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Traditional Chinese medicine — *Angelica sinensis* root

*Médecine traditionnelle chinoise — Racine d'*Angélique chinoise

Reference number
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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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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

Angelica root is a traditional herbal remedy, derived from the dried root of *Angelica sinensis* (Oliv.) Diels, *Angelica acutiloba* (Sieb. et Zucc.) Kitagawa and *Angelica gigas* Nakai, of the Umbelliferae family, as recorded by the Chinese Pharmacopoeia, the Japanese Pharmacopoeia and the Korean Pharmacopoeia, respectively, and has a long medicinal history. *Angelica sinensis* is still one of the herbs most commonly used by traditional Chinese medicine practitioners in Asia, North America and Europe. It is commonly known as female ginseng, and widely used to invigorate blood circulation and replenish blood in treating women's reproductive problems, such as dysmenorrhea, amenorrhoea and menopause. It has also been used in over 20 countries for its significant effectiveness in the pharmaceutical and cosmetic fields.

The quality of *Angelica sinensis* root is crucial for efficacy and safety for consumers. Until now, there have been no unique requirements for *Angelica sinensis* root, although *Angelica sinensis* root has also been recorded by the American Herbal Pharmacopoeia, the European Pharmacopoeia, the British Pharmacopoeia and the Hong Kong Chinese Materia Medica Standards. It is therefore important to standardize the quality of *Angelica sinensis* root globally in order to benefit farmers, enterprises and companies involved in the planting, management and trade of *Angelica sinensis* root.

As national implementation may differ, national standards bodies are invited to modify the values given in 5.4, 5.5, 5.6, 5.7, 5.8, 5.9 and 5.10 in their national standards. Examples of national and regional values are given in Annex D.

Traditional Chinese medicine — *Angelica sinensis* root

1 Scope

This document specifies minimum requirements and test methods for *Angelica sinensis* root that is derived from *Angelica sinensis* (Oliv.) Diels.

It is applicable to *Angelica sinensis* root that is sold and used as a natural medicine in international trade, including Chinese materia medica (whole medicinal materials) and decoction pieces derived from this plant.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 1575, *Tea — Determination of total ash*

ISO 1577, *Tea — Determination of acid-insoluble ash*

ISO 18664, *Traditional Chinese Medicine — Determination of heavy metals in herbal medicines used in Traditional Chinese Medicine*

ISO 20409, *Traditional Chinese medicine — Panax notoginseng root and rhizome*

ISO 21371, *Traditional Chinese medicine — Labelling requirements of products intended for oral or topical use*

CAC/MRL01 *Maximum Residue Limits for Pesticides in Foods*

CODEX STAN 229, *Analysis of pesticide residues: Recommended methods*

World Health Organization 2011, *Quality control methods for herbal materials, General advice on sampling*

3 Terms and definitions

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

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

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
root
main underground part of a plant that can branch

