

## Chapter 7

# *Angelica sinensis* (Oliv.) Diels 当归 (Danggui, Dongkuai)

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### 7.1 Botanical Identity

*Angelica sinensis* (Oliv.) Diels is a common perennial herb in the family of Umbelliferae. Its dried roots, named *Angelicae Sinensis Radix* (Danggui, Dongkuai), have been frequently used as one of the most distinguished traditional Chinese medicines for dual medicinal and tonic purposes (Fig. 7.1). It is somewhat cylindrical, with 3–5 or more branched at the lower part, 15–25 cm long, externally yellowish-brown to brown in color, and longitudinally wrinkled and transversely lenticel-like protruded. The whole Danggui could be divided into three botanical parts: (1) root stocks (Guitou) (1.5–4.0 cm in diameter, annulated, apex obtuse and rounded or with several obvious protrudent rhizome scars), (2) main root (Guishen) (lumpy on the surface) and (3) branching roots (Guiwei) (0.3–1.0 cm in diameter, the upper portion thick and the lower portion thin, mostly twisted and exhibiting a few rootlet scars).

Danggui has been cultivated across Northwest China, in places such as Gansu, Yunnan, Sichuan, and Qinhai Province, etc. It is normally collected in late autumn, removed from the rootlet and soil, slightly dried and tied up in small bundles, placed on a shelf and then smoke-dried. It can not be used medically if the roots become woody, withered and not oily, or greenish-brown on the fracture [1]. There are several methods for preparing processed Danggui for different preferable tonic and medicinal purpose, such as slices, wine-washing and coal-frying [2].

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**Fig. 7.1** Dried roots (a) and sliced crude drug (b) of Danggui

## 7.2 Chemical Constituents

The chemical constituents in Danggui are complicated. To date, over 70 chemicals have been isolated and identified from Danggui, including carbohydrates, volatiles and organic acids, etc.

### 7.2.1 *Small Molecules*

Small molecules in Danggui have been well investigated and could be divided into two kinds, volatiles and water-soluble compounds, mainly including organic acids, vitamins, amino acids and trace elements, etc.

Danggui is very rich in volatile components, in which phthalides are dominant, for example, *Z*-ligustilide and *Z*-butylidenephthalide. Terpenes are also frequently found in the volatile components of Danggui. Of the water-soluble components, organic acids are the main compound of concern in Danggui, with ferulic acid being the most representative one (Fig. 7.2). These characteristic bioactive components are intensively employed as the chemical markers for quality evaluation of Danggui and Danggui-containing pharmaceutical and natural prescriptions and products for medicinal or tonic applications [3].

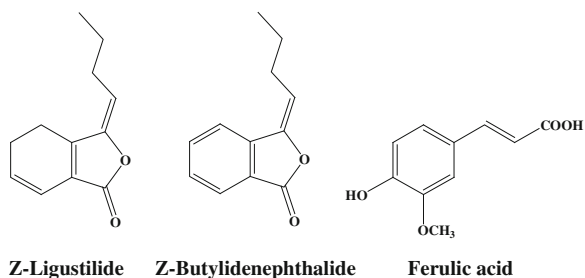


Fig. 7.2 Representative small molecular components in Danggui

### 7.2.2 Polysaccharides

There are significant amounts of polysaccharides in Danggui that have been experimentally proven to exert multiple biological properties, such as immuno-modulation, anti-tumor and anti-oxidant activity. As indicated by a recent study, polysaccharides rather than volatile oils are required in the traditional use of Danggui [4].

To date, about 40 kinds of polysaccharides have been isolated and purified from Danggui. Isolation, purification, and in-depth structural elucidation of the polysaccharides in Danggui have been intensively reported. There is much variety in the molecular weights of purified polysaccharides from Danggui, ranging from less than  $10^4$  kDa to more than  $10^6$  kDa.

Glucose, mannose, galactose, arabinose and galacturonic acid, are most frequently found, and are the five main monosaccharides and uronic acid comprising the polysaccharides isolated from Danggui. In addition, other monosaccharides such as rhamnose, xylose and glucuronic acid, also occasionally appear in the backbone or branched and terminal residues of purified Danggui polysaccharides. Moreover, diverse glucosidic bonds mainly  $1 \rightarrow 4$ ,  $1 \rightarrow 6$  or  $1 \rightarrow 3$  linkages are found in Danggui polysaccharides [5].

