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Traditional Chinese medicine — Report on the global industry and standardization development of *Panax* ginseng

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This document was prepared by Technical Committee ISO/TC 249, *Traditional Chinese medicine*.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

Panax ginseng is the dried root and rhizome of Panax ginseng C. A. Meyer. It has the effects of greatly tonifying the original qi, restoring the pulse and relieving collapse, invigorating the spleen and benefiting the lungs. It is used primarily for symptoms such as weakness, cold extremities with faint pulse and spleen deficiency with reduced appetite. [2] As a kind of rare and valuable Chinese materia medica, Panax ginseng has a long history of medicinal use. Its single and compound formulas, as well as a variety of modern preparations, play an important role in clinical practice. Furthermore, Panax ginseng is widely applied in many other fields such as food, healthcare and daily chemical products.

As one of the Chinese materia medica with the largest global trade volume, *Panax ginseng* occupies a large market scale. It is mainly cultivated in China, the Republic of Korea, the Democratic People's Republic of Korea, Japan and the Russian Federation, among which China and the Republic of Korea are the main countries for its production and consumption, accounting for over 80 % of the total yield in the world. In addition, *Panax ginseng* is also widely used in Europe and the United States, as well as some other countries in Asia.

Panax ginseng has been recorded in many national pharmacopoeias and regional standards. However, due to the restrictions on different national regulations and different purposes for standard development, the requirements specified by such pharmacopoeias and regional standards differ in their scope, items, indicators and other aspects. The lack of unified quality and safety standards gives rise to some negative phenomena, such as unqualified and fake products available on the market, substandard products sold at high prices and confusion with specification and grades of Panax ginseng products. In addition, the lack of unified standards in terms of the terminology and processing technology leads to confusion with products' names and brings lots of difficulties not only to supervision authorities but also to consumers. Therefore, it is urgent to develop unified International Standards for the whole industry chain of Panax ginseng, including the production, processing, marketing and other links.

Standards for the whole industry chain of *Panax ginseng* would guarantee the sustainable development of the industry and international trade in the aspects of promoting the manufacturing, improving the quality, regulating the market and protecting the consumers' interests. This document conducts a comprehensive survey on the industry of *Panax ginseng* in terms of its origin and application history, medicinal value, geographical distribution, cultivation methods, processing methods, the development of industry, international trade and standardization status. It will be beneficial to provide reference and information support for the follow-up formulation of the International Standards for *Panax ginseng*.

Traditional Chinese medicine — Report on the global industry and standardization development of *Panax ginseng*

1 Scope

This document reports on the global industry and standardization development of *Panax ginseng*. It includes its origin and application history, medicinal value, geographical distribution, cultivation and processing methods, industry development, international trade, current status and development demands for standardization.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

- ISO Online browsing platform: available at https://www.iso.org/obp
- IEC Electropedia: available at https://www.electropedia.org/

3.1

fresh ginseng

ginseng root harvested from the field, before being washed 4a48-b23e-ca0acfe186ef/iso-dtr-18986

[SOURCE: ISO 19610:2017, 3.1]

3.2

washed ginseng

raw ginseng root washed with drinking water to remove any foreign matter and then used as the starting material for manufacturing red ginseng

[SOURCE: ISO 19610:2017, 3.2]

3.3

steamed ginseng

ginseng produced through a process of steaming the washed ginseng to gelatinize the starch content

[SOURCE: ISO 19610:2017, 3.3]

3.4

red ginseng

ginseng root from *Panax ginseng* C.A. Meyer, treated with steam and then dried and packaged as whole or cut roots

[SOURCE: ISO 19610:2017, 3.4]

4 Origin and application history

4.1 Origin

Panax ginseng is one of the oldest relict plants on earth. The character "参" was first discovered in the oracle bone inscriptions of the Shang Dynasty of China, dating back 3 500 years. The character "参" on the oracle bone was pictographic, showing the typical characteristics of the aboveground and underground parts of Panax ginseng. [4] Fan Zi Ji Ran [5] (《范子計然》), written in the Warring States Period (465 BC), clearly recorded the origin and properties of Panax ginseng, which is the earliest available document of Panax ginseng.

4.2 Application history in China

4.2.1 Qin and Han dynasties

The Qin and Han dynasties were the initial medicinal and clinical application stages of *Panax ginseng*. As recorded in *Sheng Nong's Herbal Classics*[6] (《神農本草經》), *Panax ginseng* has rich therapeutic effects, such as calming the spirit, improving vision, enhancing intelligence and prolonging life.

