Chapter 78

*Lonicera japonica* Thunb 金银花
(Jinyinhua, Honey Suckle)

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### 78.1 Botanical Identity

Jinyinhua, a sprawling and twining lianas in the family of Caprifoliaceae, is a popular Chinese herbal medicine used for the treatment of inflammatory diseases and as a well-known dietary supplement that has been used for many centuries. The medicinal part of the plant is the dried flower buds or flowers before blooming. The bloomed flowers undergo six stages, i.e. the juvenile bud stage, green stage, white stage, complete white stage, silver flowering stage, and golden flowering stage [1]. The color of the last two stages are silvery and golden respectively, so the medicinal material is called Jinyinhua because Jin means gold in Chinese, Yin means silver in Chinese and Hua means flower in Chinese. Although four other species of genus *Lonicera*, similar to Jinyinhua, have been used for medicinal purposes [2], only *Lonicera japonica* Thunb. has been used as a legal source of Jinyinhua, recorded in The Pharmacopoeia of People’s Republic of China [3]. As the typical botanical traits, *L. japonica* has young stems with pubescence; leaves ovate, elliptic, oblong or broadly lanceolate, blades 3–8 cm long, 1–3.5 cm wide; flowers in axillary cymes; corolla white, turning yellowish or tinged pink, 2-lipped. Figure 78.1 showed the flowering plant and crude drug of *Lonicera japonica*.

Besides natural wild growth, Jinyinhua is cultured as a ground cover for ornamental and conserving water and soil due to its beautiful flowers and strong roots. Both wild and cultured materials are the source of supply. The flowers are typically harvested between May to June when they change from green to white and are in buds. The quality of medicinal materials will be lowered if the harvest is too early or too late. After drying 1–2 days and picking up impurities, cleaned and dried raw
material can be obtained and marketed. During drying procedures, do not directly expose the flowers to strong sunlight because it will darken the flowers. Other processing methods are further performed for some specific medicinal purposes, such as fried Jinyinhua and charcoaled Jinyinhua etc. In recent years, sulfur-fumigation has been used to replace natural drying processing for efficiency and pest control [4].

### 78.2 Chemical Constituents

Organic acids, flavonoids and volatile oil are the three major classes of bioactive compounds found in Jinyinhua [1]. In addition, shuangkangsu (shown in Fig. 78.2 (8)), which has the marked anti-viral activity against influenza B virus, influenza A3 virus and respiratory syncytial virus, is an important chemical constituent with a novel skeleton structure of cyclic peroxide. It was found in 2008.

#### 78.2.1 Organic Acids

Organic acids are the main and effective components of *L. japonica*. Chlorogenic acid (1), isochlorogenic acid (2), neochlorogenic acid (3), and caffeic acid (4) (shown in Fig. 78.2) are representative compounds. Among them, chlorogenic acid is received considerable attention for its part in the human diet with potential biological effects [5], and is used as a standard compound for evaluation of the quality of Jinyinhua and related pharmaceutical or natural health product containing the herb. According to the Chinese Pharmacopoeia, its content must be not less than

Fig. 78.1  Flowering plant (a) and crude drug (b) of *Lonicera japonica*
1.5 % in the dried crude drug. The highest level of chlorogenic acid was found in the white and complete white flowering stages. So far, about 32 organic acids have been isolated from Jinyinhua [1]. Figure 78.2 illustrated the representative organic acids, flavonoids and volatile components isolated from Jinyinhua.

78.2.2 Flavonoids

Because flavonoids have a wide spectrum of biological activities, especially with antioxidative and anti-inflammatory properties, they play a part in the qualitative and quantitative analysis of Jinyinhua. Luteoloside (5) was added in Chinese Pharmacopoeia with chlorogenic acid to control the quality of medical material by HPLC method. The content of luteoloside in the Jinyinhua should be not less than 0.05 %. Besides luteoloside, other flavonoids, such as luteolin (6) and lonicerin (7) (shown in Fig. 78.2), have exerted anti-inflammatory activity [6]. Up to now, about 30 flavones have been isolated from L. japonica.
78.2.3 Volatile Oil

As one of the important compositions, volatile oil is significant in both the wide activity and utilization of Jinyinhua. A total of about ninety compounds of volatile oil were identified, the main compound being linalool [7]. Due to the differences in harvesting time and processing technics, the contents and components of volatile oil are different. Existing research showed that the complete white and silver flower period are the preferable harvest times for volatile oil, which match with the best time to harvest for chlorogenic acid. Low temperature and no-lighting were in favor of the volatile oil in the dry and extract processes [1].

