

# Systematic review for geo-authentic *Lonicerae Japonicae Flos*

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**Abstract** In traditional Chinese medicine, *Lonicerae Japonicae Flos* is commonly used as anti-inflammatory, antiviral, and antipyretic herbal medicine, and geo-authentic herbs are believed to present the highest quality among all samples from different regions. To discuss the current situation and trend of geo-authentic *Lonicerae Japonicae Flos*, we searched Chinese Biomedicine Literature Database, Chinese Journal Full-text Database, Chinese Scientific Journal Full-text Database, Cochrane Central Register of Controlled Trials, Wanfang, and PubMed. We investigated all studies up to November 2015 pertaining to quality assessment, discrimination, pharmacological effects, planting or processing, or ecological system of geo-authentic *Lonicerae Japonicae Flos*. Sixty-five studies mainly discussing about chemical fingerprint, component analysis, planting and processing, discrimination between varieties, ecological system, pharmacological effects, and safety were systematically reviewed. By analyzing these studies, we found that the key points of geo-authentic *Lonicerae Japonicae Flos* research were quality and application. Further studies should focus on improving the quality by selecting the more superior of all varieties and evaluating clinical effectiveness.

**Keywords** *Lonicerae Japonicae Flos*; geo-authentic; herbal quality; chemical fingerprint; component analysis

## Introduction

*Lonicerae Japonicae Flos*, also known as *Jin Yin Hua*, is a dried flower of *Lonicera japonica* Thunb., which originates from East Asia. In traditional Chinese medicine (TCM), it is commonly used as anti-inflammatory, antiviral, and antipyretic herbal medicine for some diseases, such as acute tonsillitis, pneumonia, dysentery, and arthritis in clinic [1,2]. According to statistics, *Lonicerae Japonicae Flos* is one of the most frequently used herbs in the treatment and precaution of severe acute respiratory syndromes (SARS) and influenza A virus A (H1N1), which are serious viral diseases [3]. *Lonicerae Japonicae Flos* is also an economic plant with high value and is widely recognized as tea, food, and ornamental plant

in Asia and Europe because of its unique aroma and beautiful flowers [4].

*Lonicerae Japonicae Flos* is widely planted in China, but its quality is influenced by many factors, such as the product area, planting and processing, and ecological system. Research showed that these herbs are different in qualities and morphological characteristics from different regions [5]. In TCM, geo-authentic herbs, which are planted in specific areas, are believed to present the highest quality among all samples from different regions, and they have been considered with appropriate and classic planting and processing; they have highly effective pharmaceutical use and contain the highest contents of active constituents [6]. Currently, with the standardization of TCM, the quality of Chinese herbs, including the planting and processing, contents of active constituents, and injurious ingredients, is becoming more and more important to control. Therefore, the geo-authentic herb is becoming the hot research point.

As for *Lonicerae Japonicae Flos*, it has been confirmed

that Henan and Shandong Provinces in China are geo-authentic product areas [7]. The research about geo-authentic *Lonicerae Japonicae* Flos is growing in recent years, but no systematic review exists. Thus, in this article, we searched the studies about geo-authentic *Lonicerae Japonicae* Flos to discuss the current situation and trend, to find out the difference between geo-authentic and non-authentic product, and to assess the quality of geo-authentic *Lonicerae Japonicae* Flos.

## Methods

### Inclusion/exclusion criteria

We planned to discuss the studies about geo-authentic *Lonicerae Japonicae* Flos. The studies should meet the inclusion criteria of geo-authentic *Lonicerae Japonicae* Flos (cultivated in Shandong or Henan Province). Additionally, reviews, news reports, or studies discussing other varieties, such as *Lonicera hypolauca* Miq, *Lonicera confusa* DC, *Lonicera dasystyla* Rehd, or the main study objects that do not focus on geo-authentic *Lonicerae Japonicae* Flos, were excluded.