Medicine Inscribed Wooden Slips of the Han Dynasty in Wuwei^[2] (《武威漢代醫簡》), the earliest literature on the clinical application of *Panax ginseng*, summarized the medication rules of *Panax ginseng* in treating various diseases. In the Eastern Han Dynasty, the clinical application of *Panax ginseng* was expanded and it was widely used in various formulas. In the *Treatise on Febrile Diseases*[8] (《傷寒論》), 23 of a total of 113 formulas contained *Panax ginseng*.

4.2.2 Jin and Southern-Northern dynasties

The clinical application of $Panax\ ginseng$ was further explored in the Jin and Southern-Northern dynasties. The single prescription of $Panax\ ginseng$ "Ginseng Powder" was first recorded in the $Handbook\ of\ Prescription\ for\ Emergency^{[9]}$ (《时後備急方》) in the Eastern Jin Dynasty. It is mainly used for the treatment of sudden reversed flow of qi and life-threatening diseases. $Annotation\ of\ Materia\ Medica^{[10]}$ (《本草經集注》), written during the Liang Dynasty, elaborated the therapeutic effects of $Panax\ ginseng$ on diseases occurring in specific Zang-fu organs, which extended the scope of functions and indications of $Panax\ ginseng$. The cultivation of $Panax\ ginseng$ in gardens was first recorded in the $Panax\ ginseng$ in $Panax\ ginseng$ in P

4.2.3 Tang and Song dynasties

The Tang and Song dynasties witnessed the rapid development of application and dissemination of *Panax ginseng. Tang Materia Medica*[12] (《新修本草》), the first official pharmacopoeia of China, recorded in detail about the functions, indications, usage, properties and main production areas of *Panax ginseng*. In addition, a large number of prescriptions containing *Panax ginseng* is included in *Prescriptions Worth Thousand Gold for Emergencies*[13] (《備急千金要方》) and *Supplement to Invaluable Prescriptions for Ready Reference* [14] (《千金翼方》), with 445 and 310 prescriptions, respectively. With frequent foreign trade and exchange activities, *Panax ginseng* spread more widely overseas in the Tang Dynasty. *Panax ginseng* produced in the Bohai State (an ancient kingdom existing from 698 AD to 926 AD) was continuously paid to the central plains as tributes. Master Jianzhen, an eminent Chinese monk in Tang Dynasty, propagated the herb of *Panax ginseng* and its application to Japan. This herb is still preserved in Shosoin of Japan today. [15]

Traditional Chinese medicine writings flourished in the Song Dynasty. Illustrated Classics of Materia $Medica^{[16]}$ (《本草圖經》) first systematically described the morphological characteristics of the original plant of $Panax\ ginseng$ in the form of illustrations. Classified Materia $Medica^{[17]}$ (《證類本草》) further explained the medicinal theory of $Panax\ ginseng$. In the Song Dynasty, the resources of $Panax\ ginseng$ increased with the eastward expansion of its main production areas. Meanwhile, a quantity of $Panax\ ginseng$ was imported through border trade to ensure domestic demand for medicinal use. [15]

4.2.4 Ming and Qing dynasties

The Ming Dynasty was the peak period of clinical theory and practical application of $Panax\ ginseng$. $Biography\ of\ Panax\ ginseng\ (《人參傳》)$, the first monograph of $Panax\ ginseng$, comprehensively summarized its pharmacology and medicinal properties. On this basis, $Compendium\ of\ Materia\ Medica^{[18]}$ (《本草綱目》) made a detailed collation of the prescriptions and indications of $Panax\ ginseng$, including 67 prescriptions applied to 15 kinds of diseases. However, due to the severe destruction of resources, the production areas of $Panax\ ginseng$ moved northward. Thus, the supply of $Panax\ ginseng$ in the Ming Dynasty fell into a difficult period. Under such circumstances, the government opened cross-border markets to import large quantities of $Panax\ ginseng$ from the Liao Dynasty and the Joseon Dynasty of Korea in order to ease domestic demand for supply. At the same time, large-scale artificial cultivation of $Panax\ ginseng$ was realized through seed propagation among the people. [19]