78.3 Pharmacological Studies

As described previously, Jinyinhua is one of widely used herbs in TCM, especially for almost all infectious diseases, due to its antimicrobial and anti-inflammatory activities. The two activities act synergistically to accelerate wound repair [8]. Moreover, the modern pharmacological studies showed that Jinyinhua and its active principles also possess the wide pharmacological actions, such as antiendotoxin, antipyretic, antihyperlipidemic, anti-thrombotic, anti-oxidative and anti-carcinogenic activities, and hepatoprotective etc. [1]. In addition, anti-lipase, insecticidal and acaricidal activities were also found in the crude extract of Jinyinhua. In recent years new bioactivities, such as the potent anti-Parkinsonism activity [9] and protecting neuronal cells against glutamate excitotoxicity via antioxidative activity [10], inhibition of the allergic contact dermatitis [11], and a possible use for antidiabetes, have been discovered and suggested to be in the compounds isolated from Jinyinhua due to its potent inhibitor action for maltase [12]. Researchers thought most of these effects may be related to the active compositions of volatile oil, chlorogenic acid, and flavones. Chlorogenic acid and luteoloside, officially used as the indicator compound to characterize the quality of this herb and its related preparations, were shown to have beneficial effects in the aspects of anti-oxidation and antitumor [1, 13]. Moreover, chlorogenic acid showed the antibacterial, antiviral, anti-inflammatory, hypoglycemic activities, and allergy-preventive properties [1, 14]. Meanwhile, luteolin, another major flavonoid in Jinyinhua, and volatile oil also showed significant anti-inflammatory activity. Luteolin has significant bioactivities in the aspects of antifibrotic and anti-5-lipoxygenase activities [6, 15]. Taken together, most of these activities matched to traditional usage.
**78.4 TCM Applications, Dietary, and Daily Life Usage**

### 78.4.1 TCM Applications

Jinyinhua with heat-clearing and detoxifying effect has been called little fairyhood of herb store. In TCM clinical practice, Jinyinhua is usually used to treat various infectious diseases. As the most famous herb of anti-inflammatory, it is constantly used for upper respiratory tract infections. 1500 years ago, Jinyinhua had been used for the treatment of exopathogenic wind-heat, epidemic febrile diseases, carbuncles, sores, furuncles and infection diseases. Also, it has also been made in preparations to treat chronic enteritis, pneumonia, acute tonsillitis, nephritis, acute mastitis, and leptospirosis in clinic. More than 500 prescriptions containing Jinyinhua have been used to treat various diseases [1]. Common Jinyinhua preparations clinically used include the following forms:

#### 78.4.1.1 Oral Liquids

Yinhuang Oral Liquid and Shuanghuanglian Oral Liquid [9, 12] are two typical examples of oral liquid. Yinhuang Oral Liquid is composed of two herbal components: Jinyinhua and Huangqin (roots of *Scutellaria baicalensis*), where Shuanghuanglian Oral Liquid has an additional component: Lianqiao (fruits of *Forsythia suspensa*) besides Jinyinhua and Huangqin. There are hundreds of manufacturers making these two products based on the same formula in China. These two products are two of the best-selling drugs on market. They are mainly used for the treatment of fever, cough, sore throat, acute and chronic tonsillitis, acute and chronic pharyngitis through its function clearing away the heat and toxic material, antibacterial, anti-inflammatory and antiviral effects.

#### 78.4.1.2 Buccal Tablets

Yinhuang buccal tablets and Shuanghuanglian buccal tablets have the same compositions as oral liquid but are in a different form. The buccal table form is particularly suitable for swelling and pain of the throat caused by acute and chronic tonsillitis, pharyngitis and upper respiratory tract infections.

#### 78.4.1.3 Injections

Yinhuang Injection, Shuanghuanglian Injection, and Compound Acetaminophen Jinyinhua Injection are three common used preparations containing Jinyinhua. Compound Acetaminophen Jinyinhua Injection is composed of the extract of Jinyinhua, baicalin, and acetaminophen. These products have been used clinically for
the treatment of upper respiratory tract infections, sore throat, tonsillitis, mumps and pneumonia, and Compound Acetaminophen Jinyinhua Injection has also been used to relieve moderate pain, such as arthralgia, headache, and toothache. Adverse reactions of these products after intravenous injection were detected so these injections are better to be administered by intramuscular injection.

**78.4.1.4 Granular Form**

Jinyinhua granula prepared by itself is an extract in a convenient form that is used by being mixed with other herbs.

