tonifying drugs [28]. Huangqi

is one of the 50 fundamental herbs used in TCM and was included in many TCM preparations with a wide range of biological functions [23]. In traditional Chinese medicine, *A. membranaceus* has been used for the treatment of general weakness and chronic illness and to increase overall vitality. Modern pharmacological studies indicated that *A. membranaceus* showed different peripheral effects such as immune modulation [29], anti-diabetic activity [30], anti-oxidative and anti-inflammatory actions [31], antitumor activity [32], antiviral actions [33] and enhancement of cardiovascular functions, the protection of cardiovascular function might be explained in terms of protection against membrane lipid peroxidation [34].

3.4. Application in formulation

A. membranaceus has been formulated as the main ingredients TCM formulations to treat patients with "qi"-deficiency symptoms, which present as a lack of strength, anorexia, edema, abscesses and spontaneous sweating. Other indications include shortness of breath, spontaneous sweating and frequent cold, night sweating and edema [35]. Some TCM herbal formulations included *A. membranaceus* have been evaluated and screened. A TCM formulation called "Shi-quan-da-bu-tang", comprising Astragalus and Ligusticum, has shown to improve the therapeutic efficacy of chemotherapy and radiation in various animal and clinical studies [36]. The prescription is capable of prolonging survival, preventing the recurrence of malignancies and increasing resistance to immunosuppression that resulted from antineoplastic and radiotherapy drugs through stimulation of the macrophages to produce IL-6 and tumor necrosis factor (TNF), and is most effective in stimulating hematopoietic factors and interleukin (IL) production [29]. Bu-Zhong-Yi-Qi-Tang was determined to be the most commonly prescribed formula for treating elderly patients with weakness and fatigue, especially for female AD patients. Bu-Zhong-Yi-Qi-Tang led to elevated levels of dopamine and noradrenaline in the cortical tissues of mice, as well as improved attention, learning function and memory [37]. Bu-Zhong-Yi-Qi-Tang was also used to treat elderly patients with weakness and fatigue [38].

3.5. Safety

Generally, *R. astragali* was regarded as a safe drug, no incidence of poisoning related with the use of *R. astragali* or its main active ingredients, has been reported *in vivo* or *in vitr*o so far. It is determined that the LD50 of a crude extract of *R. astragali* is 40 g/kg using intraperitoneal injection (i.p.) in rats [39], and that did not show any adverse effects when raw herb was given to rats by lavage at the high dose 100 g/kg [40]. Moreover, the herbal extract (0.5 g/kg, i.p.) was injected to rats for 1 month, which caused no abnormal changes in food intake, urine/fecal production or behavior [41] Recently, the sub-chronic toxicity of the Astragalus extract, consisting of its active polysaccharides and saponins, has been evaluated the safety dosage range in clinical application. The application ranges 5.70–39.90 g/kg in rats, which are equivalent to 70 and 35 times in humans (0.57 g/kg, say, average body weight 70 kg), respectively [23, 42].

3.6. Cultivation practices

R. astragali is fond of coolness and drought tolerance but could not endure high temperature. An appropriate altitude of cultivating sites is from 1000 to 1500 m above sea level. The annual average temperature of 2–5°C and average rainfall of 250–350 mm are suited for cultivating. Sandy loam with rich organic matter content, good drainage and deeper is preferred. Seed coat of *R. astragali* is hard and difficult to germinate after sowing, so seed treatment should be done before sowing seeds. Seed was soaked with 70–80% sulfuric acid for 3–5 min, then quickly rinse, wash with running water. The sowing time of nurturing seedlings begins the early April. In cultivation practices, combined with soil preparation before planting, applying 45,000 to 60,000 kg/ha of manure and 25 to 30 kg/ha of phosphate fertilizer were recommended. Adopting

Seedling transplanting is usually used in the spring, by 20 cm apart in the row, 40 cm spacing between rows and 225,000 plants/ha. Combined with tillage, weeding should be carried out timely during growing period. The main disease in growing periods of *R. astragali* is powdery mildew; it can be used by 1000 time liquid mildothane 1000 time liquid spraying 2–3 time. The harvest period of *R. astragali* is during October to November and is dried using technology of freeze drying or solar drying.