In the Qing Dynasty, the theories and management of *Panax ginseng* were well developed. *Essential of Materia Medica*[20] (《本草備要》) divided *Panax ginseng* into "raw" and "cooked" ginseng. *Ginseng spectrum*[21] (《參譜》) discussed ginseng production, purchase and sales, identification of quality, processing methods and value in detail. At the same time, the authorities tightened the control over *Panax ginseng* by establishing monopoly institutions and implementing various policies and systems for the management of *Panax ginseng*. In addition, the grades and specifications of *Panax ginseng* were clearly specified. [22] In the late Qing Dynasty, the garden cultivation of *Panax ginseng* was rapidly developed to make up for the shortage of its natural resources. [15]

4.2.5 Modern times

Panax ginseng has been greatly developed covering such aspects as modern basic research, industrial scale and regulation supervision. With the development of modern medicine, biology and chemistry, people have a growing understanding of the pharmacological effects of Panax ginseng. Meanwhile, remarkable achievements have been made in the research of the material basis of Panax ginseng. Supported by modern science and technology, the industry of Panax ginseng continues to expand. The manufactured products of Panax ginseng, such as general food, health functional food, cosmetics and drugs have become the main components of the international industry of Panax ginseng. In order to promote the rapid and healthy development of this industry, relevant regulations and standards have been successively issued by various countries.

Panax ginseng was one of the first Chinese materia medica included in Chinese Pharmacopoeia 1963, with a detailed description of its source, processing, usage and dosage. [2] The industry development of Panax ginseng in the People's Republic of China can be roughly divided into four periods:

- Expansion period (1970 to 1990): A production model of high quality and high yield was achieved in terms of the planting of *Panax ginseng*.[23]
- Turbulent period (1990 to 2002): The conflict between the lands and forests on *Panax ginseng* cultivation led to a drop in price and a slowdown in the industry.
- Recovery period (2003 to 2012): The government paid more attention to the industry of *Panax ginseng* and facilitated with modern technology to promote its industry development.
- Growth period (2012 to present): The industry of *Panax ginseng* developed rapidly after its approval as "new resource food".

4.3 Application history in Korea

4.3.1 The Samhan Period

According to literature, [24,25] *Panax ginseng* has been cultivated and used to make medicine since the Samhan Period. It is recorded that *Panax ginseng* grown on the Korean peninsula was traded to the Tang Dynasty, China, during the periods of Kings Jinpyeong (A.D. 627) and Sungdeok (A.D. 723) of the Silla Dynasty.

4.3.2 Goryeo Dynasty (Goryeo Period)

The Goryeo period was characterized by active trade with neighbouring nations. Naturally, *Panax ginseng* was one of the major commodities actively traded with the outside world, including the Khitans, the Song Dynasty, the Yuan Dynasty and the Ming Dynasty. [26] During the period of King Injong (1123), *GoryeoDogyeong* [25] (《高麗圖經》) contains information regarding ginseng steamed (red ginseng of today) due to distribution issues, showing that people of the time steamed and dried ginseng for long-distance transport.

Panax ginseng was actively traded not only with China but also with Japan. In the reigning period of King Wu, Goryeo delivered ginseng as a gift when sending envoys to Japan to effectively handle trouble caused by Japanese pirates. [26] *Panax ginseng*, which was used as medicine and tributes during the Samhan period, was regarded as a commodity that royal families trade for profit and was subject to taxation in the Goryeo Dynasty. In particular, it was one of the nation's representative items considered significant in terms of diplomatic relations with China and Japan.

4.3.3 Joseon Dynasty

The clinical application and processing and cultivation method of *Panax ginseng* were greatly developed in the Joseon Dynasty. *Principles and Practice of Eastern Medicine*^[27] published during the reign of King Seonjo contains more than 170 prescriptions based on *Panax ginseng*. Moreover, steamed ginseng in the Goryeo Dynasty was converted into pasam (steamed, compressed and threaded ginseng) and pansam (steamed, compressed and pasted ginseng) that are the ancestors of red ginseng.^[28] During the periods of Kings Sukjong and Jeongjo, the red ginseng production method was fully developed to enable the stable and long-distance transport.

In the Joseon Dynasty, trading ginseng privately was thoroughly controlled, so that ginseng was used as medicine or tributes by the royal families or those in authority for profit. [28] However, the prices of *Panax ginseng* were sharply raised due to lack of wild ginseng, which requires the development of ginseng cultivation methods. *Imwongyeongjeji* shows that ginseng cultivation methods were fully established in the mid-Joseon Dynasty. [29] Against this backdrop, the development of *Panax ginseng* and red ginseng cultivation methods greatly contributed to the financial health of the nation and the royal families.

