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An ethnopharmacological investigation of medicinal *Salvia* plants (Lamiaceae) in China

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Abstract In China, over 40 species of the genus *Salvia* have been used as medicinal plants for various diseases, some for thousands of years. Recently, research has focused on the biological activities of *Salvia* medicinal plants used in traditional Chinese medicine (TCM). However, to date a scientific survey of the genus *Salvia* in China has not been carried out. In this paper, we report the results of 10 field surveys of *Salvia* medicinal plants collected in 17 provinces including detailed information on their local names, growing environment, distribution and therapeutic effects. We also summarize the results of research on the materia medica, phytochemistry and pharmacology of some of the important *Salvia* medicinal plants. Our study reveals that 35 *Salvia* plants have been used in TCM in different regions of China, including 20 species used as Danshen to treat heart diseases, and 15 species used to treat a range of other conditions including gynecological diseases, muscular or skeletal problems, hepatitis, urological diseases, and mouth and eye conditions. It is clear that some species of *Salvia* L. possess significant pharmacological activity in the context of ethnopharmacological knowledge, especially in the treatment of heart disease. Further studies of the phytochemistry and pharmacology of *Salvia* species will no doubt improve their medical utilization and contribute to the development of new natural drugs.

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1. Introduction

Salvia L. species constitute the largest genus in the family Lamiaceae with over 1000 species distributed mainly in Central and South America (500 spp.), Central Asia/Mediterranean (250 spp.) and Eastern Asia (100 spp.). Most species are perennial herbs but annuals, shrubs and a few trees and vines also exist¹. 84 *Salvia* species are native to China with their distribution located in South-West China, notably in the Hengduan Mountain region².

Salvia species have been used in herbal medicine for thousands of years. In fact, the name *Salvia* comes from the Latin word “*salvare*” meaning “to heal” and *S. officinalis* (Sage) has long been an important herb in Europe. *Salvia* species have been used in the treatment of more than sixty different ailments ranging from aches and pains to epilepsy although their main application has been in treating colds, bronchitis, tuberculosis, hemorrhage and menstrual disorders³. Until the discovery of antibiotics, Sage was a frequent ingredient of herbal teas recommended to patients with tuberculosis to prevent sudation. The leaves of Sage exhibit a range of biological activities based on their astringency and antibacterial, micostatic, virustatic and antihydrotic properties and are included in the British Herbal Pharmacopoeia (1983) for use as a gargle or mouthwash. Sage has also been included in combined herbal preparations for treating acute and chronic bronchitis⁴.

In China, over 40 species of *Salvia* have been used as medicinal plants for various diseases, some for thousands of years. One of the most well-known herbs is the roots of *S. miltiorrhiza* Bunge (Red Sage, called Danshen in Chinese) which is endemic to Eastern Asia, and is included as an official drug in the Chinese Pharmacopoeia (2010). Traditionally Danshen has been used to promote blood circulation, remove stagnation, tranquilize the mind, clear heat from the blood and resolve swelling⁵. In more recent times, the most important and frequent clinical use of Danshen has been in the treatment of coronary heart disease for the alleviation of angina pectoris, coronary artery spasm and myocardial infarction^{6,7}. Although there is increasing interest in the biological activity of *Salvia* species^{8,9}, to date a scientific survey of the genus *Salvia* in China has not been reported. Given that the indigenous uses of many *Salvia* medicinal plants remain undocumented, we undertook the survey to collect information relating to the resource and use of *Salvia* plants in Traditional Chinese Medicine (TCM) in order to provide baseline data for future pharmacological and phytochemical studies.

2. Materials and methods

During the period 2006–2011, we conducted 10 field surveys in 17 provinces and regions of China (Beijing, Hebei, Henan, Shandong, Anhui, Jiangsu, Zhejiang, Hubei, Hunan, Jiangxi, Fujian, Shanxi, Gansu, Chongqing, Sichuan, Guangxi and Yunnan provinces) based on analysis of ancient medicinal works and local knowledge of herbal medicines that include *Salvia* species. With the assistance of local herbalists, we collected plant samples and recorded detailed information on their local names, growing environment, distribution and therapeutic effects (Table 1). Voucher specimens of each plant species were identified by professional experts and their scientific names confirmed by consulting the *Flora of China*². The specimens were pressed and deposited at the Pharmaphylogeny Laboratory of the Institute of Medicinal Plant Development, Chinese academy of Medical Sciences, and the Molecular Pharmacognosy Laboratory of the Institute of Chinese Materia Medica, China Academy of Traditional Chinese Medicine.