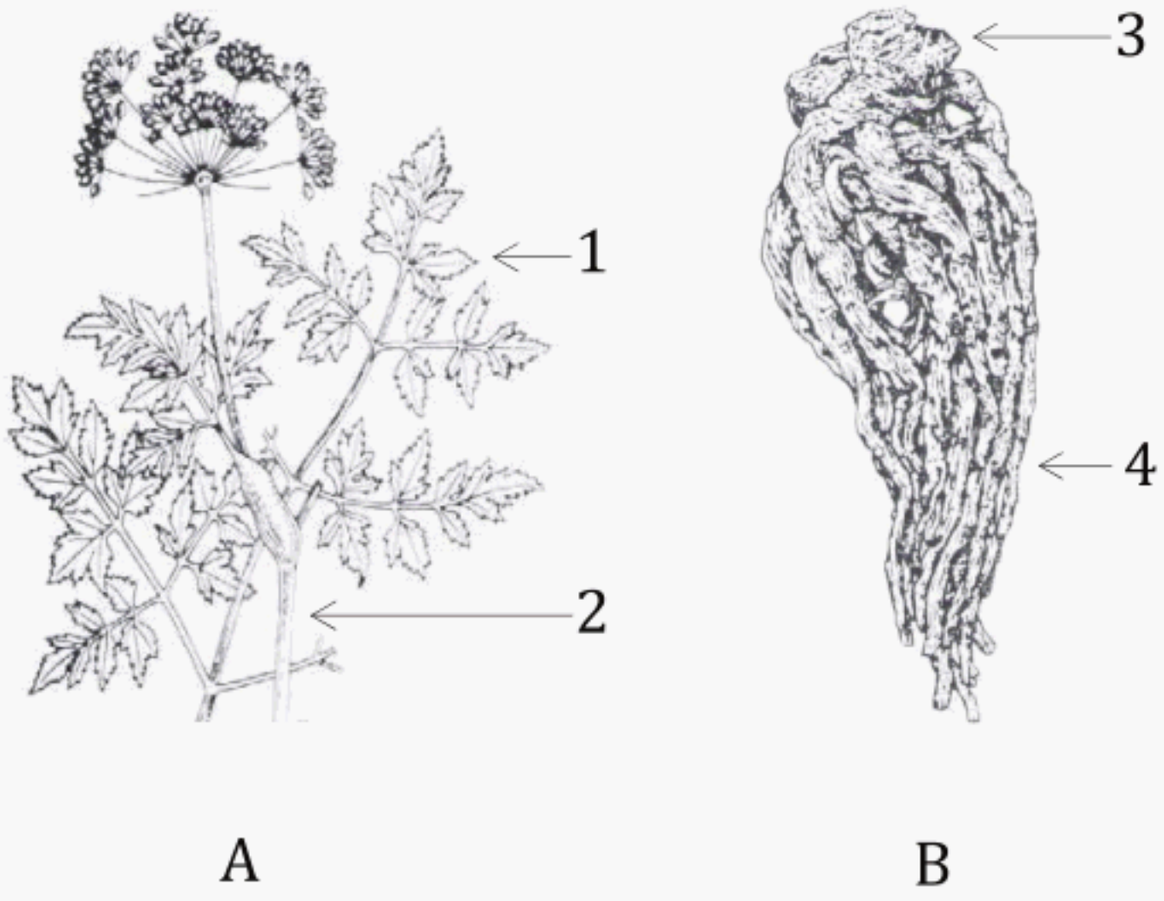
3.2
root stock
top part of the dried main *root* (3.1), which is closest to the stem

3.3
total ash
residue obtained after incineration at 525 °C ± 25 °C

3.4
acid-insoluble ash
part of the *total ash* (3.3) remaining after treatment with hydrochloric acid

4 Description

Angelica sinensis root is shown in Figure 1.



Key

A *Angelica sinensis* plant
B *Angelica sinensis* dried root
1 leaf
2 flowering branch
3 root stock
4 branching root

Figure 1 — Structure of *Angelica sinensis* (Oliv.) Diels

5 Requirements

5.1 General characteristics

The following requirements shall be met before separating the bulk sample into test samples.

a) *Angelica sinensis* root shall be clean and free from foreign matter.

b) The presence of living insects, mould and external contaminants which are visible to the naked eye shall not be permitted.

5.2 Morphological features of *Angelica sinensis* root

a) The root is slightly cylindrical.

b) The outer surface is yellowish brown to reddish brown with longitudinal wrinkles and transversely elongated lenticels.

c) The root stock is known as "Angelica head" (or *guitou*). The main root is known as "Angelica body" (or *guishen*). The branching root is known as "Angelica tails " (or *guiwei*). The entire root is known as "entire Angelica" (or *quangui*).

d) The root stock is 15 mm to 40 mm in diameter, annulated with obtuse and rounded apex or with purple or yellowish green remains of stems and leaf sheaths.

e) The main root is thick and short with numerous branching roots in the lower part. The upper portion of the branching root is thick, while the lower portion of the branching root is thin and mostly twisted with a few rootlet scars.

f) The texture is flexible.

g) The fracture is yellowish white or pale yellowish brown with numerous brown-spotted secretory cavities in the thick bark. The wood is paler in colour than the bark with radial lines. The cambium ring is yellowish brown.

h) The core of the root stock contains a pith and a cavity.

i) The odour is strongly aromatic; the taste is sweet, pungent and slightly bitter.

5.3 Identification of *Angelica sinensis* root

The identification of *Angelica sinensis* root by a thin-layer chromatogram (TLC) shall present spots or bands with the same colour and positions corresponding to those of reference solutions.

5.4 Moisture

The mass fraction of moisture should not be more than 15,0 %.

5.5 Total ash

The mass fraction of total ash should not be more than 7,0 %.

5.6 Acid-insoluble ash

The mass fraction of acid-insoluble ash should not be more than 2,0 %.