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4.3.4 Modern times

Throughout the history of Korea, *Panax ginseng* has been traded as one of Korea's major commodities. ^[30] In 1899, the Ginseng Policy Team (Samjeonggwa) initiated producing red ginseng under the leadership of the central government. In 1908, the *Red Ginseng Monopoly Act* and the *Ginseng Tax Act* were promulgated to lead the government to monopolize the red ginseng market. The *Ginseng Policy Handbook (Samjeongyoram)* ^[30] published by the Ginseng Policy Team shows that research on ginseng cultivation methods, pest control, red ginseng manufacturing processes and the age of *Panax ginseng* optimized for red ginseng manufacturing was systematically conducted.

In 1996, the *Red Ginseng Monopoly Act* and the *Ginseng Industry Act* were abolished and established, respectively, thereby transferring the authority to control *Panax ginseng* and red ginseng to the private sector for the first time in 600 years. The *Ginseng Industry Act* specifies matters required for the cultivation, manufacturing and testing of *Panax ginseng* and ginseng products, leading *Panax ginseng* to be protected and promoted as a speciality and significantly increasing the number of related firms and red ginseng products. [30] After diverse animal and clinical tests, the functionality of *Panax ginseng* has been officially recognized in several areas by the Ministry of Food and Drug Safety. [31]

4.4 Application history in other countries

Panax ginseng is mainly used for Kampo medicines and health food in Japan. In ancient Japan, *Panax ginseng* was frequently used by Kampo practitioners. With the prosperity of Kampo medicine, prescriptions containing *Panax ginseng* were more widely used in the treatment of several diseases. Japan attaches great importance to the quality standards of Kampo medicine preparations and *Panax ginseng* varieties with high extract content and short leaching time are often used as raw materials.

Wild *Panax ginseng* is listed in the *Red Book of Primorsky Krai* as an endangered species in the Russian Federation. Cultivated *Panax ginseng* has been planted in Siberia since the 19th century. In 1968, it was included in the State Pharmacopoeia of the Soviet Union. *Panax ginseng* is popular in the Russian Federation as medicine, health products and food. [34]

5 Medicinal value

5.1 Traditional use

Panax ginseng has the effects of greatly tonifying the original qi, restoring the pulse and relieving collapse, invigorating spleen and benefiting lung, engendering fluid and nourishing blood, quieting the spirit and sharpening the wits. It is used primarily for symptoms such as weakness, cold extremities with faint pulse and spleen deficiency with reduced appetite.^[2]

Both single and formulas of *Panax ginseng* can be used in traditional clinical application. Nevertheless, there are some incompatibilities. For example, *Panax ginseng* is antagonized by *Veratrum nigrum* root and rhizome, restrained by *Trogopterori* faeces and inhibited by *Raphanus sativus* seed. [18]

5.2 Modern application

5.2.1 Phytochemistry and pharmacological effects

Panax ginseng is mainly composed of saponins, polysaccharides, volatile oils, organic acids and esters, sterols, flavonoids, lignans, inorganic elements and vitamins. [35] A variety of pharmacological actions also have been proven in *Panax ginseng*, including anti-fatigue, anti-stress, anti-mutagenesis, anti-oxidation, anti-cancer, as well as protection of the cardiovascular system. [36]

Ginsenosides are well believed as the primary bio-active ingredients in *Panax ginseng*. More than 170 kinds of ginsenosides have been reported,^[37] which can be mainly divided into protopanaxadiol type (PPD), protopanaxatriol type (PPT) and oleanolic acid type (OA) according to their structure properties. Ginsenosides of different types possess varied of pharmacological characteristics. For example, PPT is recognized for the effects of stimulating central nervous system, improving memory, nourishing and promoting protein synthesis, whereas OA exerts the effects of anti-inflammation and anti-platelet release.

Besides, polysaccharides and volatile oils are also important ingredients of *Panax ginseng*. Up to now, there have been reports of 64 polysaccharides^[38] and 160 volatile oils from *Panax ginseng*.^[39] Ginseng polysaccharides are mainly composed of neutral and pectin-like acidic polysaccharides, which play critical roles in enhancing immunity, anti-aging, anti-tumour and reducing liver injury. Ginseng volatile oils with special fragrance are primarily made up of sesquiterpenes, long-chain saturated acids and aromatic hydrocarbons. Among them, sesquiterpenes are the mostly constituents, while polyacetylenols such as panaxynol and panaxyloxynol are regarded as the principalcharacteristic compounds.^[40] Ginseng volatile oil has significant effects on antifungal, anti-inflammatory, central nervous system depression and bi-directional regulation of blood pressure.