3. Results and discussion

In the *Flora of China*, Chinese *Salvia* species are classified into four subgenera namely *Salvia*, *Sclarea*, *Jungia* and *Allagospadonopsis*¹⁰. Table 1 lists the species identified in this study arranged according to this classification system together with their local names, collection location, growing environment and therapeutic use.

3.1. Ethnopharmacological investigation

According to our field survey, 35 *Salvia* plants have been used as folk medicine in multiple therapeutic remedies in different regions of China. All four subgenera are represented with *Sclarea* (15) being the dominant subgenus, followed by *Salvia* (12), *Allagospadonopsis* (6) and *Jungia* (2).

Of the 35 *Salvia* species identified, 20 are used as Danshen to treat heart disease, 7 are used to treat respiratory diseases (cough, pneumonia and tracheitis), 8 for gynecological diseases (mastitis, dysmenorrheal and irregular menstruation), 2 for muscular or skeletal problems (muscular twitching pain and rheumatic arthritis), 3 for hepatitis, 2 for urological diseases (nephritis and urethritis), 2 for mouth and eye conditions (keratitis, faucitis and toothache), and 5 for other conditions (snakebite, sexual dysfunction, fever, hypertension and pyogenic infection of the skin) (Fig. 1A).

Parts of *Salvia* species used in the preparation of herbal remedies were the roots (20 species), herbs (14 species), leaves (2 species), flowers (2 species), seeds (1 species) and fruits (1 species) (Fig. 1B). It is well known that different parts of plants contain different concentrations of active constituents and different phytochemicals¹¹. For example, flavonoids, triterpenoids and monoterpenes are found in the aerial parts of *Salvia* plants particularly the flowers and leaves, whereas diterpenoids and phenolic acids are mainly found in the roots³. In our survey, it emerged that, generally, only one part of a medicinal plant is used in the preparation of a particular herbal remedy. For example, the herbs of *S. roborowskii* are used to treat hepatitis, while its flowers are employed to treat toothache. Sometimes *Salvia* plants have been used as the sole ingredient in a herbal medicine but often they are used in combination with more than one medicinal plant. For example, the leaves of *S. officinalis* are used in a tea to prevent and treat hypertension whereas the roots of *S. miltiorrhiza* and its related species are used in combination with other herbal medicines (Rhizoma ligustici wallichii, Radix astragalus, Radix notoginseng) for the management of heart disease.

Decoctions or infusions are most commonly used for oral administration and only one species, *S. cavaleriei*, has been prepared for external use involving topical application of its crushed leaves to the site of pyogenic infection.

3.2. Details of some widely used Chinese *Salvia* species

According to our field survey, ethnopharmacological knowledge of Chinese *Salvia* species is indicative of their pharmacological activity especially in the treatment of heart disease and cancer. Based on the limited research into their phytochemistry and pharmacology, only those *Salvia* species of significant medicinal value are described below.

3.2.1. *S. miltiorrhiza* and related species

S. miltiorrhiza is designated as the official source of Danshen in the Chinese Pharmacopoeia (2010). The earliest record of Danshen

Table 1 Names, distribution and therapeutic use of *Salvia* medicinal plants in China.