4. *Radix glycyrrhizae*

甘草 (Gan cao, *R. glycyrrhizae*)

4.1. Botanical identity

R. glycyrrhizae is an ancient Greek word for the "sweet root," which was later called liquiritia and finally liquorice in Latin. As perennial shrub, it belongs to the leguminous Fabaceae (Leguminosae) family and exists about 20 species and grows mainly in Central Asia, Southwestern Asia and the Mediterranean region. The Chinese liquorice, *Glycyrrhiza uralensis Fish.* (*G. uralensis*), and the European liquorice, *Glycyrrhiza glabra L.* (*G. glabra*), are the most common ones among cultivated species. *G. glabra* is a more western species, found in Spain, Italy, Turkey, the Caucasus, Central Asia and the western China, whereas *G. uralensis* is distributed in Central Asia, Mongolia and China [43]. Photographs of *G. uralensis* are shown in **Figure 5**.

In the Northwest of China, *G. uralensis* mainly contains botanical characteristic as follows: calyx 5-lobed, two teeth than under three short; anther size (five big, five small), anther cell united at the top, different length of filaments. The ground part of different level is glands, glandular hairs and bristles, cilia, viscose or shen raised. A variety of underground part of the root and rhizome sweet taste needs to supplement the characteristics of some legumes as moniliform, ovule 1–11. The root and rhizome sweet including glycyrrhizin, glycyrrhizic acid, not sweet taste is some kind of glycyrrhetinic acid or glycyrrhetinic acid compounds (glycyrrhizic acid two yuan), some kinds of the above substances are not contained [44].

Figure 5. Photographs of *G. uralensis* are shown.

4.2. Chemical constituents

G. uralensis, commonly known as Chinese licorice, is an ancient herb of the legume family that is native to Asia. Its root is known to produce a variety of phytochemicals, plant secondary metabolites, including many terpenoids saponins (glycyrrhizic acid and glycyrrhetinic acid) and flavonoids flavonoids (liquiritin, isoliquiritin, liquiritigenin, isoliquiritigenin and glabridin). Among them, glycyrrhizin (I), liquiritin (II), isoliquiritin (III), liquiritigenin (IV) and isoliquiritigenin (V) (**Figure 6**) are believed to be bioactive contents [45].

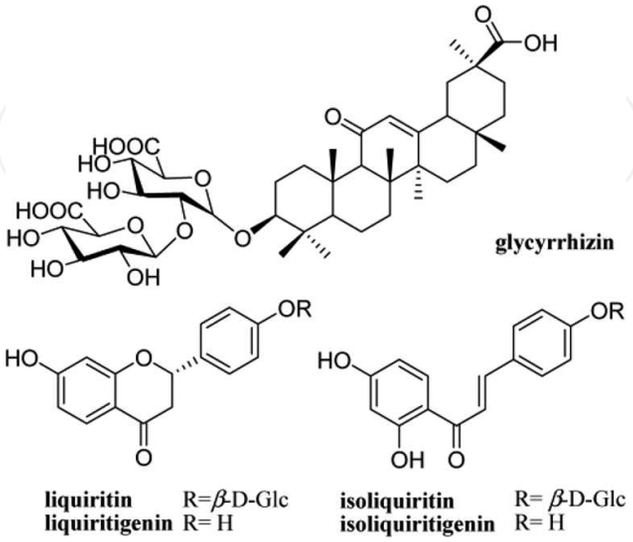

Figure 6. Structure of glycyrrhizin (I), liquiritin (II), isoliquiritin (III), liquiritigenin (IV) and isoliquiritigenin (V) [45].

4.3. Pharmacological studies

R. glycyrrhizae is one of the most famous herbal drugs used in TCM and has been used for several centuries. It has been frequently used in different formulations for the purposes of nourishing Qi (vital energy and functional activity of life), reducing spasms and pain, moistening the lungs and relieving coughs, detoxification, anti-inflammation and treating gastric ulcers [46]. According to modern pharmacological studies, its major constituents revealed various activities, providing concrete evidence for its extensive therapeutic use. The main saponin, glycyrrhizin, and its aglycone, glycyrrhetinic acid, has shown anti-inflammatory, anti-ulcer, hepatoprotective, immunomodulatory [47] and antivirus activities; flavonoids, including flavanones such as liquiritin apioside, liquiritin and liquiritigenin, and chalcones, such as isoliquiritin apioside, isoliquiritin, isoliquiritigenin, etc., have shown antitussive, anti-inflammatory, anti-allergic and anti-tumor effects [48]. In addition, glycycoumarin, a species-specific compound to *G. uralensis*, has antispasmodic and antibacterial activities.