5.7 Extractives

The mass fraction of 70 % ethanol-soluble extractives should not be less than 40,0 %.

5.8 Content of maker compound

The content of marker compound shall be determined. For example, ferulic acid shall be determined taking into account relevant national or regional pharmacopoeias, legislation and norms.

The mass fraction of ferulic acid ($C_{10}H_{10}O_4$) should not be less than 0,050 %.

5.9 Heavy metal

The content of heavy metals such as arsenic, mercury, lead and cadmium shall be determined.

The limit value should take into account the requirements of the regulatory bodies of the destination country or region. If there is none, the limit value of a national or regional pharmacopoeia listed in ISO 18664 shall be chosen.

5.10 Pesticide residues

The content of pesticide residues such as benzex, dichloro-diphenyl-trichloroethane (DDT) and quintozene shall be determined.

6 Sampling

Sampling of *Angelica sinensis* root shall be carried out according to the World Health Organization's *Quality control methods for herbal materials, General advice on sampling*.

7 Test methods

7.1 Macroscopic identification

Samples not less than 500 g are taken from each batch randomly and observed with the naked eye.

7.2 TLC identification

See Annex A for additional information.

7.3 Determination of moisture content

The testing method specified in ISO 20409 applies.

7.4 Determination of total ash

The testing method specified in ISO 1575 applies.

7.5 Determination of acid-insoluble ash

The testing method specified in ISO 1577 applies.

7.6 Determination of extractives

See Annex B for additional information.

7.7 Determination of ferulic acid

See Annex C for additional information.

7.8 Determination of heavy metal

The testing method specified in ISO 18664 applies.

7.9 Determination of pesticide residues

The testing methods specified in CODEX STAN 229 and CAC/MRL01 apply.

8 Test report

For each test method, the test report shall specify the following:

a) all information necessary for the complete identification of the sample;

b) a reference to this document, for example “determined in accordance with ISO 22584:2019";

c) the sampling method used;

d) the test method(s) used;

e) the test result(s) obtained;

f) all operational details not specified in this document, or regarded as optional, together with details of any incidents which may have influenced the test result(s);

g) any unusual features (anomalies) observed during the test;

h) the date of the test.

9 Packaging, storage and transportation

Packaging shall not transmit any odour or flavour to the product and shall not contain substances which may damage the product or constitute a health risk.

Angelica sinensis root should be preserved in a cool and dry place, and protected from light, pollution, moisture, moths and foreign substances during storage and long-distance delivery.

10 Marking and labelling

The method specified in ISO 21371 shall apply. The following items shall be marked or labelled on the packages:

a) product name and plant scientific name;

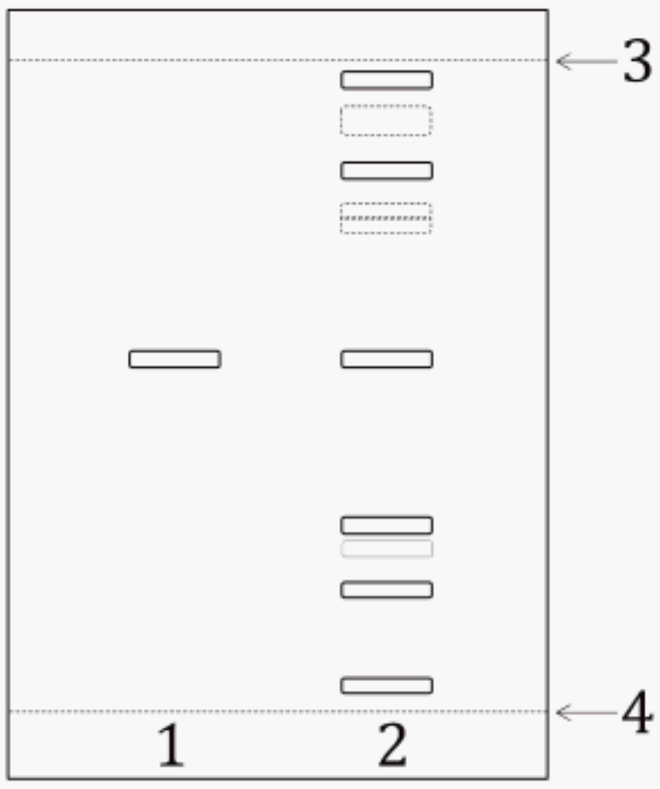
b) all quality features indicated in Clause 5;

c) country and province/state of the products;

d) date of production, batch number and expiry date of the products;

e) storage and transportation method;

f) items required by the regulatory body of the destination country.