Original plant (voucher number)	Local name	Collecting location and time	Growing environment	Used part and therapeutic effects
Subg. <i>Salvia</i> Benth.				
Sect. <i>Eurysphace</i> Stib.				
<i>S. bulleyana</i> Diels HLQ-SBU-1101-1	Zi Danshen	Dali, Yunnan Aug 2011	Hillsides, valleys (Alt. 2500–3100 m)	The roots were used as Danshen.
<i>S. brachyloma</i> Stib HLQ-SBR-1001-8	Duan Guan Danshen	Muli, Sichuan Aug 2010	Hillsides, valleys (Alt. 3000–3300 m)	1. The roots were used as Danshen. 2. The flowers could be used to treat cough.
<i>S. campanulata</i> Wall. 2006070808	Huang Hua Danshen	Deqin, Yunnan Jul 2006	Forests, hillsides, grasslands (Alt. 2800–3500 m)	The roots were used as Danshen
<i>S. castanea</i> Diels 2006070803	Rong Mao Danshen	Muli, Sichuan Jul 2006	Forests, hillsides, grasslands (Alt. 2500–3200 m)	The roots were used as Danshen.
<i>S. digitaloides</i> Diels HLQ-SDI-1001-1	Yin Zi Danshen, Bai Yuan Shen	Lijiang, Yunnan Aug 2010	Dry shady pine forests, grassy hillsides, valleys (Alt. 2200–2800 m)	The roots were used as Danshen.
<i>S. evansiana</i> Hand.-Mazz. 2006090805	Danshen	Xianggelila, Yunnan Sep 2006	Alpine meadows, hillsides, forests (Alt. 3400–4150 m)	The roots were used as Danshen.
<i>S. flava</i> Forrest. HLQ-SFL-1001-8	Huang Hua Danshen	Lijiang, Yunnan Jul 2010	Forests, hillsides, grasslands (Alt. 2300–3500 m)	The roots were used as Danshen.
<i>S. kiametiensis</i> Lévl. HLQ-SQM-1001-7	Shan Bian, Danshen	Zhaotong, Yunnan Jul 2010	Hillsides (Alt. 2200–2800 m)	The roots were used as Danshen.
<i>S. przewalskii</i> Maxim. HLQ-SPZ-1101-8	Zi Danshen, Hong Qinjiao	Xianggelila, Yunnan Jul 2011	Forest margins, hillsides, banks of streams, thickets (Alt. 2000–3500 m)	1. The roots were used as Danshen. 2. The roots were used as Qinjiao which has the effects of expelling wind, dredging, removing the heat from the blood and relieving swelling.
<i>S. roborowskii</i> Maxim. HLQ-SRO-1001-5	Ye Zhi Ma	Kangding, Yunnan Jul 2010	Hillsides (Alt. 2600–3500 m)	1. The flowers could be used to treat toothache. 2. The herbs could be used to treat hepatitis. 3. The fruits could be used to treat keratitis.
<i>S. umbratica</i> Hance HLQ-SUM-1001-7	Shan Su Zi	Ningqiang, Shanxi Aug 2010	Hillsides, banks of streams, forests, valleys (Alt. 600–1500 m)	The herbs and seeds could be used to treat irregular menstruation.
Sect. <i>Eusphace</i> Benth.				
<i>S. officinalis</i> L. HLQ-SOF-1001-4	Sai Er Wei Ya	Beijing Aug 2010	Cultivated in gardens	The leaves could be used to treat faucitis and hypertension.
Subg. <i>Sclare</i> (Moench) Benth.				
Sect. <i>Drymosphace</i> Benth.				
<i>S. bowleyana</i> Dunn 2007081601	Danshen, Zi Gen	Jinhua, Zhejiang Aug 2007	Hillsides, banks of streams, valleys (Alt. 300–800 m)	The roots were used as Danshen.
<i>S. cavaleriei</i> Lévl HLQ-SCA-1001-2	Xue Pen Cao	Emeishan, Sichuan Jul 2011	Hillsides, banks of streams, forests, valleys (Alt. 300–1500 m)	1. The herbs were used to treat irregular menstruation. 2. The leaves could be used to treat pyogenic infection of the skin.
<i>S. dabieshanensis</i> J.Q.He 2007062004	Danshen, Hong Gen	Shucheng, Anhui Jun 2007	Hillsides, margins of thicket (Alt. 600–1000 m)	The roots were used as Danshen.
<i>S. honania</i> L.H.Bailey 2007061503	Danshen	Xinyang, Henan Jun 2007	Hillsides (Alt. 600–900 m)	The roots were used as Danshen.
<i>S. meiliensis</i> S.W.Su 2007062101	Hong Gen, Danshen	Liuan, Anhui Jun 2007	Hillsides, roadsides (Alt. 800–1100 m)	The roots were used as Danshen.

