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Table: 1, Figs :

An overview of Processing methods and applied aspects of Sanchi (Notoginseng Radix et Rhizoma) in human health

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CONTENTS

ABSTRACT

The *Panax notoginseng* (Burk.) F.H. Chen is mainly grown in China, and Notoginseng Radix et Rhizoma is widely used in Traditional Chinese Medicine (TCM). Ancient Chinese medical books recorded that Sanchi processed products were used to treat various diseases. However, its extracts were used for clinical applications. Currently, more attentions are paid to using the Sanchi for dietetic and health-care, hence, many products of *Panax notoginseng* are available for medicine and food. This review summarizes the present uses of Notoginseng Radix et Rhizoma products worldwide.

Key words: Clinical applications, current status of use, medicinal and edible, Notoginseng Radix et Rhizoma, *Panax notoginseng*, processed drugs, Sanchi.

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1. INTRODUCTION

Sanchi is the dried roots of *Panax notoginseng* (Burk) F.H. Chen (family Araliaceae) is a ginseng specie (1). It is called Tianqi, Tiansanqi, Kaihua Sanqi, Shanqi, Jinbuhuan, Sanqirenshen, and Renshen Sanqi, etc. in China (8,50). Presently wild *Panax notoginseng* is rare in China. According to the historical documents ["*Guangxi Tongzhi* (*General Records of Guangxi*) (1733)", the "*Shiyao Bianwei* (*Chinese medicine herbs identification*)" and the "*Bencao Gangmu Shiyi* (*Supplement to the Grand Compendium of Materia Medica*)"], the original producing area of Sanchi were in south-central, southeastern, northeastern Yunnan Province and in southwestern Guangxi Province, China (50,57). Present production areas of *Panax notoginseng* are in Wenshan and several regions in Yunnan Province (9). According to "*The Chinese Pharmacopoeia* (2020 edition)", the main effective components of Notoginseng Radix et Rhizoma are : (i). Ginsenoside Rg1, (ii). Ginsenoside Rb1 and (iii). Panax notoginosides R1, etc. (31). Notoginseng Radix et Rhizoma has several medicinal applications viz., stops wound bleeding, promotes blood circulation, relieves pain, prevents hemoptysis, hematemesis, traumatic hemorrhage and swelling (31,48).

In ancient China, Sanchi was mostly used in medicine as the processed products. Currently, the active ingredients in Notoginseng Radix et Rhizoma are used in the clinic (17,37,56,64). This paper reviews the development of the applied aspects of Sanchi from the Yuan Dynasty to modern times in China and overseas.

2. SANCHI APPLICATIONS IN TCM

The historical records showed that Sanchi has existed on earth for > 25 million years, and the Chinese have used it for > 3,000 years (11,20). In China, the Sanchi-related products are unprocessed, hence, their effects are variable (23). The name 'Shensanqi' appeared first in the Ming dynasty, [the earliest record of Sanchi as a medicinal material (14)]. Later, the processing methods of Sanchi were developed, which increased its traditional uses.

2.1 Sanchi's processing methods

The Mo (made flour) method was first recorded in the "*Wanshi Nvke* (*The Wan's Treatment of Gynecological Diseases*)" in the Ming Dynasty (1368-1644). For Sanchi

Table 1. Historical evolution of processed Sanchi (20)

Processing Method	Description	Period
Qie (Cut)	Mo (Made flour)	Ming Dynasty (1368-1644)
	Xi Mo (Ground into a very fine powder)	Qing Dynasty (1636-1912)
	Dao (Mashed)	
	Jue (Chewed)	
	Yan (Ground)	
Zheng	Steamed	
Zhi	Frying with liquid auxiliary ingredients	
Qingchao	Stir-fried without auxiliary ingredients	
Bei	Baked over a slow fire	Modern (1949-today)

Reference: 20

processing, the methods used were : (i). Qie (Cutting), (ii). Zheng (Steaming), (iii). Zhi (Frying with liquid auxiliary ingredients, like honey, lard, etc.) and (iv). Qingchao (Stir-fried without auxiliary ingredients) and (v). Bei (Baked over a slow fire) (Table 1) (20).

(i). Qie method (Cutting). In Qie method (58) Notoginseng Radix et Rhizoma is cleaned and cut into thin slices. In Mo method (25) Sanchi is ground with wine or vinegar, which is similar to Qie method. Wine or vinegar are added, so that the heat generated by friction in grinding does not destroy the effective components. Besides, the wine promotes blood circulation to remove the meridian problem. While, vinegar removes the blood clots to relieve pain (7).

