INTERNATIONAL STANDARD

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# Traditional Chinese Medicine — Determination of heavy metals in herbal medicines used in Traditional Chinese Medicine

*Médecine traditionnelle chinoise — Dosage des métaux lourds dans les herbes médicinales utilisées dans la médecine traditionnelle chinoise*



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# Foreword

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The committee responsible for this document is ISO/TC 249, *Traditional Chinese medicine*.



 

# Introduction

Heavy metals are natural constituents of the environment, and are commonly detected in air, water and soil. However, technical and industrial processes may release heavy metals into the environment, and they have gained attention as contaminants. At present, there is no uniformly accepted International Standard which defines maximum limits for heavy metals in materials used in Traditional Chinese Medicine (TCM), resulting in disputes about what levels should be considered acceptable in TCM materials.

ISO 18664 was developed in response to worldwide demand for harmonization of the determination of heavy metals in herbal medicines used in TCM. The International Standard is applicable to Traditional Medicine systems derived from ancient Chinese medicine.

For reference, the maximum limits of heavy metals in natural materials of TCM have been provided in Annex A.

# Traditional Chinese Medicine — Determination of heavy metals in herbal medicines used in Traditional Chinese Medicine

## 1 Scope

This International Standard specifies determination methods of lead (Pb), arsenic (As), cadmium (Cd) and mercury (Hg) in herbal medicines used in Traditional Chinese Medicine (TCM). It is applicable to natural materials of TCM that are sold and used as food supplements, functional foods or natural medicines in international trade, including Chinese materia medica (whole medicinal materials) and decoction pieces derived from plants or animals. It is not applicable to mineral drugs used in TCM.

This International Standard is not intended to set maximum limits (ML) for individual nations; rather, it is intended to give a reference for standardized testing method and risk assessment.

## 2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 6561-2:2005, *Fruits, vegetables and derived products — Determination of cadmium content — Part 2: Method using flame atomic absorption spectrometry*

ISO 11212-1:1997, *Starch and derived products — Heavy metals content — Part 1: Determination of arsenic content by atomic absorption spectrometry*

ISO 11212-2:1997, *Starch and derived products — Heavy metals content — Part 2: Determination of mercury content by atomic absorption spectrometry*

ISO 11212-3:1997, *Starch and derived products — Heavy metals content — Part 3: Determination of lead content by atomic absorption spectrometry with electrothermal atomization*

ISO 11212-4:1997, *Starch and derived products — Heavy metals content — Part 4: Determination of cadmium content by atomic absorption spectrometry with electrothermal atomization*

ISO 11885:2007, *Water quality — Determination of selected elements by inductively coupled plasma optical emission spectrometry (ICP-OES)*

ISO 17239:2004, *Fruits, vegetables and derived products — Determination of arsenic content — Method using hydride generation atomic absorption spectrometry*

ISO 17294-1:2004, *Water quality — Application of inductively coupled plasma mass spectrometry (ICP-MS) — Part 1: General guidelines*

ISO 17294-2:2003, *Water quality — Application of inductively coupled plasma mass spectrometry (ICP-MS) — Part 2: Determination of 62 elements*

ISO/TS 21033:2011, *Animal and vegetable fats and oils — Determination of trace elements by inductively coupled plasma optical emission spectroscopy (ICP-OES)*

ISO 27085:2009, *Animal feeding stuffs — Determination of calcium, sodium, phosphorus, magnesium, potassium, iron, zinc, copper, manganese, cobalt, molybdenum, arsenic, lead and cadmium by ICP-AES*

## 3 Terms and definitions

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

**3.1**
**arsenic content**
quantity of arsenic determined in accordance with the conditions specified in this method and expressed as arsenic (As), in micrograms per kilogram of the product as received

[SOURCE: ISO 11212-1:1997, 2.1]

**3.2**
**mercury content**
quantity of mercury determined in accordance with the conditions specified in this method and expressed as mercury (Hg), in micrograms per kilogram of the product as received

[SOURCE: ISO 11212-2:1997, 2.1]

**3.3**
**lead content**
quantity of lead determined in accordance with the conditions specified in this method and expressed as lead (Pb), in micrograms per kilogram of the product as received

[SOURCE: ISO 11212-3:1997, 2.1]

**3.4**
**cadmium content**
quantity of cadmium determined in accordance with the conditions specified in this method and expressed as cadmium (Cd), in micrograms per kilogram of the product as received

[SOURCE: ISO 11212-4:1997, 2.1]

## 4 Analytical methods

### 4.1 Instrumental methods

#### 4.1.1 Atomic Absorption Spectrometry (AAS)

AAS methods can be used for the individual determination of lead, mercury, arsenic and cadmium in natural materials used in TCM. The detailed information is specified in the following documents.