Recently, Jinyinhua, as ‘bouvardin’, has been used extensively to prevent and treat some serious viral diseases of humans and animals, such as SARS corona virus, H1N1 (Swine) flu virus [16].

**78.4.2 Dietary Usages**

Jinyinhua is a well-known dietary supplement due to its valuable bioactivities and because it’s easy to obtain since it is planted in many areas as one of ornamental groundcover. It can be used in many ways historically. These include Jinyinhua beverage, Jinyinhua candy, and Jinyinhua soup etc. The following dietary forms can be easily bought at a market or made at home.

**78.4.2.1 Jinyinhua Beverage and Wine**

Jinyinhua has been used to make healthy beverage through various technologies, such as Jinyinhua tea, Jinyinhua dew, Jinyinhua nutritive dew, Jinyinhua nutritive beverage, and Jinyinhua yogurt etc. These beverages are employed to improve the body and prevent illnesses in China [1].

Jinyinhua tea has a variety of practices, such as Jinyinhua by itself, combined with tea, combined with honey, or combined with other herbs. All of them are popular ways to use Jinyinhua. They are typically drunk in the hot season for clearing heat, detoxicating and strengthening the body’s response against disease by improving the activity of the immune system. Some examples are: Jinyinhua dew composed of the distilled liquid of Jinyinhua and water. Jinyinhua Tea can be drunk after boiling water of 150 ml to soak Jinyinhua (5 g) and green tea (3 g) for 5–10 min. According to further needs, Jinyinhua can be combined with other herbs with bioactivities for enhancing its effect. Jinyinhua Shanzha Tea composed of Jinyinhua (10 g), Juhua (flowers of *Chrysanthemum morifolium*, 10 g), and Shanzha (fruits of *Crataegus pinnatifida*, 10 g) for headache, fever and thirst caused by hotness. Jinyinhua Bohe Tea composed of Jinyinhua (15 g), Bohe (aerial parts of *Mentha haplocalyx*, 5 g), and Gouqi (fruits of *Lycium chinense* or *L. barbarum*, 15 g).
Jinyinhua itself or combined with different herbs can be used to make herbal wine for various specific needs of functions. Some examples are: the extracting solution of Jinyinhua (alcohol content 55 %) is added before fermentation, the following process is the same as used to brew wine [17]; Jinyinhua (45–55 g), Gancao (roots and rhizomes of Glycyrrhiza uralensis, G. inflata, or G. glabra, 5–10 g), Gouqi (fruits of Lycium chinense or L. barbarum, 25–30 g) and Baizhi (roots of Angelica dahurica, 5–10 g) are soaked in 500 ml wine of alcohol content between 55–60 % for more than 25–50 days, then it can be adjusted into different contents of alcohol according to needs.

78.4.2.2 Jinyinhua Candy

Jinyinhua, the material which can be used as medicine and food, is often made into candy together with other herbs. Some examples are: Jinyinhua Qingguo Pipa candy composed of Jinyinhua, Qingguo (Chinese olives, fruits of Canarium album), Pipa (fruits of Eriobotrya japonica), Jiegeng (roots of Platycodon grandiflorum) and Baimaogen (rhizomes of Imperata cylindrica); Jinyinhua cool candy is composed of Jinyinhua, Qingguo, Luohanguo (fruits of Siraitia grosvenorii), Pangdahai (seeds of Sterculia lychnophora) and Bohe (aerial parts of Mentha haplocalyx); Jinyinhua Juhua candy is composed of Jinyinhua, Bohe and Juhua (flowers of Chrysanthemum morifolium). White granulated sugar and liquid glucose are usually added to adjust the taste. You can buy the candy in the supermarket for the purpose of moistering and clearing the throat.

78.4.2.3 Jinyinhua Used in Medicated Foods

Jinyinhua can be used to make soups or porridge with rice, or mung bean etc. A typical way is to boil 100 g mung bean and a piece of ginger in 1 liter of water before adding 30 g Jinyinhua, then continuously boil until the mung bean cracks and are fully cooked. Other ingredients, such as wax gourd, lily bulbs, lotus root, almond, pears, and ham etc., can be boiled together with Jinyinhua. Beautiful white and yellow color, nutrient, and health-maintaining effect of Jinyinhua can be employed simultaneously. The taste of Jinyinhua-contained foods can be adjusted by adding honey, white granulated sugar or licorice.

In addition, the oil and extracts from Jinyinhua may be a potential source of preservatives for the food industries [1].