### Search strategy

The following sources were up to November 2015. We searched four Chinese databases, including Chinese Biomedicine Literature Database (CBM), Chinese Journal Full-text Database, Chinese Scientific Journal Full-text Database, and Wanfang Database. The keywords were “*Jinyinhua*,” “*Shuanghua*,” “*Rendonghua*,” “*Erhua*,” “*Yinhua*,” or “*Rendong*.” Moreover, we refined the titles or abstracts of these studies with the word “*Daodi*” or “*Didao*.” We also searched the English databases, including PubMed, Cochrane Central Register of Controlled Trials, and EMBASE database. The main keywords were “*Lonicera japonica*,” “*Lonicerae Japonicae Flos*,” “*Jinyinhua*,” “*Shuanghua*,” “*Rendonghua*,” “*Erhua*,” “*Yinhua*,” or “*Rendong*.” We continued to refine these studies through the geo-authentic habitats. Each database was used independently. For example, we searched CBM using “*Jinyinhua*,” “*Shuanghua*,” “*Rendonghua*,” “*Erhua*,” “*Yinhua*,” or “*Rendong*” and “*Daodi*” or “*Didao*” in Title/Abstract/Keyword/Mesh. Finally, we obtained 75 articles from this database.

### Screening

Two reviewers assessed whether the studies should be accepted or excluded. Both reviewers independently assessed studies, and disagreement was resolved by discussion or through the third reviewer.

### Data extraction

We made a data extraction table based on the detailed situations of studies regarding geo-authentic *Lonicerae Japonicae* Flos. The table included the basic information of articles and the main information about geo-authentic *Lonicerae Japonicae* Flos, such as chemical fingerprint, component, discrimination, pharmacological effects, planting, and processing. We accomplished the data extraction table after screening these articles.

### Data analysis

We performed a descriptive analysis as it was not possible to undertake a meta-analysis due to the heterogeneity of these studies. We classified all these studies into different parts according to the main discussing point, and in each part, we clearly listed the main point.

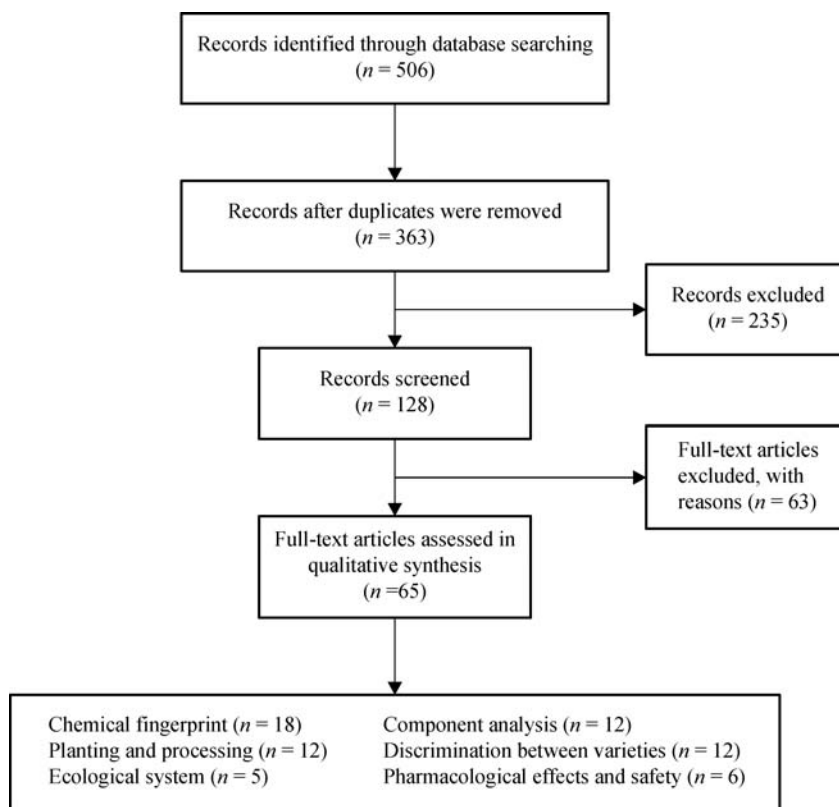
## Results

We initially searched 363 potentially relevant articles. A total of 235 articles were excluded based on the headings and abstracts. Of the 128 articles remained, 61 articles were excluded according to the inclusion and exclusion criteria. In this work, 67 articles were supposed to be reviewed; however, we could not access the full text of two articles. Hence, we analyzed 65 articles in our review. Data are shown in Fig. 1.