ISO 6561-2:2005, *Fruits, vegetables and derived products — Determination of cadmium content — Part 2: Method using flame atomic absorption spectrometry*

ISO 11212-1:1997, *Starch and derived products — Heavy metals content — Part 1: Determination of arsenic content by atomic absorption spectrometry*

ISO 11212-2:1997, *Starch and derived products — Heavy metals content — Part 2: Determination of mercury content by atomic absorption spectrometry*

ISO 11212-3:1997, *Starch and derived products — Heavy metals content — Part 3: Determination of lead content by atomic absorption spectrometry with electrothermal atomization*

ISO 11212-4:1997, *Starch and derived products — Heavy metals content — Part 4: Determination of cadmium content by atomic absorption spectrometry with electrothermal atomization*

ISO 17239:2004, *Fruits, vegetables and derived products — Determination of arsenic content — Method using hydride generation atomic absorption spectrometry*

### 4.1.2 Inductively-Coupled Plasma-Atomic Emission Spectrometry (ICP-AES)

ICP-AES methods can be used for the simultaneous determination of lead, mercury, arsenic and cadmium in natural materials used in TCM. The detailed information is specified in the following documents.

ISO 11885:2007, *Water quality — Determination of selected elements by inductively coupled plasma optical emission spectrometry (ICP-OES)*

ISO/TS 21033:2011, *Animal and vegetable fats and oils — Determination of trace elements by inductively coupled plasma optical emission spectroscopy (ICP-OES) — First Edition*

ISO 27085:2009, *Animal feeding stuffs-Determination of calcium, sodium, phosphorus, magnesium, potassium, iron, zinc, copper, manganese, cobalt, molybdenum, arsenic, lead and cadmium by ICP-AES — First Edition*

### 4.1.3 Inductively-Coupled Plasma Mass Spectrometry (ICP-MS)

ICP-MS methods can be used for the simultaneous determination of lead, mercury, arsenic and cadmium in natural materials used in TCM. The detailed information is specified in the following documents.

ISO 17294-1:2004, *Water quality — Application of inductively coupled plasma mass spectrometry (ICP-MS) — Part 1: General guidelines*

ISO 17294-2:2003, *Water quality — Application of inductively coupled plasma mass spectrometry (ICP-MS) — Part 2: Determination of 62 elements*

## 4.2 Comparison of instrumental methods

All of these instrumental methods have advantages and disadvantages. Table 1 below provides a tabular overview, including detection limits, sample throughout, linear dynamic range, interferences, precision, and ease of use, applicability, unattended use, method development, initial costs, operating costs, and cost per sample.

**Table 1 — Comparison of various instrumental techniques**

| | FAAS | GFAAS | ICP-AES | ICP-MS |
|---|---|---|---|---|
| **Detection limit** (µg/L) | Very good for some elements Arsenic 150<br>Cadmium 0,8<br>Lead 15<br>Mercury 300 | Excellent for most elements<br>Arsenic 1<br>Cadmium 0,002<br>Lead 0,5<br>Mercury 0,6 | Very good for some elements<br>Arsenic 20<br>Cadmium 0,1<br>Lead 1<br>Mercury 1 | Excellent for most elements<br>Arsenic < 0,05<br>Cadmium < 0,05<br>Lead < 0,05<br>Mercury < 0,05 |
| **Analytical capability** | Single element | Single element | Multi-element | Multi-element |
| **Linear dynamic range** | $10^3$ | $10^2$ | $10^5$ | $10^5$ |
| **Precision** | 0,1 % to 1 % | 1 % to 5 % | 0,3 % to 2 % | 1 % to 3 % |
| **Interferences spectral** | Few | Very few | Common | Few |
| **Interferences chemical** | Many | Many | Very few | Some |
| NOTE Comparison of various instrumental techniques is selected from The American Herbal Products Association (AHPA), Heavy Metals: Analysis and Limits in Herbal Dietary Supplements. AHPA, US, 2009. | | | | |

**Table 1** *(continued)*

| | FAAS | GFAAS | ICP-AES | ICP-MS |
|---|---|---|---|---|
| **Interference physical** | Some | Very few | Some | Some |
| **Method development** | Easy | Fairly easy | Fairly easy | More difficult |
| **Ease of use** | Easy | Easy | Easy | Easy |
| **Initial cost** | Low | Medium | High | Very high |
| **Operating cost** | Low | High | Medium | High |
| **Cost per sample** | Low | Medium | Low | Medium |

NOTE Comparison of various instrumental techniques is selected from The American Herbal Products Association (AHPA), Heavy Metals: Analysis and Limits in Herbal Dietary Supplements. AHPA, US, 2009.