78.4.3 Jinyinhua Used in Daily Life

In Qing dynasty of China, about 375 year ago, Jinyinhua was used to moisturize the skin and for rejuvenation. Recently, the extract of Jinyinhua, as natural source of
bioactive compounds, have been applied in cosmetics, extensively to exert its marked antibacterial and antisepticize activities, such as Jinyinhua facial mask, Jinyinhua facial cleanser, and Jinyinhua shower Gel. It could be made into toothpaste which could have the effects of preventing and treating the oral cavity’s diseases [1]. In addition, the volatile oil isolated from Jinyinhua would cover the smell from cigarettes. And chlorogenic acid and its analogues, which are beneficial to health, are rich in Jinyinhua. It can be added into cigarettes to serve a useful role in improving the quality of cigarettes and preventing disease.

78.5 Clinical Evidences

Jinyinhua is mostly used in combination with other herbs with heat-clearing and detoxifying effect, such as Huangqin (roots of Scutellaria baicalensis), Lianqiao (fruits of Forsythia suspensa) etc. More than 12 preparations, in which Jinyinhua was the main and active compositions, were listed in Chinese Pharmacopoeia (2010 edition) and used to cure fever, cough and pharyngalgia and the swell of throat, constipation, conjunctival congestion, etc. Except the aforementioned preparations: injection, oral solution, granular, or suppository of Yinhuang, Shuanghuanglian and Yinzhihuang, SimiaoYongan decoction, Yinqiao Jiedu Tablets, and Xiaoyin Tablets etc. are the most commonly used preparations.

There are large numbers of clinical related reports or observational studies published on the effects of Jinyinhua and its related preparations for various diseases. Clinical report showed Shuanghuanglian oral solution’s effect of antipyretic on wind and warm syndrome was 100 % within 72 h in 48 cases [18]; and the preparation could effectively relief the cold symptom of cough, headache, nasal discharge, sore throat. It could also stop the cheek swelling of child with epidemic parotitis [19]. Yinzhihuang oral solution, which is composed of four herbal components: Jinyinhua, Yinchen (aerial parts of Artemisia scopariae or A. capillaris), Huangqin (roots of Scutellaria baicalensis), and Zhizi (fruits of Gardenia jasminoides), may inhibit further increase in bilirubin levels, and reduced the phototherapy requirement in 1177 cases of neonatal indirect hyperbilirubinemia in term newborn infants [20]. Simiao Yongan (Trade name: Mailuoning) is used in treating ischemic cardiovascular and cerebrovascular diseases for many years in clinical and comprises Jinyinhua, Xuanshen (roots of Scrophularia ningpoensis), Danggui (roots of Angelicae sinensis) and Gancao (roots and rhizomes of Glycyrrhiza uralensis, G. inflate or G. glabra), clinical studies have shown that it can inhibit the inflammatory response and antagonize the blood clotting process [21].
78.6 Safety Evaluation and Toxicity Data

Because Jinyinhua is an edible herb and commonly used as raw material in health food, clinical reports on the toxicity or side effects were done to determine its safety at least 10 years ago. The extract of Jinyinhua was found to be fairly nontoxic when oral taken by rats or mice. The detail was as follow. Acute toxicity test showed its LD<sub>50</sub> was more than 15 g/kg body weight on mice orally. According to the classification standard of chemicals acute toxicity, it belongs to non-toxic level. Micronucleus test of bone marrow cells up to 7.5 g/kg in mice orally and Ames test/mammals microsomal enzyme test showed it was safe without mutagenesis. Meanwhile, sperm abnormalities and antifertility effect were undetected on male mice and SD female rats, respectively [22]. In addition, Jinyinhua combined with the dried Zhimu (rhizomes of <i>Anemarrhena asphodeloides</i>) showed no signs of acute or chronic toxicity in terms of general behavior, gross appearance of the internal organs, blood chemistry, or mortality in male or female rats when orally administered a single dose of 5,000 mg/kg in acute toxicity test or 500, 1000 or 2,000 mg/kg daily for 13 weeks in chronic toxicity test. They didn’t cause significant gastric mucosal damage after single or repeated doses, instead appearing to protect the mucosa from diclofenac-induced gastric damage [23].

To sum up, as a material of being used as medicine and food, Jinyinhua is definitely a safe herbal medicine, and often used for the treatment of infectious diseases and health maintaining purpose. It can also be used for relieving cold and cleaning away poison. But the close attention must be paid when deciding to use this herb for cold because it is obvious that the cold treated by Jinyinhua refers only to a pyretic cold rather than a frigid cold, and this herb is inapplicable for the hypofunction of person’s constitute with cold manifestation consideration of its strong clearing heat activity.