Only 1 article was published in English, whereas 64 articles were published in Chinese. All of these studies were classified into 6 parts, based on the main idea of articles, mainly discussing the following points: chemical fingerprint, component analysis, planting and processing, ecological system, pharmacological effects and safety, and discrimination between different varieties. We also analyzed the years that these studies were published. Only one study was published before 2000, and most of the studies regarding *Lonicerae Japonicae* Flos were published between 2001 to 2015. Data are presented in Table 1.

### Chemical fingerprint

From Table 1, we could see that there were 18 studies using chemical fingerprint to analyze the quality of *Lonicerae Japonicae* Flos. Among the 18 studies, HPLC was the most commonly used method, accounting for 88%. Many other methods were also used, such as gas chromatography, polyacrylamide gel electrophoresis, infrared spectrum, rapid resolution liquid chromatography. Most of these articles used these methods to analyze the content of main components, including chlorogenic acid and galuteolin;



**Fig. 1** Flow chart showing the number of studies included and excluded from the systematic review.

**Table 1** Classification of all studies

Classification	Before 2000	2001–2005	2006–2010	2010–2015	Total
Chemical fingerprint	0	4	5	9	18
Component analysis	0	7	2	3	12
Planting and processing	1	1	7	3	12
Discrimination between varieties	0	3	3	6	12
Ecological system	0	4	0	1	5
Pharmacological effects and safety	0	3	1	2	6
Total	1	22	18	24	65

these were also used to form the standard chemical fingerprint. The details are shown in Table 2.

### Component analysis

A total of 12 studies mainly discussed the component of geo-authentic *Lonicerae Japonicae* Flos. We put emphasis on the main component, chlorogenic acid, and galuteolin. Out of the 12 studies analyzed, 10 showed chlorogenic acid content, and only 2 of them showed galuteolin. Other

components, such as volatile oil, heavy metal, and total ash, were also accessed in some studies. The details are shown in Table 3.

### Planting and processing

Twelve studies discussed the planting and processing of geo-authentic *Lonicerae Japonicae* Flos. Two studies [37,38] investigated the germplasm resources from the main producing areas of *Lonicerae Japonicae* Flos in

**Table 2** Primary details of the studies mainly discussing chemical fingerprint

Study ID	Technology		The main components analysis		
	HPLC	Others	Chlorogenic acid	Galuteolin	Others
He [8]	Y	GC	Y		Volatile oil
Li a [9]	Y	PAGE, TLC, IR			
Zhao [10]		IR			
Sun [11]	Y	HNMR	Y		
Zhao [12]	Y		Y		Total ash, acid insoluble ash
Shi [13]	Y		Y	Y	Caffeic acid, rutin, quercetin
Liang [14]	Y				Volatile oil
Zhang a [15]	Y	PAGE, RAPD	Y	Y	Residual pesticide, heavy mental, total ash, acid insoluble ash
Xiang [16]	Y				
Li b [17]	Y	HS-GC-MS			Volatile oil
Li c [18]	Y		Y	Y	Chiratin, hyperin, heavy mental
Zhang b [19]	Y		Y	Y	Residual pesticide
Li d [20]	Y		Y	Y	
Kang [21]	Y	ISSR	Y	Y	Isochlorogenic acid
Li e [22]	Y		Y	Y	
Liu a [23]	Y				
Liu b [24]		RRLC			
Liu c [25]	Y	RRLC	Y		

Y indicates the study included in the current research on this point; HPLC, high-performance liquid chromatography; GC, gas chromatography; PAGE, polyacrylamide gel electrophoresis; TLC, thin-layer chromatography; IR, infrared spectrum; HNMR, nuclear magnetic resonance spectra; RAPD, random amplified polymorphic DNA; HS-GC-MS, headspace solid-gas chromatography-mass spectrometry; ISSR, inter-simple sequence repeat; RRLC, rapid resolution liquid chromatography.