4.4. Application in formulation

A systematic database was constructed to investigate the frequency of reporting formulations and crude drugs described in Shang-Han-Lun (known as the Treatise on Cold Damage Disorders), a famous prescription in TCM. It consists of 112 kinds of genuine formulations from a total of 430 formulations but due to overlapping or repetition. The best three frequently mentioned prescription were Da-cheng-qi-tang (DCQT), Guizhi-tang (GZT) and Shaoyao-gancao-tang (SYGCT) [46]. Da-cheng-qi-tang, also known as Dai-joki-to in Japanese, is a formulation composed mainly of Rhizoma Rhei and Cortex Magnoliae used for the treatment of interior heat- and excess-syndrome. Clinically, DCQT was widely prescribed to promote the recovery of gastrointestinal motility after abdominal surgery and to treat acute abdominal diseases, such as acute pancreatitis, adhesive bowel obstructions and acute appendicitis [49]. Guizhi-tang contains *R. glycyrrhizae*, Ramulus Cinnamoni and Radix Paeoniae as major crude drugs and is used for the treatment of exterior cold- and deficiency-syndrome [46]. Shaoyao-gancao-tang (SYGCT) in Chinese or Shakuyaku-kanzo-to in Japanese is a traditional herbal formula used for analgesic purposes and consists of two herbs, the Radix of Paeonia lactiflora Pall.; PL and the Radix et Rhizome of *G. uralensis*; GU, in a ratio of 1:1. SYGCT has been clinically and pharmacologically applied to prevent muscle cramps and inhibit the contraction of skeletal muscle [50], reduce uric acid, regulate autonomic functions [51], relax intestinal smooth muscle [52] and relieve painful peripheral neuropathy [53].

4.5. Safety

The acute toxicities of licorice extract containing approximately 53% glycyrrhizin have similar acute toxicity doses and are low in mice and rats. Glycyrrhizin administered 70 mg/kg intravenously has shown acute toxic effects of convulsions and slight hemolysis in mice, whereas toxic effects did not see at lower doses of glycyrrhizin. The majority of short-term

toxicity effects on the pituitary-adrenal axis have indicated that glycyrrhizin induced the pseudoaldosteronism at dose and time dependent manner, but the establishment of a clear no observed effect levels (NOEL) is difficult due to the differences in agents tested, animals used and end-points studied. The 90-day NOEL for licorice extract (53% glycyrrhizin) in rats is at the range of 0.31–0.63 g/kg, which delivers approximately glycyrrhizin 165–334 mg/kg [54]. However, for glycyrrhizin, the 30-day NOEL in rats is below 15 mg/kg [55]. In contrast, a two-year disodium glycyrrhizinate administered as high as 229 mg/kg/day or females administered as high as 407 mg/kg/day in mice showed no significant effects on average body weights or mortality, nor any signs of tumorgenicity among male animals. Other studies *in vivo* showed no teratogenic effects when glycyrrhizin salts were given maternally to mice, rats, hamsters or rabbits during gestation at doses up to 1000 mg/kg/day. However, dominant lethal testing in male rats suggests that an intake of glycyrrhizin 4000–5000 mg/kg/day could result in mutagenic effects in offspring [56]. Microbial experiments indicated that licorice extract and glycyrrhizinates were non-genotoxic and had some anti-genotoxic effects.

4.6. Cultivation practices

A climate condition with an average height of 1000–1500 m above sea level, annual average temperature of 6–8°C and average rainfall of 150–300 mm is suited for cultivating glycyrrhiza. Soil types of chestnut soil, brown soil, sierozem, dark loessial soils, salinized desert meadow soil and a weak alkaline (pH of 8–9) are the most suited for the cultivation of glycyrrhiza. The seedling fields should be chosen in the land of flat terrain, layers deep and fertile soil. Sow the seeds in drills 3–4 cm deep and 20 cm apart. The proper seed sowing time is in the end of April to early of May. Lifting seedling is in the day before transplanting. Transplanting is same as sowing time. Each plot at planting time, spacing of 10–15 cm and 25–30 cm row spacing planting are generally adopt. An under-mulch-drip irrigation or drip irrigation is usually a much better irrigation mode. Combined with tillage, weeding should be carried out timely during growing period. About 45,000 kg/ha of organic manure as base fertilizer with irrigation topdressing PK should be combined depending on soils and plant nutrition. Adopting measure of agricultural and biological prevention and cure control the diseases of rust disease, powdery mildew and brown spot, as well as insects of leaf beetle and *Porphyrophora sophorae* (Arch.). Seed breeding for 3–4 years, rhizomes multiply for 2–3 years can be harvested. When the stems and leaves withered in late September and early October, licorice roots could be excavated. Owing to deep roots, licorice should dig deep and not be broken or hurt the root bark. After sorting taproot and lateral root and removing reed head and bristles dried in the sun to a half dry state, tied into small, and then the sun to totally dry.

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