Key

1 ferulic acid
2 *Angelica sinensis* root
3 solvent front
4 origin position

Figure A.1 — Schematic diagram of a typical TLC identification by ferulic acid of *Angelica sinensis* root

A.2.2 TLC identification by *Z*-Ligustilide

A.2.2.1 Preparation of test solution

Weigh 250 g of sample to grind and pass it through an 80 mesh or finer sieve. Weigh approximately 1 g of the powder, add 20 ml of diethyl ether, and shake occasionally for 2 h. Evaporate the filtrate to dryness in a warm water bath (<50 °C) and dissolve the residue in 1 ml of ethyl acetate as the test solution.

A.2.2.2 Preparation of reference solution

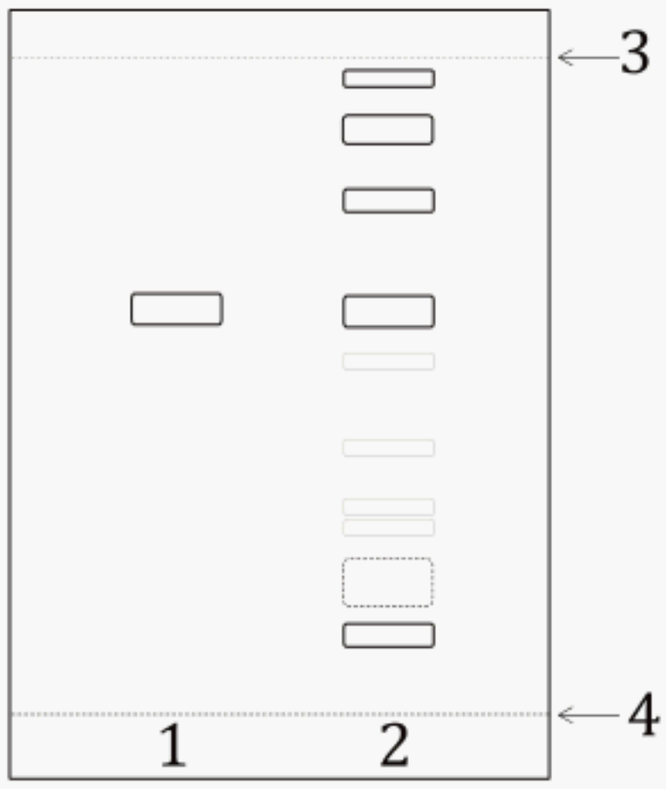
Dissolve *Z*-Ligustilide CRS in ethanol to prepare a reference solution containing 1 mg/ml of *Z*-Ligustilide.

A.2.2.3 Developing solvent system

Prepare a mixture of n-hexane and ethyl acetate in the volume ratio of 5:1 as the mobile phase.

A.2.2.4 Identification by TLC

Apply 10 µl of both the test solution and the reference solution on the same TLC plate (silica gel) previously dried at 110 °C for 15 min in the oven. Develop the plate in the mobile phase for a path of about 8 cm, take the plate out and air-dry. Examine the plate under ultraviolet light at 365 nm. Identify the spots of the test solution by comparing the positions and colours with those of the reference drug solution. A typical reference TLC identification by *Z*-Ligustilide is shown in Figure A.2



Key

1 *Z*-Ligustilide
2 *Angelica sinensis* root
3 solvent front
4 origin position

Figure A.2 — Schematic diagram of a typical TLC by *Z*-Ligustilide of *Angelica sinensis* root

Annex B
(informative)

Determination of extractives

The determination of extractives is performed as follows.

a) Weigh 250 g of sample to grind and pass it through a 24 mesh or coarse sieve. Dry the powder in a desiccator to constant mass. Weigh accurately 2 g to 4 g of the dried sample into a 100 ml to 250 ml stopper conical flask. Accurately add 100 ml of 70 % ethanol and weigh.

b) Allow the conical flask to stand for 1 h. Boil gently under reflux for 1 h. Cool and weigh again. Replenish the loss of mass with 70 % ethanol, mix well and filter.

c) Transfer accurately 25 ml of the successive filtrate into a dried evaporating dish. Evaporate the filtrate to dryness in a water bath.

d) Dry at 105 °C for 3 h and allow to cool for 30 min in a desiccator. Weigh the extracts rapidly and accurately.

e) Calculate the mass fraction of ethanol-soluble extractives, W_e, on the dried basis (%) using Formula (B.1):

$$W_e = (m_1 - m_0) \times 4 / m_s \times 100 \quad \text{(B.1)}$$

where

m_1 is the mass of the evaporating dish and residue after drying (g);

m_0 is the mass of the evaporating dish (g);

m_s is the mass of the sample (g).