**Table 3** Primary details of the studies mainly discussing component

Study ID	Chlorogenic acid	Galuteolin	Others
Xing a [26], Xing b [27], Gou [28]	Y		
Xing c [29]			Volatile oil
Zhang a [7], Zhang b [30]	Y		Flavonoids, saponins ivy, oleanolic acid, iridoid Glycoside, trace elements
Xiang [31]			Organochlorine insecticid, heavy mental, acid insoluble ash
Cui [32]	Y		Total ash
Liu [33]	Y		Isochlorogenic acid
Ye [34]	Y	Y	Endophytic fungi
Yan [35]	Y	Y	
Zhang c [36]			Mineral element

Y indicates the main focus of the study.

China. Through the investigation, they analyzed the existent problems about producing areas and germplasm resources, including aimless introduction of new strain, lack of strain selection technology, and unreasonable management. They also provided some suggestions and methods, such as setting standards, assessment, and screening of good strain.

Four studies [39–42] discussed the processing methods of geo-authentic *Lonicerae Japonicae* Flos. Wang *et al.*'s research [39] indicated that different plucking time and processing methods made a great effect on the quality of *Lonicerae Japonicae* Flos through measuring the content of chlorogenic acid. To make sure of the high effectiveness, the more appropriate time to pluck *Lonicerae Japonicae*

Flos was at the beginning of May when the flowers start to bloom and then dried in the sun or placed in a stove after drip washing.

Additionally, other research [43–46] suggested that the plucking time and processing methods, influenced by the natural and man-made factors, determined the quality and production of *Lonicerae Japonicae* Flos; they also discussed the standard operation procedure of planting, including the technical requirements for the production suitability, growth, field management, diseases, and pest control, picking and processing, packing and storing, transporting, and quality monitoring of *Lonicerae Japonicae* Flos.

Another two articles [47,48] reported the hybridization and induction of allotetraploid of *Lonicerae Japonicae* Flos and culturing *in vitro* to satisfy the need of modern market and make a foundation to generalize new varieties and rapidly propagate *in vitro* through biotechnology and industrial production.

### Discrimination between different varieties

#### *Morphological characteristic discrimination*

Five studies mainly discussed the morphological characteristics discrimination of geo-authentic *Lonicerae Japonicae* Flos. We could see from these studies that they observed the leaves and buds, such as exterior of petal and corolla, pollen grain seen under the microscope, the skin hair of buds, and the length or width or diameter or number of the leaves and buds. The details are shown in Table 4.

#### *Heredity discrimination*

Three studies discussed the heredity of *Lonicerae Japonicae* Flos using different methods. To study the formation of geohybridism of *Lonicerae Japonicae* Flos on the gene level, Li *et al.* [54] extracted genomic DNAs from different populations, amplified, and sequenced the 5S-rRNA gene spacer region. They found that the sequences were different between genuine and ungenue drugs and could be identified by sequencing. Sun *et al.* [55] and

Han *et al.* [56] used the intersimple sequence repeat (ISSR) to analyze genetic polymorphism of *Lonicerae Japonicae* Flos, providing evidence of molecular biology for the genetic resources, genetic relationship, and planting. The results showed that there were obvious genetic differences among regions and plant sources. In the research of Kang [21], except the HPLC fingerprint, he also discussed the genetic diversity using ISSR, revealing that geographical factors had a significant effect on the variety of *Lonicerae Japonicae* Flos.

#### *Others*

HPLC, PAGE, and RAPD were used to compare the content of main available components, isozyme, and gene sequence to offer scientific basis for the discrimination of different varieties of *Lonicerae Japonicae* Flos. The amino acid content and extracorporeal bacteriostatic effectiveness were also compared [57].

Li *et al.* [58] used electron probe method to analyze the element weight in the cell of two different species to identify the quality of *Lonicerae Japonicae* Flos and distinguish the geo-authentic and non-authentic species. The results showed that the method of electron probe was effective in appraising and distinguishing the quality of *Lonicerae Japonicae* Flos because it could be used to distinguish the content of elements in the cell of different *Lonicerae Japonicae* Flos, which was controlled by genetic factor.