(ii). Zheng method (Steaming). The time and temperature of Zheng method (58) affects the quality of traditional Chinese medicine (TCM). Ma *et al*. (24) stated that steaming of Notoginseng Radix et Rhizoma should be done at 95 °C to 105 °C for 1.0 h, till Sanchi becomes red, translucent and well-cooked (64). Xiao (46) and Sun *et al*. (38,39) compared the saponin contents of steamed powder of Notoginseng Radix et Rhizoma with raw material and found that although the saponins contents were decreased, but the ratio between different saponins increased (11,12,63). Therefore, steamed Notoginseng Radix et Rhizoma improves the blood (65).

(iii). Zhi method (Frying with liquid auxiliary ingredients). The Zhi method (25,27) refers to frying. The Book "*Waike Dacheng* (*Compendium of Surgery*)" in the Qing dynasty (1636-1912) reported a method to process the lard-fried Sanchi. Xiao (46) pharmacological research results showed that the contents of ginsenoside Rb1/ notoginsenoside R1, and ginsenoside Rg1/notoginsenoside R1 were increased after Zhi method processing, which improves the invigoration effects of Notoginseng Radix et Rhizoma.

(iv). Qingchao method (Stir-fried without auxiliary ingredients). In Chao method (33) Sanchi is stir-fried without other ingredients, which is the traditional method of processing. The book "*Yaolong Xiaopin* (*Doctor's Dialogues in Youyuzhai*)" described that the "stir-fried Sanchi is more suitable for healthy tonic prescriptions" as it increases the Qi to nourish body fluids (33).

(v). Bei method (Baked over slow fire). The Bei method (35) was first recorded in the book "*Waike Dacheng*", it was believed that the Sanchi processed by Bei method could remove putridity, engender flesh, and also used to treat wounds from beaten by sticks (45).

2.2 Applied aspects of Sanchi

(i). Stops bleeding. When Notoginseng Radix et Rhizoma is used for treating traumatic injuries and pain with congestion, it can be considered as a single-ingredient prescription. The patient can decoct it with water for 3~9 g of herb or swallow for 1~3 g of powder to recover from traumatic injuries (34). According to the ancient books, Sanchi and its processed products were mainly used to treat hematemesis, hemoptysis, hematochezia, stab wounds, gynecology hemorrhage and insect bites. Sanchi can treat

hematemesis or hemoptysis by taking 3-Qian (unit of weight, equals to 5 g) of Huaruishi (Ophicalcitum), 2-Qian of Sanchi and 1-Qian of Xueyu (Charred Human Hair) as prescription could treat hematemesis or hemoptysis (30). Mix three Qian of Sanchi powder with rice soup and then drink it, or take chewed Sanchi herb and apply it to the injury can treat insect stings (30). In addition, powder of *Notoginseng Radix et Rhizoma* is commonly used to stop wound bleeding, which is related to the presence of special amino acid, dencichine and can promote the production of thrombin and then effectively shortens the bleeding time and accelerates clotting time (45).

(ii). Invigorates blood. Sanchi has the nature of "Shengxiao Shubu (unprocessed Sanchi for stop bleeding and processed Sanchi for blood-enriching)" (15). In modern society, the main application of Notoginseng Radix et Rhizoma is to "activate blood" and "stop bleeding". For example, patients who suffered from acute necrotizing segmental enteritis can be treated with *Notoginseng Radix et Rhizoma* powders mixed with boiled water with three times a day (30).

In summary, the extant processing methods are Mo, chewed, grinding with wine or vinegar, Bei, Chao, steamed and juiced (47). Among them, Mo, chewed, grinding with wine or vinegar and juiced methods all use unprocessed Notoginseng Radix et Rhizoma, while Bei, Chao and steamed methods all use processed Notoginseng Radix et Rhizoma. The modern processing methods are also inherited from ancient times.

3. MODERN CLINICAL APPLICATIONS

The traditional clinical application of Sanchi used the unprocessed or processed products to cut into slices, fragments or grind into powder (2,45). Nowadays, the modern clinical application of Notoginseng Radix et Rhizoma has become more precise (19,29). The most widely used components are saponins, while the application aspects of polysaccharides and dencichine are being explored. Tu (24,60,64) found that the extraction of ginsenoside Re from the powder of Notoginseng Radix et Rhizoma by ether defatting-methanol ultrasonic extraction method is the best among the 5-methods viz., (i). Aqueous ultrasonic extraction-macroporous resin column separation and purification method, (ii). Ether degreasing-soxhlet extraction method, (iii). Methanol soxhlet extraction method, (iv). Ether degreasing-methanol ultrasonic extraction method and (v). Water extraction method. Cai *et al*. (1), reported that to determine the polysaccharides' contents the anthrone-sulfuric acid method was better.

