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Schisandra *Schisandra chinensis*, *S. sphenanthera* Family: Schisandraceae

by Gayle Engels, Josef Brinckmann

HerbalGram. 2015; American Botanical Council

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INTRODUCTION

The plant genus *Schisandra* contains 19 species; of the 12 that are endemic in China,¹ there are two main species – *Schisandra chinensis* and *S. sphenanthera*. These are used interchangeably in traditional Chinese medicine (TCM) for the same indications at the same dosage.² Both are deciduous climbers with a medium rate of growth, with *S. chinensis* growing to about 29 feet (9 meters) and *S. sphenanthera* growing to 23 feet (7 meters).^{3,4} Both have clusters of small white flowers in April through May, followed by red berries. *S. sphenanthera* fruit ripens July through September, while *S. chinensis* fruit ripens a little later, August through October.^{3,4} Both species are exported and traded under the genus and standardized common name schisandra.⁵

The Chinese common name for schisandra is *wu wei zi*, which refers to the five flavors of the fruits – *wu* (五, “five”) *wei* (味, “flavor”) *zi* (子, “fruit and seed”).¹ Depending on the species, the common name *wu wei zi* is preceded by a qualifying prefix. For example, *S. chinensis*, or northern schisandra, is differentiated as *bei wu wei zi* (*bei* means northern), and *S. sphenanthera*, or southern schisandra, is differentiated as *nan wu wei zi* (*nan* means southern).¹

Southern schisandra is dioecious (individual flowers are either male or female, and only one sex is found on any given plant) and mainly grows in broad-leaved forests in temperate and subtropical regions of central and southern China at altitudes of 2300-6560 feet (700-2000 meters).¹ Northern schisandra is monoecious (both male and female flowers are borne on the same plant) and commonly occurs in deciduous and coniferous forests of northeastern China at altitudes of 3937-5577 feet (1200-1700 meters), as well as in parts of North Korea, far northern Japan, and the Russian Far East (RFE).¹

Most of the commercial supply of southern schisandra is wild-collected in the Chinese provinces of Sichuan, Shaanxi, and Gansu, while the supply of northern schisandra comes from both wild collection and wild-simulated cultivation mainly from the northeastern provinces of Liaoning, Jilin, and Heilongjiang. Schisandra marketed with a protected geographical indication (PGI) designation is generally perceived to be of the highest quality and fetches the highest prices. Some wild collection also occurs in parts of neighboring North Korea and Siberia, mainly for domestic consumption, although a small amount is exported to China.

HISTORY AND CULTURAL SIGNIFICANCE

Since the two species of *Schisandra* discussed in this article are used interchangeably in TCM, attributed uses apply to both species unless stated otherwise.

The first recorded use of schisandra is in the early Chinese herbal medicine text *Shen Nong Ben Cao Jing*, the *Divine Husbandman's Classic Materia Medica*.⁶ It was believed to be one of the superior medicines that would “prolong life without aging” and was said to increase energy, treat cough and fatigue, and serve as a male sexual tonic.

The dried fruit of schisandra is said to be completely balanced because it exhibits all five classically recognized flavors in Chinese herbalism, hence its Chinese name meaning five-flavored fruit.⁶ The skin and pulp are both sweet and sour; the seed is pungent and bitter; and the fruit overall is salty.⁷ It is used as a tonic and sedative, and for the treatment of anxiety, asthma and chronic cough, diarrhea, dream-disturbed sleep, frequent urination, insomnia, night sweats, and palpitations.⁸⁻¹¹ Conditions displaying the following symptoms are treated with schisandra: dry cough, dull complexion, fatigue, labored breathing or shortness of breath, and weakness.⁹ It is also used in combination with other herbs to inhibit sweating, relieve wasting and thirst, and to treat spermatorrhea (involuntary discharge of semen), nocturnal emissions, and urinary incontinence.⁹ In TCM, schisandra is said to have warm properties, to act on the heart, lung, and kidney channels, and to have the following actions: antibacterial, analgesic, antitussive and expectorant, cardiotoxic, central nervous system and uterine stimulant, bile secretion promotion, and gastric secretion inhibition.^{10,11}