Wang *et al.* [59] used restriction fragment length polymorphism analysis to confirm geographical authenticity. The results showed that the cleavage rate of PCR products by *Eco*N I correlated remarkably with the geographical origin of *Lonicerae Japonicae* Flos. Therefore, this method could also be used to classify geo-authentic *Lonicerae Japonicae* Flos.

Wang [60] sought for further research on Shandong provincial *Lonicerae Japonicae* Flos cultivars, and three cultivars, Jizhuahua, Maohua, and Sijihua, were studied on original, macroscopical, and microscopical identification, HPLC fingerprint atlas, and RAPD fingerprint atlas. The results showed that these methods could distinguish the characteristic identification of three cultivars.

**Table 4** Primary details of the studies mainly discussing morphological characteristic discrimination

Study ID	Exterior of petal and corolla	Pollen grain	Skin hair of bud	Branches and leaves	Buds
Pu [49]	Y	Y	Y		
Guo [50]			Y	Y	Y
Shao [51]				Y	Y
Li [52]				Y	
Zhang [53]			Y		

Y indicates the main focus of the study.

**Table 5** Primary details of the studies mainly discussing ecological system

Study ID	Geological background			
	Longitude, latitude, altitude	Geology, soil type	Vegetation regionalization	Climatic elements
Zhang a [61]	Y	Y	Y	Y
Zhang b [62]				
Zhang c [63]	Y	Y	Y	Y
Xing [64]	Y			Y
Fu [65]	Y	Y	Y	Y

Study ID	Soil characteristics					
	Soil texture	Trace element	pH	Organic material	N,P,K	Base saturation
Zhang a [61]	Y	Y	Y	Y	Y	Y
Zhang b [62]		Y				
Zhang c [63]	Y	Y	Y	Y	Y	
Xing [64]		Y		Y	Y	
Fu [65]	Y	Y	Y	Y	Y	Y

Study ID	Component				Economic benefits
	Cation exchange	Chlorogenic acid	Flavone	Measurement	
Zhang a [61]	Y				
Zhang b [62]					
Zhang c [63]					
Xing [64]		Y	Y	HPLC	
Fu [65]	Y	Y	Y	HPLC	Y

Y indicated the study included in the current research on this point; HPLC, high-performance liquid chromatography; N, P, K, meant nitrogen, phosphorus, and potassium; climatic elements, including annual average temperature, highest temperature, annual rainfall, humidity, annual illumination, wind speed, etc.; trace element, including sodium, calcium, strontium, potassium, magnesium, chromium, lead, etc.

## Ecological system

Five articles discussed the ecological system, including the geological background and soil characteristics. Detailed points, such as longitude, latitude, altitude, geology, soil type, vegetation regionalization, climatic elements (annual average temperature, rainfall, sunshine), soil texture, trace element, pH, organic material, and base saturation, were mentioned. Some studies analyzed the component and economic benefits of geo-authentic *Lonicerae Japonicae* Flos to investigate the effect of ecological system. The details are shown in Table 5.

## Pharmacological effects and safety

Two of these studies were randomized clinical trials [66,67], investigated the clinical effectiveness for gum inflammation and oral ulcer of honeysuckle from geo-authentic product area and Sichuan Province, and the results showed that the effects of authentic production were better than that from Sichuan Province in the treatment of mouth ulcers and gum inflammation. However, the problems were that these two studies did not clearly express the randomized and blinded methods, inclusive criteria, and efficacy assessment

standards. Thus, the qualities of these two studies were low.

Furthermore, Li *et al.* [68] found that the scavenging capacities on free radicals, O<sub>2</sub>, ·OH, and H<sub>2</sub>O<sub>2</sub> varied from locality and species and were highly relative to the contents of phenolic acids. As the same species, the scavenging capacities of the samples from Henan and Shandong Provinces were stronger than those from Jiangsu Province.