In addition, the traditional processing methods of *Panax ginseng* could alter its chemical composition and pharmacological effects to achieve the purpose of efficiency enhancing. Various processed *Panax ginseng* products have been exploited to better the therapeutic demands (see <u>Clause 8</u>).

5.2.2 Modern traditional Chinese medicine preparations

Ginsenoside monomer compounds, extract and preparations of *Panax ginseng* have been widely developed into drugs for the treatment of different diseases. Ginsenoside Rg3, 20 (S) -ginsenoside Rg3 and Ginsenoside Rd^[41,42] have been developed into new anticancer and antiviral drugs. Capsules developed from the fruits and total saponins of *Panax ginseng* leaves have been used as adjuvant medicine for the treatment of coronary heart disease, climacteric syndrome, diabetes and tumours. ^[43,44] Ginseng polysaccharide injection has been also mainly used for fighting various chronic infections, diabetes and various immune diseases. ^[45]

5.3 Healthcare and functional products

Except for medicinal value, *Panax ginseng* has been widely developed into healthcare and functional products because of its rich nutrients. These products are mainly helpful for immunity enhancement, anti-aging, blood sugar control and auxiliary protective effects against liver injury, sleep improvement and anti-oxidation. [46]

Functional foods with *Panax ginseng* include capsules, sticks, ampoules, pills, drinks, baked food, prepared food and condiments For example, ginseng polysaccharide fermented milk beverage^[47] is used for improving immunity, preventing and treating hypertension, and fermented ginseng rice wine is used for anti-oxidation, with rare saponin CK produced and the content of ginsenoside increased significantly after fermentation.^[48]

The use of natural and non-toxic botanical sources has become the trend of cosmetics industrial development. Ginseng extracts and ginsenoside have been used in the field of cosmetics since the 1980s and nowadays have become the most widely used starting materials in plant cosmetics. [49] For example, moisturizing cream, whitening cream, facial mask, eye cream and shampoo made with *Panax ginseng* are mainly used to improve the antioxidant activity of skin cells, inhibit melanin transfer, improve skin colour and reduce hair loss. [50,51]

In addition, as a non-edible product, it is used in various ways such as cosmetics and toothpaste, and premium pet food and products using ginseng fruit, not the root, are being released. [52]

6 Geographical distribution

The production areas of *Panax ginseng* are mainly distributed in northeast Asia between latitude 33° N and 48° N. Information on the main production areas and climatic features is listed in Table 1.

Panax ginseng grows in special and strict conditions, mostly in deciduous broad-leaved forests or mixed coniferous broad-leaved forests hundreds of metres above sea level. It prefers sandy loam with loose texture, good ventilation, good drainage and high nutrient availability. As shade-tolerant plants, it is well adapted to a cool and moist climate. In addition, Panax ginseng is resistant to low temperature and prefers weakly scattered light rather than strong direct light. The relative moisture of the soil is usually maintained at 35,0 % to 50,0 % during the growth of Panax ginseng. [53] High soil moisture can restrain to root growth and result in root rot, while low soil moisture can lead to its poor growth.

Tabla 1 —	Main production a	ranc and climatic fa	atures of <i>Panax ainsena</i>
rame r —	Maill Di Odilici Ioli a	i eas ano cumancie	alules of <i>Fullux ullisellu</i>

Country	Main production areas	Latitude	Climatic features
People's Re- public of China	From Kuandian, Liaoning province in the south, to Yichun, Heilongjiang province in the north. Main production areas: Fusong, Changbai, Jingyu, Ji'an, Dunhua, Antu and other counties or cities of Jilin province	35° N to 48° N	Affected by multiple continental and mon- soon climates, with annual rainfall of about 1 000 mm
Republic of Korea	Gyeonggi province, Gangwon province, north Chungcheong province, south Chungcheong province, south Jeolla province, north Jeolla province, north Gyeongsang province, etc. Main production area: Geumsan county	33° N to 42° N	Temperate monsoon climate with annu- al rainfall of around 1 500 mm
Democratic People's Re- public of Korea	Kaesong, Kumchon, Pyongsan, So- hung, etc. Main production area: Kaesong	35° N to 42° N	Ocean climate with annual rainfall of 1 000 mm to 1 500 mm