3.1. Cardiovascular diseases

Recently, the prevalence of cardiovascular disease (CVD) has become a serious threat to humans as a common disease (6). *Panax notoginseng* saponins (PNS) are as the main effective components to treat the CVD (10,32). It is known that PNS improves the blood lipid concentration, vasorelaxation, lower blood pressure, anti-platelet agglutination and anti-thrombosis by inhibiting the inflammatory response for the treatment of CAD by inhibiting the cardiomyocyte apoptosis and other mechanisms (10,22). PNS is useful in the treatment of coronary heart disease, hypertension, heart failure and coronary microvascular

disease (CMVD). In addition, Luo (21), Wang (43) and Li *et al* (13) found that the Xueshuantong injection significantly improved the angina pectoris and electrocardiogram.

3.2. Immune System Diseases

Notoginseng Radix et Rhizoma can be used as an immunomodulator. The total PNS can regulate the too low or too high immune functions to the normal level (29). PNS increases the activity of C3b receptors on the red blood cell membrane, thereby improving the combination of red blood cells and immune complexes to maintain the immune stability of the body (53). The clinical trials have confirmed that ginsenoside Rg1 can increase the proliferation ability of lymphocytes and promotes the expression of interleukin-2 (IL-2) gene (29,44).

3.3. Tumor and cancer

Tumors generally occur due to human immunosuppression or dysimmunity. With the development of medical treatment, researchers have developed the therapeutic drugs. According to the analysis of the anti-cancer effect of Notoginseng Radix et Rhizoma extracts *in vitro* by Yang *et al* (51), the PNS inhibits the proliferation of human gastric cancer cell line MKN-28. However, their inhibitory effects on the proliferation of human laryngeal carcinoma cell line Hep2, skin T-cell lymphoma Hut-97 and leukemia cell line K562 were not seen (51).

Multi-Drug Resistance (MDR) is a current problem. Tumor cells can develop resistance in short period even though antitumor drugs effects different targets and mechanisms, thus making difficult to investigate antitumor (25,29). However, *P. notoginseng* polysaccharide has the characteristics of multi-target anti-tumor. In addition, it does not produce drug toxicity in normal cells and plays an important role in killing tumor cells and inhibiting their growth or metastasis with ideal anti-tumor effects (25).

4. CURRENT STATUS OF SANCHI USES WORLDWIDE

Sanchi has been used in traditional Chinese medicine since ancient times but was not known internationally. Recently, China has vigorously promoted the Chinese medicinal materials abroad, this increased the Notoginseng Radix et Rhizoma's popularity internationally (38). In 2017, the International Organization for Standardization (ISO) approved the international standard for *P. notoginseng* (ISO 20408), which stipulated the provenances, scopes, definitions, technical requirements, grading standards and inspection rules. To internationally promote the Sanchi, the "II Wenshan-Sanchi International Summit (2018)" was successfully held in Wenshan, Yunnan Province. These actions have greatly promoted the use of Sanchi worldwide (3,58).

4.1 International status

With the adoption of International standards for production of Notoginseng Radix et Rhizoma, more and more countries are recognizing and using Notoginseng Radix et Rhizoma products from Chinese market (4). *P. notoginseng* extract "*P. notoginseng* Triol Saponins" which was discovered in China was included in "*German Pharmacopoeia* (2018

edition)". In 2019, the American Botanical Council unanimously included the *P. notoginseng* in US Botanical Catalogue for research and development of botanicals (13). Besides, the research on the allelopathy of *P. notoginseng* has also increased, for example, the changes of root soil microorganisms and the exploration of planting patterns etc. This showed that Notoginseng Radix et Rhizoma had been recognized by various countries as TCM medicinal material and paved the way for its industries to enter the international markets.

The application areas of Notoginseng Radix et Rhizoma in the international arena are the same as those in China, where PNS are most widely used, with effectiveness in anti-blood cell condensation, slowing down of stomach diseases and anti-aging, etc. (49). Although Notoginseng Radix et Rhizoma is currently used to a limited extent in other countries, we believed that with the joint efforts of many scholars, more people will study, develop and manufacture of new drugs related to Notoginseng Radix et Rhizoma, so that its beneficial uses to health became widely known.