Different qualities and values are assigned to schisandra fruits of different geographical origins. One of the more famous is “Fushun Liao Schisandra,” produced only in certain ecoregions of Liaoning province.¹² For schisandra to be labeled and marketed with a PGI designation, the berries must be produced in compliance with technical requirements and quality specifications established by China's General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ).¹³

This is one example of “geothermalism,” an important concept in TCM that correlates the use of “geo-authentic” (referred to as *daodi*) medicinal materials with the highest clinical efficacy.¹⁴ *Daodi* herbs account for the highest volume and economic value of botanicals used in TCM; of the 500 most commonly used Chinese medicinal plants, about 200 are classified as materials of *daodi* origin, which account for about 80% of total medicinal plant usage in terms of volume.¹⁵ In China, there is a relationship between the practice of geothermalism and intellectual property laws governing products of “geographical indication” (GI).¹⁶ As such, geothermalism can be protected as “traditional Chinese medical knowledge” under the GI regulatory framework.¹⁷

Furthermore, for use of schisandra fruit as an active ingredient in medicines, quality standards monographs for both species have been published in the *Hong Kong Chinese Materia Medica Standards*, Vol. 4 (HKCMMS, 2012)¹⁸ and in *The Pharmacopoeia of the People's Republic of China* (PPRC, 2010).² Additionally, for northern schisandra only, quality monographs are available in the current editions of the *European Pharmacopoeia* (Ph. Eur. 8.0),¹⁹ *Japanese Pharmacopoeia* (JP XVI),²⁰ *Korean Pharmacopoeia* (KP X),²¹ *United States Pharmacopoeia Herbal Medicines Compendium* (USP-HMC Version 1.0, 2015),²² and *WHO Monographs on Selected Medicinal Plants*, Vol. 3 (2007).²³ The unofficial American Herbal Pharmacopoeia also provides quality standards and analytical methods.⁶

CURRENT AUTHORIZED USES IN COSMETICS, FOODS, AND MEDICINES

In China and other Asian regions where TCM is recognized and practiced, as well as in some Western countries, both species are used as active substances indicated for treating conditions including chronic cough and dyspnea (shortness of breath), nocturnal emission and spermatorrhea, enuresis (urinary incontinence) and frequent urination, chronic diarrhea, spontaneous sweating and night sweating, thirst caused by fluid consumption and interior heat-wasting thirst,* palpitations, and insomnia.²

In the United States, schisandra is permitted as a component of dietary supplement products, requiring Food and Drug Administration (FDA) notification within 30 days of marketing (if a “structure-function” claim is made) and product manufacturing according to dietary supplement current Good Manufacturing Practices (cGMPs).²⁴ The USP has developed draft dietary supplement quality standards monographs for “Northern Schisandra Fruit” and “Northern Schisandra Fruit Powder,” which are scheduled to become official in the first supplement to the 38th revision of the USP in August 2015.²⁵ Certain licensed healthcare practitioners, such as licensed acupuncturists (LAc) and naturopathic doctors (ND), may also dispense schisandra-containing preparations to their patients.

In Canada, both species are classified as medicinal ingredients listed in Table 1 (General Medicinal Ingredients) of the Natural Health Product (NHP) Traditional Chinese Medicinal Ingredients monograph.²⁶ Schisandra is also listed in the draft Cognitive Function Products monograph as an adaptogenic active ingredient “to help increase energy and resistance to stress (e.g., in case of mental and physical fatigue related to stress).”²⁷ At the time of this writing, there were 622 licensed NHPs containing schisandra as a medicinal ingredient.²⁸

In the European Union (EU), although the use of schisandra berries as food or a food ingredient is established — due to evidence of significant human consumption prior to May 15, 1997²⁹ — when claim statements are made, schisandra is regulated as an active ingredient of herbal medicinal products that require pre-marketing authorization and product registration (EPCEU 2004).³⁰ There are no known schisandra mono-preparations with marketing authorization for sale in the EU, although there are some poly-preparations. For example, in 2013, Sweden’s Medical Products Agency granted Bringwell AB (Stockholm, Sweden) traditional herbal registrations for two schisandra-containing products manufactured by the Swedish Herbal Institute (Vallberga, Sweden) called “Chisandra” (coated tablets) and “Chisan” (an oral suspension). The liquid form contains, per mL, 10 mg northern schisandra fruit soft extract (2.0-5.0:1), 2.6 mg eleuthero (*Eleutherococcus senticosus*, Araliaceae) root soft extract (17-30:1), and 3 mg of rhodiola (*Rhodiola rosea*, Crassulaceae) root and rhizome soft extract (2.5-5.0:1). Both products are labeled with the same indication of “traditionally used as an adaptogen in case of reduced performance ability such as tiredness and fatigue.”^{31,32}