# Annex A
(informative)

# Reference of national, regional and organizational limits of heavy metals in natural TCM materials and calculated limits using Target Hazard Quotients based on USEPA and WHO

Different countries, regions and organizations give their own limits of heavy metals in natural materials of TCM. Table A.1 shows these limits in various types of herbal products. Also, some health authorities provide risk assessment methods (USEPA) and recommend heavy metals intake per week (WHO). According to these information and TCM's characteristics, the calculated limits using Target Hazard Quotients are also listed with the summarized maximum and minimum limits from previous references in Table A.1.

**Table A.1 — The national, regional and organizational limits of heavy metals in natural TCM materials and calculated limits using Target Hazard Quotients based on USEPA and WHO (mg/kg)**

| | Pb[a] | As[a] | Cd[a] | Hg[a] | Object | Analytical methods | Authority organization or regulation |
|---|---|---|---|---|---|---|---|
| Australia | 5,0 | — | –1 | 0,1 | Unprocessed herbal material | AAS, ICP-AES or ICP-MS | Therapeutic Goods Administration |
| China | 5 | 2 | 0,3 | 0,2 | Crude herbal drugs | AAS and ICP-MS | Chinese Pharmacopoeia 2010 edition |
| Hong Kong | 5 | 2 | 1 | 0,2 | Chinese material medica | ICP-MS | Hong Kong Chinese Materia Medica Standards |
| Macao | 20 | 5 | — | 0,5 | Crude herbal drugs and Chinese patent medicines for external use | AAS and ICP-MS (The same as in Chinese Pharmacopoeia) | Written instructions No. 10/SS/2013 |
| Germany | 5 | — | 0,2 | 0,1 | Herbal medicines | — | Draft recommendation for limits of heavy metals in medicinal products of plant and animal origin 1991 |
| India | 10 | 3 | 0,3 | 1 | Herbs | AAS | Pharmacopoeia of India |
| Japan | 20 | 5 | — | — | Crude herbal drugs | Colourimetric method | Japanese Pharmacopoeia 16th edition |

**Table A.1** *(continued)*

| | Pb[a] | As[a] | Cd[a] | Hg[a] | Object | Analytical methods | Authority organization or regulation |
|---|---|---|---|---|---|---|---|
| Malaysia | 10 | 5 | 0,3 | 0,5 | Traditional medicine products | — | Nationa Pharmaceutical Control Bureau |
| Singapore | 20 | 5 | — | 0,5 | Chinese Proprietary Medicines, traditional medicines and raw medicinal herbs | In accordance with the latest edition of the following pharmacopoeias: British Pharmacopoeia, China Pharmacopoeia, European Pharmacopoeia, United States Pharmacopoeia, etc. | Health Sciences Authority |
| South Korea | 5 | 3 | 0,3 | 0,2 | Crude herbal drugs | AAS and ICP-MS | Korean Pharmacopoeia |
| Thailand | 10 | 4 | 0,3 | — | Herbal plants | AAS | Thai Herbal Pharmacopoeia 2000 |
| UK | 5 | 5 | 1 | 0,1 | Herbal drugs | AAS | British Pharmacopoeia 2012 |
| U.S.A | 5 | 2 | 0,3 | 0,2 | Herbs | ICP-AES, ICP-MS, | US. Pharmacopoeia 35 /National Formulary-Herbal Medicines Compendium |
| USA-California | 0,5[b] | 10[b] | 4,1[b] | — | Herbs | — | State of California Proposition 65 |
| Vietnam | 10 | 4 | 1 | 0,5 | Herbs | AAS | Pharmacopoeia of Vietnam |
| WHO | 10 | — | 0,3 | — | Crude herbal drugs | Colourimetric method and AAS | WHO Guidelines for Assessing Quality of Herbal Medicines with Reference to Contaminants and Residues |
| EU | 5 | — | 1 | 0,1 | Herbal drugs | AAS | European Pharmacopoeia 8,0 |
| Minimum MLs from different nations[c] | 0,5 | 0,5 | 0,2 | 0,1 | / | / | / |