Table 1 (continued)

Original plant (voucher number)	Local name	Collecting location and time	Growing environment	Used part and therapeutic effects
<i>S. miltiorrhiza</i> Bunge HLQ-SMI-1101-05	Hong Gen, Danshen,	Jiangxian, Shanxi Jun 2011	Hillsides, banks of streams, plains, forests (Alt. 0–1100 m)	The roots were used as Danshen.
<i>S. paramiltiorrhiza</i> H.W. Li et X.L.Huang HLQ-SPA-1001-01	Danshen, Hong Gen	Qingtian, Anhui Jun 2010	Hillsides, banks of streams (Alt. 350–900 m)	The roots were used as Danshen.
<i>S. plectranthoides</i> Griff. HLQ-SPL-1001-07	Hongshen, Jin Zhi Danshen	Wudu, Gansu Jun 2010	Hillsides, banks of streams, valleys, sparse forests (Alt. 800–2200 m)	1. The roots were used as Danshen. 2. The roots were used for treatment of arthralgia due to dampness, muscular twitching pain and hemiplegia. 3. The roots were used to treat cough.
<i>S. prionitis</i> Hance HLQ-SPR-100001-07	Hong Gen Cao	Jinhua, Zhejiang Sept 2010	Hillsides, banks of streams (Alt. 150–800 m)	The herbs were used to treat cough, antiaditis tracheitis, diarrhea, hepatitis and cancer.
<i>S. sinica</i> Migo 2006070401	Danshen	Jinzhai, Anhui Jul 2006	Hillsides, banks of streams (Alt. 350–800 m)	The roots were used as Danshen.
<i>S. trijuga</i> Diels. HLQ-STR-1001-03	Xiao Hongshen, Zi Danshen	Lijiang, Yunnan Aug 2010	Foothills, riverbanks, banks of streams, grasslands (Alt. 2100–3500 m)	1. The roots were used as Danshen. 2. The roots could be used to treat deficiency in kidney and deficiency of yang.
<i>S. vasta</i> H.W. Li 2007062103	Danshen	Enshi, Hubei Jun 2007	Hillsides (Alt. 800–1000 m)	The roots were used as Danshen.
<i>S. yunnaensis</i> C.H.Wright. 2006092002	Dian Danshen, Yunnan Danshen	Kunming, Yunnan Sep 2006	Grassy hillsides, dry thin forests (Alt. 2000–3300 m)	1. The roots were used as Danshen. 2. The roots could treat mastitis.
Sect. Plethiosphace Benth. <i>S. deserta</i> Schang HLQ-SDE-1001-3	Xinjiang Shu Wei Cao	Buerjin, Xinjiang Aug 2010	Foothills, hillsides, grasslands (Alt. 300–1500 m)	The herbs were used to treat cough and urethritis.
Sect. Notiosphace Benth. <i>S. plebeia</i> R.Br. HLQ-SLZ-1001-1	Li Zhi Cao	Jinhua, Zhejiang Sep 2010	Foothills, hillsides, riverbanks, grasslands (Alt. 100–2500 m)	The herbs were used to treat faucitis, bronchitis, nephritis and urethritis.
Subg. Jungia (Moench) Briq. Sect. Calosphace Benth. <i>S. splendens</i> Ker-Gawl. 2006081702	Yi Chuan Hong	Beijing Aug 2006	Cultivated in gardens	The herbs were used to treat fever.
<i>S. coccinea</i> Linn HLQ-SZC-1001-2	Zhu Chun	Beijing; Aug 2011	Cultivated in gardens	The herbs were used to treat snakebite.
Subg. Allagospadonopsis Briq. <i>S. chinensis</i> Benth. HLQ-SXC-1002-10	Shi Jian Chuan	Chuzhou, Anhui Aug 2010	Foothills, hillsides, riverbanks, grasslands (Alt. 100–500 m)	The herbs were used to treat hepatitis, dysmenorrhea and acute mastitis.
<i>S. japonica</i> Thunb. 2007070802	Ba Wang Bian, Qiu Danshen	Badong, Hunan Aug 2007	Foothills, riverbanks, banks of streams, grasslands (Alt. 400–1000 m)	The herbs were used to clear heat from blood, treat hepatitis, dysmenorrhea, acute mastitis and irregular menstruation.
<i>S. kiangsiensis</i> C.Y.Wu HLQ-SKI-1001-08	Guan Gong Xu, Gen Xia Hong	Nanfeng, Jiangxi Aug 2011	Forests; (Alt. 600–800 m)	The herbs were used to clear heat from blood, treat acute mastitis and irregular menstruation.
<i>S. liguliloba</i> Sun HLQ-SSB-1001-03	Chang Ye, Danshen	LinAn, Zhejiang Aug 2010	Foothills, riverbanks, banks of streams, grasslands; (Alt. 600–800 m)	The herbs were used to clear heat from blood, treat rheumatoid arthritis and irregular menstruation.
<i>S. substolonifera</i> Stib. HLQ-SSU-1001-5	Fo Guang Cao	LinAn, Zhejiang Aug 2010	Foothills, banks of streams, grasslands; (Alt.300–800 m)	The herbs were used to clear heat from blood and treat cough and pneumonia.
<i>S. scapiformis</i> Hance HLQ-SDG-1001-8	Po Luo Zi, Bai Bu Yao	Leshan, Sichuan Aug 2010	Foothills, banks of streams, grasslands; (Alt. 900–1100 m)	The herbs were used to clear heat from blood, treat cough and pneumonia.