A few *S. chinensis* ingredients are also authorized for use in cosmetic products, including callus extracts (grown in culture), essential oil of the fruit, extracts of the fruit and of the seed (usually supercritical CO₂ soft extracts), fruit powder, and fruit water (aqueous solution of the steam distillates obtained from the fruit). Extracts of *S. sphenanthera* are also listed for functions including antioxidant, antiseborrhoeic (oil-production regulating), skin conditioning, and skin protecting.³³

MODERN RESEARCH

Pharmacological, animal, and clinical studies have shown schisandra to have adaptogenic, antioxidant, anti-inflammatory, anti-stress, astringent, cardiogenic, energy-enhancing, hepatoprotective, and immune-enhancing properties.³⁴

In the former Soviet Union, interest in schisandra was stimulated by the Nanai (Siberian) hunters who used the herb to improve stamina and night vision and to reduce hunger and thirst. Research conducted in the USSR between 1940 and 1960 supports many of the modern uses of schisandra, specifically for improved mental performance and increased work capacity.³⁴

Most of the modern clinical trials have used fixed combination products containing schisandra. Many of these studies were performed in China and, unfortunately, are of questionable design.

In a 2013 randomized, parallel, placebo-controlled study investigating the effect of a combination product containing schisandra and sesame (*Sesamum indicum*, Pedaliaceae) seed extracts on liver function, 40 patients with borderline liver dysfunction were randomly assigned to experimental or placebo groups (n=20 for each group).³⁵ The subjects were given 34.4 mg/kg per day of *S. chinensis* fruit extract with sesamin (BRAND’S® SCH; containing 0.06-0.12 mg schisandrin B plus 2.25-2.95 mg sesamin, extraction method not specified; Cerebos International Health Ltd., Taipei, Taiwan) or placebo for five months. Blood samples were taken and assayed at pre-intake and each month for six months post-intake. After five months of SCH administration, liver function and fatty liver were improved, antioxidant capacity was increased, and oxidative stress was greatly reduced. The authors recommended further study of SCH’s detailed mechanisms of action.

A number of clinical studies have been conducted using a Chinese prescription herbal drug called Wuzhi or Wu-Zhi (registration number in China: Z20025766) in combination with other drugs to test their efficacy in addressing liver function.³⁶ It is difficult to determine if all Wuzhi tablets are made by the same company because the information is not provided in study reports. However, it is probable that, since it is a prescription drug, all of the tablets are made to the same specifications (i.e., an ethanolic extract of *S. sphenanthera* containing 7.5 mg schisandrin A per tablet).

In a 2011 letter to the editor of the *European Journal of Clinical Pharmacology*, one researcher described a study in which 64 renal transplant patients were randomly assigned to receive either tacrolimus (Tac) and mycophenolic acid (immunosuppressive drugs used after organ transplant) plus the anti-inflammatory drug prednisone, or Wuzhi tablets in addition to Tac, mycophenolic acid, and prednisone (n=32 in each group).³⁷ The results indicated that the addition of *S. sphenanthera* extract in the form of Wuzhi tablets increased the bioavailability of Tac. In a 2010 study, researchers investigated the effects of co-administration of Wuzhi and Tac on liver transplant patients.³⁸ During the first phase, all 46 patients received the same dose of Tac. In the second phase, 21 patients (group A) received the same dose of Tac while 25 patients (group B) received a lower dose; both groups also received Wuzhi. Subsequently, all patients experienced increased Tac concentration in the blood (339% in group A and 262% in group B), improved liver function, and reduced incidence of Tac-associated side effects.