## 7.3 Pharmacological Studies

In the light of traditional Chinese medicine theories, Danggui is historically used for nourishing blood. Based on modern research, multiple pharmacological effects of Danggui have been experimentally proven, such as hematopoietic effect, cardiovascular effects (protection of the cardiovascular system against ischemia, relaxation of blood vessels and vascular protection effect in endothelial cells, anti-oxidation, anti-platelet aggregation, and regulation of hemorrheology), effects on gynecological imbalances (dysmenorrhea alleviation, estrogenic activity, and anxiolytic effects), neuro-protective activity, wound healing, and anti-cancer effects

[6]. In addition, the bioactive effects of Danggui fractions and individual components were also intensively studied. For example, polysaccharide fractions in Danggui are hematopoietic, anticancerous, antioxidative, and immunoregulatory [7] while essential oil fractions possess the effects of anti-platelet aggregation, muscle relaxation and antianxiety [8]. Vessel relaxation, neuro-protective and anti-tumor effects of Z-Ligustilide as well as anti-oxidation, anti-platelet aggregation, anti-bacterial activities of ferulic acid have also been undoubtedly verified [9].

## 7.4 TCM Applications and Dietary Usage

### 7.4.1 TCM Applications [10]

As one of the most important Chinese medicines, Danggui has been used in the treatment of cardiovascular and cerebrovascular conditions in China for years and is usually combined with other herbs for clinical use. For instance, Danggui plus Radix Astragalus in a 1:5 ratio form a famous prescription: Danggui Buxue Tang which is traditionally used for blood deficiency disorders. Thanks to its positive effect, this formula has been getting more and more attention in recent years and many experimental studies have been conducted to provide scientific testimony to its favourable effects in promoting hematopoiesis, regulating immunity, and protecting cardiovascular aspects. Another example of a well known tradition prescription is Siwu Tang. It consists of *Angelica sinensis*, *Ligusticum chuanxiong*, *Paeonia lactiflora* and *Rehmannia glutinosa* (processed), and is a well regarded ancient Chinese prescription that is prized throughout East Asia and used to enrich the blood and regulate menstruation. Moreover, other Danggui-containing formulas with more complicated compositions, such as Guipi Tang, Xiaoyao San, Danggui Sini Tang and Danggui Liuhuang Tang, are also widely used in individuals for blood-related diseases.

Apart from use in traditional medicinal formulas, Danggui is also employed in many medicinal products with modern dosage forms, for example, ointments (Danggui fluid extract), tablets (Danggui Tablets and Danggui Longhui Tablets), pills (Danggui Yangxue Pills and Concentrated Danggui Pills), oral solution (Danggui Buxue Oral Liquid), granules (Danggui Shaoyao Granules), injections (Danggui Jisheng Injections and Fufang Danggui Injections) and mixtures (EJiao Danggui Mixtures).

### 7.4.2 Dietary Usage

Due to the outstanding tonic effects, Danggui is also well-accepted in dietary usage as a popular food supplement to treat many conditions. It is used mainly for the

treatment of dysmenorrhea, amenorrhoea and other female reproductive problems. Danggui is also used to enrich blood as an aid to recovery from blood loss after child birth or surgery [11]. Danggui itself or combined with other herbs can be used to prepare herbal wine, herbal tea, and medicinal foods such as congees and other dishes, which could be easily made at home.

#### 7.4.2.1 Danggui Wine

Herbal wine made of Danggui itself or mixed with other herbs is commonly used for irregular menstrual cycles as well as coronary diseases. For example, Guiqi Wine, prepared by Danggui (150 g), Huangqi (roots of *Astragalus mongholicus*, 150 g), Dazao (fruits of *Ziziphus jujuba var. inermis*, 100 g) and Chinese spirit (500 mL), is a well-known kind of tonic wine for regulating menstruation. Drinking 20–30 mL daily for 3 months is recommended [12]. Danggui can also be used to make herbal wines in combination with Cordyceps and Sanqi (roots of *Panax notoginseng*) for treating coronary diseases [13].