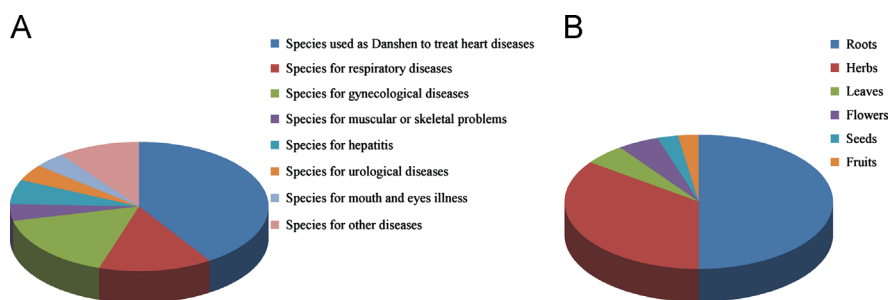


Figure 1 (A) The proportion of *Salvia* plants used to treat different diseases and (B) the proportion of the parts of *Salvia* plants used in their preparation.

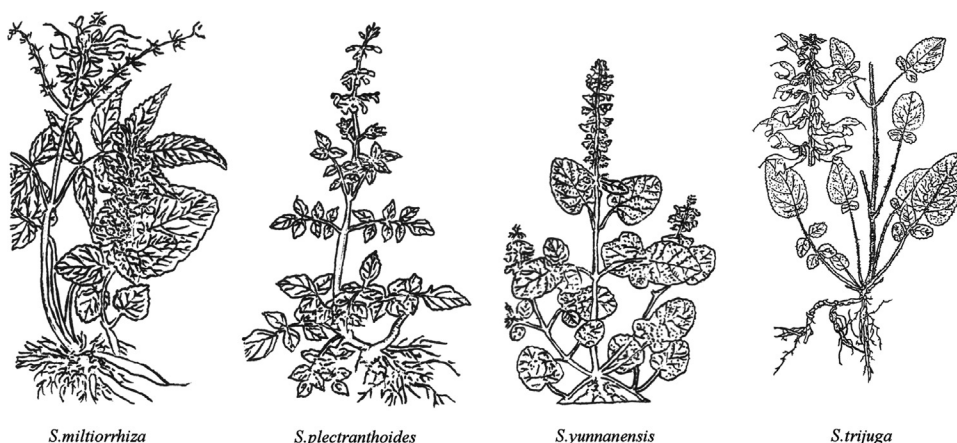


Figure 2 Images of some species of *Salvia* recorded in the *Yunnan Materia Medica*¹² and *An Illustrated Book of Plants*¹³.

appears to be from the Eastern Han Dynasty (*Shen Nong Materia Medica*, A.D. 102–200). Later, it was recorded in many other well-known medicinal texts, e.g., *Tang Materia Medica* (Tang Dynasty, A.D. 657–659), *Classic Classified Materia Medica for Emergencies* (Song Dynasty, A.D. 1082), *Compendium of Materia Medica* (Ming Dynasty, A.D. 1590) and *Illustrated Book of Plants* (Qing Dynasty, A.D. 1848), etc. In the ancient texts, the curative properties of Danshen were to promote blood circulation, remove stagnation, tranquilize the mind, clear heat from the blood and resolve swelling. In terms of morphology, the original species were described as roots red or purple and leaves comprising 5 or 7 leaflets opposited with the spica made up of purple flowers. In many ancient texts^{12,13}, the morphological characteristics were appropriate for many *Salvia* plant such as *S. plectranthoides*, *S. yunnanensis* and *S. trijuga* (Fig. 2).