Lei [69] found that antibacterial effect of *Lonicerae Japonicae Flos* from Shandong Province (Ji) was lower than that from Henan Province (Mi). *Lonicerae Japonicae Flos* had certain antipyretic effect to fevered rat caused by fresh cerevisiae. On the other hand, he also discovered that *L. macranthides* Hand-Mazz's LD50 was higher than *Lonicerae Japonicae Flos*, which meant that *L. macranthides* Hand-Mazz's had less toxicity than *Lonicerae Japonicae Flos*. Results of the study could also be confirmed in other articles [70,71].

## Discussion

*Lonicerae Japonicae Flos* is widely used clinically, and the application of geo-authentic herbs has always been paid attention by clinical experts. Many experts focus on geo-authentic *Lonicerae Japonicae Flos* because of its higher quality and better clinical effect than non-authentic product. The Chinese herbs are used to prevent and treat diseases; thus, the quality of herbs directly influences the clinical effectiveness and even sometimes affects the patients' lives to some extent. It is an important factor to the inheritance and development of TCM. Thus, most of the studies on geo-authentic *Lonicerae Japonicae Flos* focus on its quality.

Among the articles we searched, 18 studies focused on the chemical fingerprint explored the methods to access the quality of geo-authentic *Lonicerae Japonicae Flos*. Additionally, combined with the time these studies published, it indicates that chemical fingerprint is becoming a hot topic in recent years. It will provide significant scientific basis for assessment and control of the quality of geo-authentic *Lonicerae Japonicae Flos* to make a standard chemical fingerprint. The chemical fingerprint of Chinese herbs is a method used in modern technology under given conditions to analyze the chemical and biological information and expressed in image mode. Chemical fingerprint not only emphasizes the uniqueness of certain herbs but also reflects the similarity of different varieties. It has great advantages with respect to monitoring of the quality of Chinese herbs, and some developed countries have regarded it as standard of quality control. At present, the commonly used methods are HPLC, IR, GC, RRLC, RAPD, and HNMR. Among

these methods, HPLC has the most advantages, such as high separation efficiency, high sensitivity, fast analysis speed, and load liquid velocity, which is the main method used in the component analysis and fingerprint creation of geo-authentic *Lonicerae Japonicae Flos*. These studies show that it is reasonable to distinguish geo-authentic and non-authentic *Lonicerae Japonicae Flos*. Analyzing all of these studies, the chemical fingerprint is the most often used method to qualitatively analyze the component content, focusing on the content of chlorogenic acid and galuteolin, which accords with the component analysis method in *Chinese Materia Medica Grand Dictionary* and quantitatively establish the standard chemical fingerprint.

One reason for the high quality of geo-authentic *Lonicerae Japonicae Flos* is that its active component is high and stable. The active component is also the basis of quality standard of Chinese herbs. *Chinese Materia Medica Grand Dictionary* explains the content of chlorogenic acid, galuteolin, and noxious substances. In the research that focuses mainly on the component analysis, they pointed at the content of chlorogenic acid, which was also the main analyzing component in chemical fingerprint, ecological system, and other research. Chlorogenic acid is the main active component that confirmed as an anti-inflammatory agent. Flavonoid compounds, including galuteolin, are antioxidants that can remove free radicals of ultra oxygen ions in the human body, increase immunity, and has anti-aging effect. In *Chinese Materia Medica Grand Dictionary*, it also refines the content of noxious substances, such as heavy metal and residual insecticides. The high content of these noxious substances is also an important reason limiting international popularization and application of Chinese herbs. However, few studies involved the assessment of these noxious substances. Thus, further studies should improve this aspect. The content of water, total ash, and volatile oil are also seldom involved, so the studies about geo-authentic *Lonicerae Japonicae Flos* should also stress this point.

The planting and processing of *Lonicerae Japonicae Flos* is also an important factor influencing its quality. The geo-authentic *Lonicerae Japonicae Flos* with appropriate planting and processing has higher quality, but the quality and yield is unstable. Therefore, the major task is to form the scientific management and normalized planting and processing to improve the yield and effectiveness and diminish drug toxicity. From the studies we have searched, we can see that many studies have begun to explore the standardization of planting and processing of geo-authentic *Lonicerae Japonicae Flos*. The research indicates that the best picking time is *sanqing*, *erbai*, and *dabai* stage, just before the beginning of summer. These herbs are directly dried in the sun or placed in a stove, which is a

better processing method compared with other methods. This method will increase the yield and the content of the active component.