#### 7.4.2.2 Danggui Teas

Danggui alone or combined with other herbs can be used to prepare herbal tea for enriching blood. Some examples are: Danggui Tea composed of Danggui (10 g); Shanzha Danggui Tea composed of Danggui (15 g), Shanzha (fruits of *Crataegus pinnatifida*, 30 g), and moderate amounts brown sugar; Danggui Chuanxiong Yimucao Tea composed of Danggui (60 g), Yimucao (45 g), and Chuanxiong (10 g); Danggui Dihuang Tea composed of Danggui (15 g), Prepared Dihuang (roots of *Rehmannia glutinosa*, 15 g), and Dazao (fruits of *Ziziphus jujuba var. inermis*, 5 pieces). Danggui can also be used to make herbal teas in combination with many other herbs depending on the specific need of functions including enriching *Qi* and promoting blood circulation.

#### 7.4.2.3 Danggui Used in Medicinal Foods

Danggui can be used to make medicinal foods like congees and dishes as food supplement for treating women's reproductive problems such as relieving cramps, irregular menstrual cycles, infrequent periods, premenstrual syndrome (PMS) and menopausal symptoms. Danggui is commonly used with rice and other herbs for making congees. For example, Danggui Fangfeng Congee, prepared by Danggui (15 g), Fangfeng (roots of *Saposhnikovia divaricate*, 10 g) and rice (100 g); Chidou Danggui Congee, prepared by Danggui (20 g), Chixiaodou (seeds of *Phaseolus calcaratus*, 100 g) and rice (100 g).

## 7.5 Clinical Evidences

For clinical applications, Danggui is always combined with other herbal medicines as complex prescriptions, such as Danggui Buxue Tang and Siwu Tang, etc. The favorable clinical effects of these traditional formulas have been well investigated and proven for many diseases, including gynaecopathia and angiocardopathy. Danggui Buxue Tang has been clinically proven to be antanemic, liver-protective and *Qi*-beneficial therapy while the intensive clinical investigations demonstrated that Siwu Tang was an ideal formula for nourishing blood and regulating menstruation [14]. Some modern dosages of Danggui or Danggui-containing combinations are also clinically investigated. For Compound Danggui Huoxue Tablets, a clinical study showed that the compound could be used for treating thromboangiitis obliterans in 40 cases, which was better than Compound Danshen Tablets used in control groups [15]. For Compound Danggui Pills, clinical research was carried out on 200 cases with the symptoms of dysmenorrheal and irregular menstruation. The efficiency of the treatment group was as high as 95.1 %, showing the significant difference compared with the control group [16]. For Danggui Buxue Tang (DBT) which is a famous Chinese herbal medicine preparation, a randomized, double-blind, multiple-dose escalation trial (phase II clinical trial) was completed. This clinical study investigated the dose-response relationship of DBT on 60 postmenopausal women experiencing severe hot flashes and night sweats. The resulted showed that DBT preparations at 6.0 g/day significantly improved physical and psychological scores and significantly reduced vasomotor symptoms from baseline [17].

The clinical effects of Danggui Buxue Oral Liquid for mild and moderate anemia [18], Danggui Shaoyao Granules for menoxenia [19], Danggui Buxue Decoction No.1 for auxiliary therapy in treating patients of non-small-cell lung cancer at peri-operational stage [20] have all been experimentally proven as well.

## 7.6 Safety Evaluation and Toxicity Data [17]

In “Shennong Bencao Jing”, an ancient book on medicinal herbs, Danggui was recorded as a “top grade” non-toxic herbal medicine. Few clinical reports on the toxicity or side effects of Danggui are available. According to toxicity studies on animals, the MLD (Minimum Lethal Dose) of Danggui fluid extract by intragastric administration for SD rats is 30–90 g/kg, the LD<sub>50</sub> of Danggui water extracts by single dose i.g. and i.p. (mice) are more than 8 and 6.58 g/kg, respectively. The LD<sub>50</sub> of Danggui diethyl ether extracts by single dose i.g. and i.p. (mice) are more than 10 and 5 g/kg, separately, and the LD<sub>50</sub> of Danggui methanol extracts by single dose i.g. and i.p. (mice) are both more than 6 g/kg. Furthermore, 0.06 and 0.02 mL/kg diethyl ether extracts of Danggui by single dose i.v. could lead to the death of dogs and cats, respectively.

As described above, Danggui is a relatively safe herbal medicine often used for the treatment of gynaecopathia and angiocardopathy. However, there are several issues you must be aware of when you decide to use this herb without doctor's advice. Breast cancer sufferers should not take Danggui since its estrogen components could significantly promoting the proliferation of breast cancer cells. Danggui should also not be used in combination with anticoagulants because their synergistic effect could increase the risk of hemorrhage. It's strongly suggested to use Danggui under your doctor's professional advice.

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