Annex C
(informative)

Determination of ferulic acid

C.1 Principle of the test method

The high performance liquid chromatography (HPLC) method is employed to determine the content of ferulic acid. The HPLC system consists of a quaternary pump, continuous vacuum degasser, thermostated auto-sampler and column compartment coupled to a variable wavelength diode-array detector.

C.2 Preparation of test solution

Weigh 250 g of sample to grind and pass it through an 80 mesh or finer sieve. Weigh accurately 0,2 g of the powder in a stopper conical. Accurately add 20 ml of 70 % methanol. Heat under reflux for 30 min. Cool and weigh again. Replenish the loss of mass with 70 % methanol and mix well. Filter and use the successive filtrate. Filter through 0,45 µm membrane, filtrate as the test solution.

C.3 Preparation of reference standards solution

Weigh accurately a quantity of ferulic acid CRS, add to a brown volumetric flask, then dissolve with 70 % methanol to prepare a solution containing 12 µg per ml as the reference solution.

C.4 Chromatographic condition

Column:

a) stationary phase: octadecylsilane bonded silica gel as analysing column or equivalent;

b) size: l = 250 mm, $\varnothing$ = 4,6 mm, particle size = 5 µm;

c) theoretical plates: not less than 5 000.

Mobile phase: 0,2 % phosphoric acid solution (A) and acetonitrile (B)

Isocratic elution: a mixture of mobile phases A and B (90:10)

Flow rate: 1,5 ml/min

Injection volume: 10 µl

Column temperature: 20 °C

Detector: DAD

Detector wavelength: 316 nm

C.5 Determination

Inject accurately 10 µl of both the reference solution and the test solution into the column, then calculate the content.

C.6 Content calculation of ferulic acid

C.6.1 The percentage content of ferulic acid is calculated using Formula (C.1):

$$\frac{A_1 \times C_{\text{ref}} \times p}{A_2 \times m(1-C_{\text{m}}) \times 500} \quad \text{(C.1)}$$

where

A_1 is the area of the peak due to ferulic acid ($C_{10}H_{10}O_4$) in the chromatogram obtained with the test solution;

A_2 is the area of the peak due to ferulic acid ($C_{10}H_{10}O_4$) in the chromatogram obtained with the reference solution;