Ecological system environment, such as geology, geomorphology, soil types, and climate factors, is another important factor that influences the herbal quality. In TCM, Henan and Shandong Provinces are recognized as the authentic product areas. Analysis of the ecological system environment of these two provinces showed that they both are located in the 34°–35°N, 113°–117°E; the altitude height is 100–800 m; the soil types and geology are similar; the climate factors, such as annual sunshine, annual rainfall, and climate type, are almost the same. The accumulation of active components is closely related with ecological conditions, and the content of geo-authentic *Lonicerae Japonicae* Flos is highly above non-authentic product. By comparing the geo-authentic and non-authentic *Lonicerae Japonicae* Flos, we found that it is sunshine rather than soil style that may be the critical factor that affects the active components.

The geo-authentic *Lonicerae Japonicae* Flos, through long-term natural and artificial selection, has made obvious variations and formed different varieties in authentic product areas. The different varieties show diversity in morphological characteristics and heredity. The most common varieties are *Damaohua*, *Xiaomaohua*, *Dajizhua*, and *Xiaojizhua*. First, the varieties of the geo-authentic *Lonicerae Japonicae* Flos should be discriminated. Different organs are differently influenced by the environment. The research shows that the color, morphology of buds and leaves, density, and length of non-glandular hair outside the buds are the discrimination point between different varieties. Second, different varieties have different heredity features, which can be discriminated through technologies. From the inclusive research, we can see that the ISSR is the most commonly used method recently. ISSR combines RAPD and SSR labeling technique and has advantages such as simple, rapid, and efficient operation, high genetic diversity, and good repeatability. ISSR can provide more genome DNA information and is often used in germplasm resource discrimination, evolutionary and genetic relationship analysis, and genetic diversity research. Other technologies, such as HPLC, electron probe, RAPD fingerprint, and restriction fragment length polymorphism analysis, are also used. The aim of the discrimination of morphological characteristics and heredity is to select the superior quality of geo-authentic *Lonicerae Japonicae* Flos; however, until now, no study reports the mode of selection for superior quality and the method to improve the quality. Thus, this point should be strengthened.

The clinical effectiveness of geo-authentic *Lonicerae Japonicae* Flos is superior than that of non-authentic in TCM theory. However, scientific data to support it are

lacking as we can see little evidence from the studies we searched. The qualities of these two clinical trials are too low, and the studies about its anti-inflammation and antipyretic pharmacologic action are still with animals rather than clinical application. Thus, we should make further investigation to explore the clinical effectiveness of geo-authentic *Lonicerae Japonicae* Flos. For example, high-quality clinical trials can be conducted to compare the clinical effectiveness between geo-authentic *Lonicerae Japonicae* Flos and non-authentic ones. Furthermore, geo-authentic herbs that target illness are also important to control quality or develop Chinese herb extracts.

## Conclusions

Briefly, research shows that geo-authentic *Lonicerae Japonicae* Flos is mainly characterized by chemical fingerprint, component analysis, planting and processing, discrimination between varieties, ecological system, pharmacological effects, and safety and focuses on the quality assessment technology. The factors involve yield and quality. The key point of geo-authentic *Lonicerae Japonicae* Flos research is the quality and application. However, we are facing many problems such as identifying noxious substances of *Lonicerae Japonicae* Flos, selecting the most superior of all varieties, and evaluating clinical effectiveness. Therefore, further studies should focus on resolving these problems and focus on the application and further development of geo-authentic *Lonicerae Japonicae* Flos.

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## Compliance with ethics guidelines

Xingyue Yang, Yali Liu, Aijuan Hou, Yang Yang, Xin Tian, and Liyun He declare that they have no conflict of interest. This manuscript is a systematic review article and does not involve a research protocol requiring approval by the relevant institutional review board or ethics committee.

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