4.2 Problems

P. notoginseng is grown in Guangxi, Yunnan, Guangdong, Sichuan, Hunan, Guizhou and Fujian Province in China and the best quality is found in Wenshan, Yunnan Province. It is currently rarely cultivated outside China. Therefore, Yunnan is the main producing area of *P. notoginseng* in China and even in the world, with exports of Notoginseng Radix et Rhizoma related products > 2,000 tonnes (3).

The cultural differences between the countries are the main reasons for the hindrances in Sanchi promotion internationally. For example, some western countries import and export drug composition standard requirements are different than China. It is a major factor that cannot be ignored. Besides, the differences between Chinese and Western perceptions of medicinal herbs, the Notoginseng Radix et Rhizoma classification and formulation are not standardized (45). There is no clear and comprehensive regulation on the content of chemical components (18).

5. MEDICINAL AND FOOD USES

'Yaoshitongyuan' refers to Sanchi uses as medicine and food. In addition to medication, health care through food-adjuvant therapy and Notoginseng Radix et Rhizoma is one of the ingredients used in Yaoshitongyuan (36,66).

5.1 Treatment of rheumatoid and osteoarthritis

Rheumatoid and osteoarthritis diseases are prevalent in old people. According to Chinese historical records, Notoginseng Radix et Rhizoma, Astragali Radix and black-bone chicken cooked together with yellow wine can dispel wind and remove the obstruction in the meridian, invigorating Qi to activate the blood and relieving the rheumatoid (28,40). Modern studies have found that Notoginseng Radix et Rhizoma may play an anti-rheumatoid arthritis effect through the regulation of multiple targets and pathways such as substance metabolism, signal transduction and inflammation (61).

5.2 Treatment of hypertension

Sanchi-flower tea and Sanchi-coriander porridge relieve hypertension (54). Japonica rice, Sanchi Flower and coriander cooked together can treat hypertension (54,63). Modern pharmacological experiments have shown that the compounds in Notoginseng Radix et Rhizoma lower the blood pressure and relieving arteriosclerosis, which provides a basis for folk dietary formulas (42).

5.3 Treatment of gynecological diseases

Notoginseng Radix et Rhizoma is also used to treat gynecological diseases. The use of Notoginseng Radix et Rhizoma in soups and teas in daily life has health-preserving effects for women (16). For example, Powder of *Notoginseng Radix et Rhizoma*, Angelicae Sinensis Radix, brown sugar and eggs cooked together can relieve dysmenorrhea (16,55). Astragali Radix, Codonopsis Radix, Polygonati Rhizoma, Dendrobii Caulis, and Sanchi Flower etc. cooked together can treat poor ovarian function (52). Modern studies have shown that PNS and dencichen inhibits the release of inflammatory cytokines and adjusting vasoactive substances, which can treat some gynecological diseases (5).

6. CONCLUSIONS AND PROSPECTS

The processed Notoginseng Radix et Rhizoma has been used in China since ancient times. The processing methods were diverse and their applications lead to the development of modern Chinese medicine. The important medicinal components of Notoginseng Radix et Rhizoma are saponins, which provides the pharmacological activity. Besides the other main components are: ammarane-type tetracyclic triterpene saponins, polysaccharides, dencichine, etc. They have great effects on the blood, cardio-cerebrovascular, nerve, metabolism, immune regulation and other systems. The Notoginseng Radix et Rhizoma has rich clinical practical experience of thousands of years in China, but still there is great potential to improve the production and uses of Sanchi.

(i). **Quality :** The quality of Chinese medicine from *P. notoginseng* depends on the germplasm resources, cultivation practices and processing methods. There is great need to improve these.

(ii). **Medicinal and food uses:** There is need to develop a new Notoginseng Radix et Rhizoma medicated diet to meet requirements of medicine and food. This will be very beneficial to human health and to popularize the Sanchi.

Thus, Notoginseng Radix et Rhizoma plays an important role in the treatment of human diseases and maintenance of good health. Hence, there is need to study the pharmacological mechanisms of Notoginseng Radix et Rhizoma.

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DECLARATION

We declare that all authors of this Ms. have made substantial contributions. We did not exclude any author who substantially contributed to this Ms. We have followed our ethical norms established by our respective institutions.

CONFLICT OF INTEREST

The authors announce that they have no conflict of interest.

ETHICAL APPROVAL

The authors declare that the study was carried out following scientific ethics and conduct. However, this study did not involve any use of animals, hence no ethical approval has been obtained from the concerned committee.

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