According to the results of our ethnopharmacological investigation, about 20 species of *Salvia* L. have been used as Danshen for the treatment of coronary heart disease and stroke. Based on their morphological characteristics and geographical distribution, these Danshen related species are divided into 2 groups. Group 1 comprises 11 species *S. bulleyana*, *S. brachyloma*, *S. campanulata*, *S. castanea*, *S. digitaloides*, *S. evansiana*, *S. flava*, *S. kiaomiensis*, *S. przewalskii*, *S. trijuga* and *S. yunnanensis*; Group 2 comprises 9 species namely *S. bowleyana*, *S. dabieshanensis*, *S. honania*, *S. meiliensis*, *S. miltiorrhiza*, *S. paramiltiorrhiza*, *S. plectranthoides*, *S. sinica* and *S. vasta*.

Most Danshen related species (except *S. trijuga* and *S. yunnanensis*) in Group 1 come from sect. *Euryspace*, and are mainly distributed in the plateau area at 2500–4000 m above sea level in Sichuan and Yunnan provinces of South-West China.

S. przewalskii in this group has been widely used and is commercially available in the local herbal markets of Sichuan, Yunnan and Gansu provinces. The geographical distribution and resources of other Danshen related species in Group 1 are limited and their applications in folk medicine are restricted to remote mountain areas and minority regions of Sichuan and Yunnan provinces. In addition, some Danshen related species have been applied for other therapeutic effects in different regions. For example, the roots of *S. przewalskii* have been employed to treat rheumatism in the West of Sichuan province and the roots of *S. trijuga* have been used as a tonic in the West of Yunnan province.

All Danshen related species in Group 2 are from sect. *Drymophace*, and are distributed at low altitudes in plains and hills of North, East and Central China. *S. miltiorrhiza* is widely used in most regions of China, including some minority regions such as Inner Mongolia, and is cultivated on a large scale in Hebei, Henan, Shanxi, Shandong and Sichuan provinces. However, it is not easy to distinguish from some morphologically allied species. The farmers and villagers in rural communities generally seek to collect roots which have the red bark of *Salvia* species and use them as Danshen. As a result, in some herb markets, Danshen may come from the roots of species other than *S. miltiorrhiza*, especially in regions where several morphologically allied species are present. For example, the roots of *S. bowleyana*, known as Nandanshen, are available for purchase and use as Danshen in remote mountain areas of Zhejiang, Jiangxi and Fujian provinces and the roots of *S. dabieshanensis* and *S. paramiltiorrhiza* are used as Danshen in Dabie mountain areas of Anhui and Hubei provinces. In our previous studies, the amounts of salvianolic acid B or tanshinone IIA in some species of *Salvia* met the

requirements of the Chinese Pharmacopoeia¹⁴ but further pharmacological and phytochemical studies in relation to the application of these Danshen related species are needed.

To date, only a few Danshen related species such as *S. miltiorrhiza* have been studied extensively. Over 50 chemical constituents have been isolated and identified in *S. miltiorrhiza*, all of which can be classified as either hydrophilic phenolic acids such as salvianolic acid B and lithospermic acid or lipophilic tanshinones such as tanshinones I, IIA, and IIB and cryptotanshinone^{15–17}. Based on modern studies, the most important and frequent clinical application of the roots of *S. miltiorrhiza* has been in the treatment of heart conditions including angina pectoris, coronary artery spasm and myocardial infarction^{6,7,18}. However, they have also been used for treating neuroasthenic insomnia, hypertension dysmenorrhea, bone loss and chronic renal failure^{17,19–22}. Interestingly, the root of *S. miltiorrhiza* has been shown to reduce voluntary alcohol intake in selectively bred Sardinian alcohol-preferring rats, a finding that suggests it may have potential in treating alcoholism¹⁸. The aqueous extract has also been shown to inhibit HIV-1 integrase activity *in vitro* and viral replication *in vivo*. Since salvianolic acid B and lithospermic acid are the major biologically active constituents, the activity against HIV virus may indicate their potential as novel therapeutic drugs for AIDS²².

Another extensively studied *Salvia* species is *S. yunnanensis*. From which some 40 compounds have been isolated and identified. These include abietane diterpenes (yunnanin A, danshenol C), phenolic acids (yunnaneic acids E–H) and alkaloids (salviamines A–F)^{23–27}. Based on recent pharmacological studies, the roots of *S. yunnanensis* were shown to prevent scar-derived fibroblast formation²⁸ and the polyphenols and their derivatives to have potent anti-HIV activity^{29,30}. In addition, the roots of *S. yunnanensis* were reported to be useful in treating hepatocarcinogenesis³¹.