Several clinical trials have been conducted using a multi-herb combination formula called ADAPT-232® (containing 27.6% *R. rosea* root extracted with 70% ethanol, 51% *S. chinensis* berry extracted with 95% ethanol, and 24.4% *E. senticosus* root extracted with 70% ethanol; standardized to 0.32% rhodiolide, 0.5% rosavin, 0.05% tyrosol, 0.37% schisandrin, 0.24% schisandrin B, and 0.15% eleutherosides B and E; Swedish Herbal Institute), but the results cannot be attributed solely to the presence of schisandra.

In 2010, a randomized, double-blind, placebo-controlled study investigated the effects of a single dose of this fixed combination product on cognition.³⁹ Forty healthy females who claimed to have felt stressed over a long period of time were randomly assigned to receive a single tablet of ADAPT-232 or placebo. The ADAPT-232 group experienced significantly improved scores with regard to ability to focus, processing speed, and accuracy of task performance. A 2005 randomized, double-blind, placebo-controlled, pilot (phase III) study investigated the efficacy of ADAPT-232 in treating acute non-specific pneumonia.⁴⁰ Two parallel groups of patients (n=60) received bromhexine (an expectorant), cephalosporin (an antibiotic), and theophylline (a bronchodilator), in addition to either 20 mL ADAPT-232 or placebo, twice daily for 10-15 days as required. The group receiving ADAPT-232 in addition to the standard treatment required a shorter duration of therapy than those receiving placebo with standard treatment (5.67 days vs. 7.53 days, respectively). In a quality-of-life test, patients who received ADAPT-232 scored significantly higher than the placebo group.

A 2003 randomized, placebo-controlled, pilot study assessed the usefulness of treating Familial Mediterranean Fever (FMF) with ImmunoGuard® (a 370 mg fixed combination product containing 50 mg *Andrographis paniculata* [Acanthaceae] extract standardized to 4 mg andrographolide, 10 mg *E. senticosus* extract standardized to > 0.8 mg eleutheroside E, 100 mg *S. chinensis* extract standardized to > 0.8 mg schisandrins, and 10 mg *Glycyrrhiza glabra* [Fabaceae] extract standardized to > 0.6 mg glycyrrhizin; Swedish Herbal Institute).⁴¹ Patients with FMF (n=24) were randomly assigned into two groups; 14 were treated with ImmunoGuard three times over the course of one month with four tablets per day, and the other 10 patients with placebo at the same rate. After one month, the ImmunoGuard group experienced significantly fewer and less-severe FMF attacks.

FUTURE OUTLOOK

The current (April 2015) average market price for dried northern schisandra berries of Liaoning origin (autumn 2014 harvest) is 45.00 Chinese yuan (CNY)/kg (approximately \$7.34/kg) at both the Chengdu TCM Market (Sichuan province) and Anguo TCM Market (Hebei province).⁴² Southern schisandra berries are trading at 25.00 CNY/kg (\$4.08/kg) at the Chengdu TCM Market.⁴³

A January 2015 market research report involved a survey of 41 Chinese businesses trading in schisandra fruit at the Chengdu TCM Market, of which 35 questionnaires were evaluated (six were invalidated).⁴⁴ Of the 35 respondents, 3% believed that the current market for schisandra was better than had been expected, 37% rated the current market as worse than expected, and 60% thought it was just as expected. Regarding market outlook, 23% of the traders expected upward price movement, 3% expected downward price movement, and 74% of the surveyed companies expected no change.

Since the mid-2000s, the sustainable wild collection of schisandra berries has become an issue within broader natural resource management projects and priorities of conservation-focused non-governmental organizations (NGOs) such as the Wildlife Conservation Society (WCS), World Wide Fund for Nature (WWF), and TRAFFIC, often in collaboration with governmental and inter-governmental agencies charged with biodiversity conservation responsibilities. This has been the case particularly in ecoregions with special conservation status where schisandra berries are harvested for commercial trade by local, rural, and indigenous communities. Examples of such protected regions include the “Ussurisky taiga” and forests of the RFE, which provide habitats for the 400-500 remaining Amur (Siberian) tigers (*Panthera tigris* ssp. *altaica*, Felidae), and the Upper Yangtze ecoregion of Sichuan, Gansu, and Shaanxi provinces that is home to an estimated 1,864 giant pandas (*Ailuropoda melanoleuca*, Ursidae). In such cases, standards have been developed and tests have been implemented for sustainable resource management of the entire ecoregion in consideration of the people, plants, and animals.