References

1. Shang et al (2011) <i>Lonicera japonica</i> Thunb.: ethnopharmacology, phytochemistry and pharmacology of an important traditional Chinese medicine. J Ethnopharmacol 138(1):1–21
2. Chu et al (2011) Combination of normal light and fluorescence microscopy for authentication of five <i>Lonicera</i> species flower buds. Microsc Res Tech 74(2):133–141
3. Pharmacopoeia Committee of P. R. China (2010) <i>Pharmacopoeia of People’s Republic of China</i>. Chemical Industry Publishers, Beijing 2010 (in Chinese)
4. Cai et al (2013) Profiling and characterization of volatile components from non-fumigated and sulfur-fumigated <i>Flos Lonicerae Japonicae</i> using comprehensive two-dimensional gas chromatography time-of-flight mass spectrometry coupled with chemical group separation. Molecules 18(2):1368–1382
5. Upadhyay et al (2013) An outlook on chlorogenic acids-occurrence, chemistry, technology, and biological activities. Crit Rev Food Sci Nutr 53(9):968–984
6. Kang et al (2010) Luteolin isolated from the flowers of <i>Lonicera japonica</i> suppresses inflammatory mediator release by blocking NF-kappaB and MAPKs activation pathways in HMC-1 cells. Molecules 15(1):385–398
7. Vukovic et al (2012) Chemical composition of the essential oils from the flower, leaf and stem of *Lonicera japonica*. Nat Prod Commun 7(5):641–644
8. Chen et al (2012) Wound repair and anti-inflammatory potential of *Lonicera japonica* in excision wound-induced rats. BMC Complement Altern Med 12:226
9. Kwon et al (2012) *Lonicera japonica* Thunb. protects 6-hydroxydopamine-induced neurotoxicity by inhibiting activation of MAPKs, PI3 K/Akt, and NF-kappaB in SH-SY5Y cells. Food Chem Toxicol 50(3–4):797–807
10. Weon et al (2011) Neuroprotective activity of the methanolic extract of *Lonicera japonica* in glutamate-injured primary rat cortical cells. Pharmacogn Mag 7(28):284–288
11. Tian et al (2012) Characterization and anti-allergic effect of a polysaccharide from the flower buds of *Lonicera japonica*. Carbohydr Polym 90(4):1642–1647
12. Zhang et al (2013) α-Glucosidase inhibitory activity by the flower buds of *Lonicera japonica* Thunb. J Funct Foods 5(3):1253–1259
13. Qiu et al (2013) HPLC-ESI-MS/MS analysis and pharmacokinetics of luteoloside, a potential anticarcinogenic component isolated from *Lonicera japonica*, in beagle dogs. Biomed Chromatogr 27(3):311–317
14. Oku et al (2011) Allergy-preventive effects of chlorogenic acid and iridoid derivatives from flower buds of *Lonicera japonica*. Biol Pharm Bull 34(8):1330–1333
15. Chen et al (2010) Luteolin ameliorates experimental lung fibrosis both in vivo and in vitro: implications for therapy of lung fibrosis. J Agric Food Chem 58(22):11653–11661
16. Jiao (2009) Research and comprehensive utilization of honeysuckle. Qilu Pharm Aff 28(8):487–489 (in chinese)
17. Ren et al (2001) Studies on health food of Honeysuckle. Food Res Dev 01:63–64
18. Xi et al (2012) Research on antipyretic project of TCM emergency care for exogenous fever with analysis of 906. J Emerg Tradit Chin Med (01):1–3 + 76 (in chinese)
19. Guan et al (2005) Progress in clinical application of Shuanghuanglian oral liqui. Chin J Inf Tradit Chin Med 04:38–39 (in chinese)
20. Clinical research collaborative group of Yinzhihuang oral solution (2011) A multicenter randomized controlled study on the efficacy and safety of Yinzhihuang oral solution for the treatment of neonatal indirect hyperbilirubinemia in term newborn infants. Chin J Pediatr (Zhonghua Er Ke Za Zhi), 49(9):663–668 (in chinese)
21. Peng et al (2012) Effect of Si-Miao-Yong-An on the stability of atherosclerotic plaque in a diet-induced rabbit model. J Ethnopharmacol 143(1):241–248
22. Zhang (2003) The toxicological assessment of *Lonicera japonica* on food safety. Chin Acad Med Mag Org 02:63–64 (in chinese)
23. Huh et al (2011) Gastroprotective and safety effects of WIN-34B, a novel treatment for osteoarthritis, compared to NSAIDs. J Ethnopharmacol 137(2):1011–1017