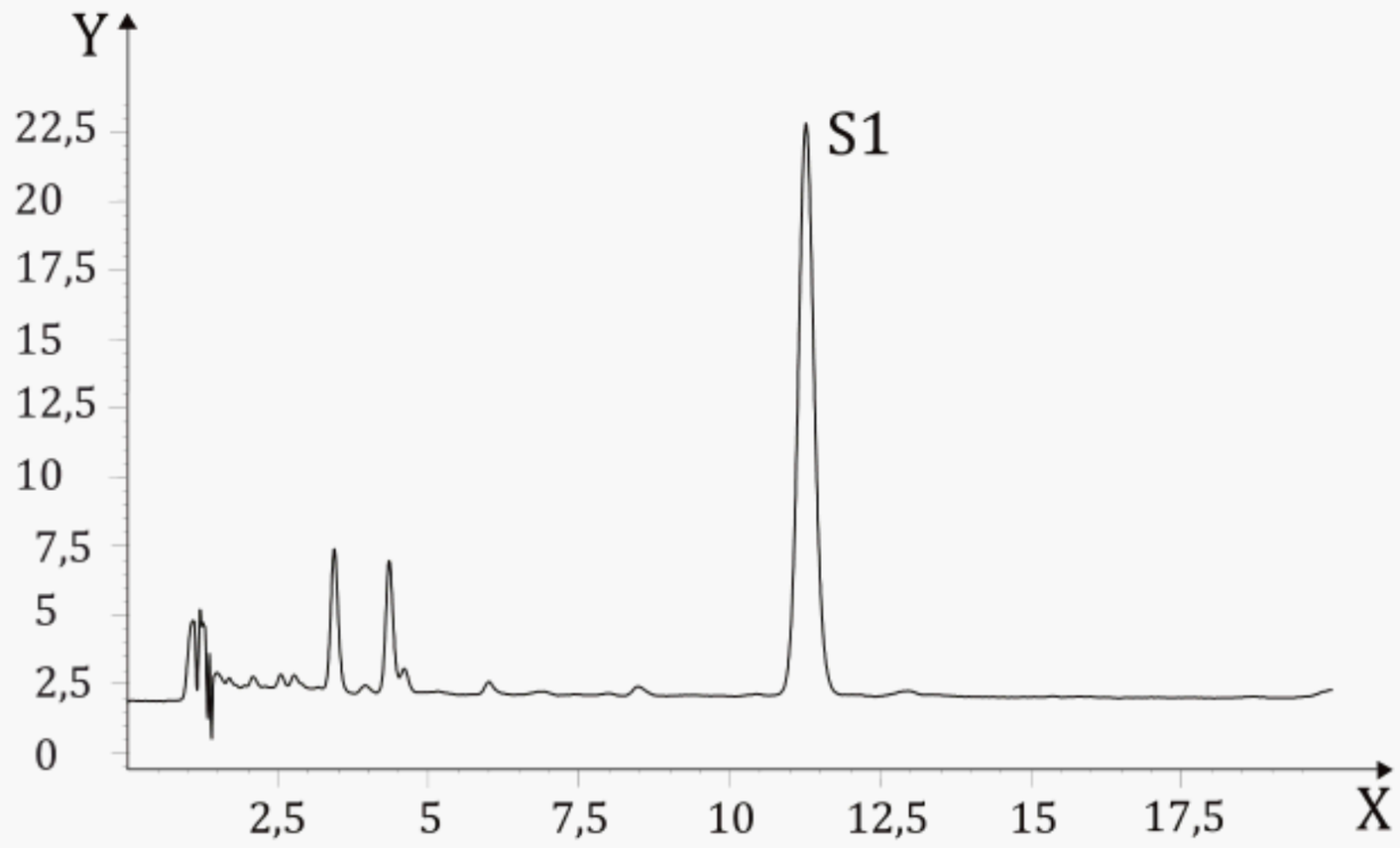
C_{ref} is the density of ferulic acid CRS in the reference solution (μg/ml);

C_{m} is the percentage moisture content of the sample;

p is the percentage content of ferulic acid ($C_{10}H_{10}O_4$) in ferulic acid CRS;

m is the mass of the sample to be examined used to prepare the test solution (g).

C.6.2 A typical HPLC chromatogram of *Angelica sinensis* root is shown in Figure C.1.



Key

S1 ferulic acid

Y absorbance in mAU

X time in min

Figure C.1 — A typical HLPC chromatogram of *Angelica sinensis* root

Annex D
(informative)

Reference values of *Angelica sinensis* root in different national and regional standards

Different countries and regions have their own limits for *Angelica sinensis* root, as shown in Table D.1.

Table D.1 — Reference values of *Angelica sinensis* root (dried drug) in different national and regional standards

Authority regulation	Ferulic acid	*Z*-Ligustilide	Volatile oil	Moisture	Total ash	Acid-insoluble ash	Ethanol-soluble extractives	Water-soluble extractives
British Pharmacopoeia, 2017 edition	≥0,050 %	≥0,1 %	—	≤12,0 %	≤7,0 %	≤2,0 %	≥45,0 %	—
Chinese Pharmacopoeia, 2015 edition	≥0,050 %	—	≥0,4 %	≤15,0 %	≤7,0 %	≤2,0 %	≥45,0 %	—
European Pharmacopeia, 2016 edition	≥0,050 %	—	—	≤12,0 %	≤7,0 %	≤2,0 %	—	—
Hong Kong Chinese Materia Medica Standards	—	≥0,6 %	—	≤13,0 %	≤6,0 %	≤1,5 %	≥55,0 %	≥48,0 %

NOTE 1 "—" means the index is not set in the pharmacopeia.

NOTE 2 The analytical method for the determination of ferulic acid, *Z*-Ligustilide, volatile oil, moisture, total ash, acid-insoluble ash, ethanol-soluble extractives and water-soluble extractives is in accordance with the latest edition of pharmacopoeias of different countries or regions.

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