In 2004, WCS Russia began working with traditional hunting associations throughout Primorskiy and southern Khabarovskiy Krai in the RFE to develop resource management tools, including a “Tiger Friendly Standard” for the certification of non-timber forest products (NTFPs) such as northern schisandra berries.⁴⁵ The following year, WCS, in partnership with the Far Eastern Association of Non-Timber Forest Producers (FEANTFP), implemented a project “Linking

Economic Development and Biodiversity Conservation in the Russian Far East through Tiger Friendly Certification.” The objective of the project was to provide economic incentives for local communities to conserve tigers and their habitats by recognizing sustainably harvested products, including schisandra, marketed with Tiger Friendly Certification.⁴⁶

Starting in 2008, WWF began a three-year project in the Amur tiger habitat. The project — which aimed to “Mitigate Impacts of Climate Change through the Protection of Large Scale Virgin Forests in the Bikin River Valley” — was financed by the German Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMU) and Development Bank of Germany (KfW Entwicklungsbank).⁴⁷ It enabled WWF and its local partners to lease the largest remaining massifs of Korean pine-broadleaf-coniferous forests and collaborate with the indigenous Udege and Nanai communities for sustainable wild collection of prioritized NTFPs, including northern schisandra berries, eleuthero root, Chaga mushrooms (*Inonotus obliquus*, Hymenochaetaceae), and Korean pine (*Pinus koraiensis*, Pinaceae) nuts, among others.

Concerning southern schisandra, the EU-China Biodiversity Programme established a five-year (2007-2011) project for the “Sustainable Management of Traditional Medicinal Plants in the High-Biodiversity Landscapes of Upper Yangtze Eco-region.” The project was funded by the EU and implemented by the United Nations Development Programme in cooperation with China’s Ministry of Environmental Protection.⁴⁸ As a result of the project, a 22-village cooperative was established to sell certified organic wild schisandra berries, and, in 2009, the Chengdu University of TCM, TRAFFIC, and WWF China collaborated to produce a Chinese-language book on sustainable wild-harvesting practices for southern schisandra berries. The collaboration also resulted in draft “Standards for Giant Panda Friendly Products,” which specifically apply to the management of three products — honey, southern schisandra berries, and bamboo (including leaves and shoots) — in the giant panda distribution areas of the Sichuan province.⁴⁹

In 2013, government officials in Jilin province estimated the annual market demand for schisandra fruit to be approximately 3-3.5 million kg (dry weight) and increasing.⁵⁰ Their report also stated that the reserve of wild schisandra was steadily declining due to habitat destruction (development) and non-sustainable harvesting practices. The annual yield of wild-harvested schisandra is beginning to fall significantly below annual market demand. Based on these data, large schisandra cultivation projects have been in the works with provincial and national governmental support. One such project is ongoing in the Yanbian Korean Autonomous Prefecture area of eastern Jilin province, adjacent to North Korea and the RFE.

Schisandra vines tend to climb trees in biodiverse forests of eastern Asia that are also inhabited by threatened and endangered large mammals. This has led to innovative approaches in nature conservation that aim to incentivize and empower local, rural, or indigenous communities, who earn some or all of their household income from wild collection of NTFPs, to become stewards of the ecosystems that they themselves are a part of — and benefit economically by offering sustainably harvested schisandra (and other forest products) at a premium price while helping to ensure the long-term survival of endangered animal and plant species. Schisandra has become a beneficiary of the considerable support from national and international governmental agencies and NGOs to effectively protect certain sensitive ecoregions. One of the authors of this article (JB) has been involved with sustainable schisandra projects in both China and the RFE, and has observed sustainable wild-collection operations in several provinces as well as wild-simulated cultivation of both northern and southern schisandra.

With these projects in place, even with the increasing global demand for schisandra, a sustainable supply should be possible in view of the new plantation projects for northern schisandra starting up within the species’ geographical origin. The future market will offer choices of wild-collected, geo-authentic berries and increasingly wild-simulated cultivated berries, which can also, in principle, be produced according to the requirements for PGI products.

—Gayle Engels and Josef Brinckmann

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