3.2.2. *S. plebeia*

S. plebeia (Lizhicao in Chinese) is another valuable medicinal plant widely distributed in Iran and throughout South East Asia as far as Eastern Australia. The earliest record of *S. plebeia* was in the *Compendium of Materia Medica* (Ming Dynasty, A.D. 1590) to treat snake bite and trauma. In the supplement to the later compendium (Qing Dynasty, A.D. 1765) the plant was said “to clear heat and toxic materials, and to remove heat from blood and diuresis”. Results of our ethnopharmacological studies indicate that *S. plebeia* has been used to treat bleeding, perineum edema resulting from hemorrhoids, swollen sore throat, bronchitis, hepatitis, cancer, nephritis and mastitis. In recent decades, about 40 chemical constituents have been isolated from this species including flavonoids, phenolic acids, diterpenes, triterpenes and others. Individual compounds in these classes include: Flavonoids nepitrin³², 2'-hydroxyl-5'-methoxybiochanin A³³, 5-hydroxy-4',7-dimethoxy-isoflavone³⁴, pectolinarigenin³⁵, luteolin-7-O- β -D-glucoside³⁶, 6-methoxynaringenin-7-O- β -D-glucoside³⁷ and luteolin³⁸; phenolic acids caffeic acid³², caffeic acid methyl ester³⁵, rosmarinic acid methyl ester³⁶ and 3,4-dihydroxybenzoic acid³⁹; diterpenes epoxysalviacocchin, salviacoccon⁴⁰, royleanonic acid⁴¹, carnosol and epirosmanol³⁵; triterpenes ursolic acid³⁵, 2 α ,3 β ,24-trihydroxy and 2 α ,3 β -dihydroxyolea-12-en-28-oic acid and oleanic acid³⁹; and other compounds conferyl aldehyde, β -sitosterol³³, scopoletin, salviaplebeiaside³⁵, β -daucosterol³⁹ and two lignin diesters^{42,43}.

Recent pharmacological studies of *S. plebeia* reveal it displays a variety of biological activities consistent with its extensive use in

TCM. First, the aqueous and ethanol extracts inhibit the growth of human gastric carcinoma cell lines, suggesting it acts as a potent immunomodulator⁴⁴. Second, the extract of *S. plebeia* possesses antiangiogenic, antinociceptive, antiinflammatory, antifungal and antioxidant activities^{33,45,46}. Third, the homoplantagin isolated from *S. plebeia* was reported to be protective against hepatocyte injury⁴⁷. Finally, in combination with other herbal ingredients [the seeds of *Plantago asiatica* L., the roots of *Serissa serissoides* (DC.) Druce and the herbs of *Viola philipica* Cav. Lcons et Descr.], this species has been used to treat urinary tract infections and exhibit significant diuretic, antitubercular, antipyretic, antiinflammatory and antidyous activities⁴⁸.

3.2.3. *S. prionitis*

Another *Salvia* species valued in folk medicine for its therapeutic activity is *S. prionitis* (Honggencao in Chinese), the aerial parts of which have been used to treat cold, cancer, pneumonia, hepatitis and diarrhea. Previous phytochemical investigations revealed the presence of more than 50 secondary metabolites among which abietane diterpenes are the overwhelming majority. These include tanshinone IIA, cryptotanshinone⁴⁹, salvilenone⁵⁰, 3-ketosapiraraquinone⁵¹, 4-hydroxysapiraraquinone^{52,53}, apiraraquinone⁵⁴, de-O-ethylsalvionitin⁵⁵, prioketolactone⁵⁶, 2-isopropyl-8-methyl-3,4-phenanthraquinone⁵⁷, hongenaotone⁵⁸, 3-keto-4-hydroxysapiraraquinone⁵⁹, danshenxinkun C⁶⁰, prionoid F⁶¹, bisprionerone C⁶² and dihydrotanshinone I⁶³. It was reported that some abietane diterpenes in this plant showed significant antitumor activity both *in vitro* and *in vivo*. For example, sapiraraquinone showed cytotoxicity against P-388 and L-1210 cultured cells and a therapeutic effect against various ascites tumors in mice^{49,64}; 3-keto-4-hydroxysapiraraquinone exhibited cytotoxic activities against HL-60 human leukemia cells and the SGC-7901 and MKN-28 stomach cancer cell lines with IC₅₀ values of 4.6, 0.2 and 0.3 μ M, respectively⁵⁹; prionoid D and E also showed significant cytotoxic activity against P-388 and A-549 cell lines with IC₅₀ values of 0.41 and 0.72 μ M, respectively⁶¹. In addition, some diterpenes from *S. prionitis* showed antimicrobial activities including 7,8-seco-para-ferruginone against Gram-positive *Staphylococcus aureus* and *Micrococcus luteus* (MIC values of 20.0 and 15.0 μ M)⁵⁹. However, a full understanding of the biological effects of this plant requires the bioactivities of individual compounds to be further evaluated.

3.2.4. *S. chinensis*

S. chinensis, known as Shijianchuan (Chinese Sage) in folk medicine, was first recorded in the *Compendium of Materia Medica* (Ming Dynasty, A.D. 1590). In this famous ancient text, *S. chinensis* was recorded as a treatment for ostealgia and swollen carbuncles. However, our ethnopharmacological investigation revealed that this herbal medicine has been employed to treat breast cancer, liver cancer, stomach cancer and hepatitis.

A phytochemical investigation of *S. chinensis* revealed over 50 chemical constituents in four classes of compounds: terpenoids (monoterpenoids, sesquiterpenes and triperpenoids), phenolic acids, flavonoids and others. Individual members of each class include: Terpenoids α -boswellic acid⁶⁵, blumenol A, clovane-2 β ,9 α -diol⁶⁶ and pinfaenoic acid⁶⁷; phenolic acids salvianolic acid D⁶⁸, salvianolic acid B⁶⁹, propanoic acid, 3-(3,4-dihydroxyphenyl)-2-hydroxybenzoic acid⁷⁰, 3,5-dimethoxy-4-hydroxybenzoic acid⁷¹, 5,7,4'-trihydroxydihydroflavonol⁷¹ and protocatechuic acid⁷²; flavonoids 3,5,7-trihydroxychromone and kaempferol⁶⁷; and other compounds β -sitosterol^{65,73}, 5-hydroxymethyl furaldehyde⁷³, syringaresinol⁷¹ and various aldehydes^{65,73}.

Modern pharmacological research has revealed that the aqueous extract of *S. chinensis* can significantly inhibit the proliferation of human nasopharynx cancer CNE cells and human gastric cancer MGC-803 cells⁷⁴. Polysaccharides isolated from *S. chinensis* exhibited strong antitumor activity^{75,76} and were also reported to stimulate B-lymphocytes and, at a concentration of 20 mg/L, protect PC-12 cells against H₂O₂-induced injury^{76–78}. In addition, *S. chinensis* was reported to protect against CCl₄-induced acute liver injury in mice probably due to the antioxidant activity of the phenolic acids present in this herbal medicine⁷⁹.

Again this species has not been studied extensively and little is known about the active substances responsible for its bioactivities, especially its anticancer activity.

3.2.5. Other species

Based on our investigations of folk medicines, six *Salvia* species (*S. japonica*, *S. kiangsiensis*, *S. liguliloba*, *S. substolonifera*, *S. scapiformis* and *S. coccinea*) have been mainly used to clear heat from the blood. The results indicate that *Salvia* plants may be a source of new drugs possessing antibacterial, antiviral and anti-tumor activities. The leaves of *S. officinalis* have been used in tea to prevent and treat hypertension but the bioactivities of its individual chemical constituents remain to be assessed.

4. Conclusions

Despite the recorded use of 35 *Salvia* plants in folk medicine, only a few species have been studied extensively and many questions remain in relation to their systematic classification, identification and resource utilization. Nevertheless, it is clear that some species of *Salvia* L. possess significant potential in the treatment of heart disease. The diterpenoids and the caffeic acid derivatives are the most characteristic compounds in the genus^{14,63}, most of which are associated with antioxidant, anticoagulant and cytoprotective activities. They also possess a wide variety of other activities including anti-ischemia-reperfusion injury, antihypertensive, antifibrotic, antiviral and antitumor activities^{22,32,80,81}. However, many species of *Salvia* remain to be explored in terms of their safety or toxicity and their phytochemical and pharmacological characteristics in order to improve their medical utilization and develop effective natural drugs.

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