

BS ISO 18664:2015



BSI Standards Publication

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

bsi.

...making excellence a habit.™

National foreword

This British Standard is the UK implementation of ISO 18664:2015.

The UK participation in its preparation was entrusted to Technical Committee CH/100, Healthcare and medical equipment (European and International).

A list of organizations represented on this committee can be obtained on request to its secretary.

This publication does not purport to include all the necessary provisions of a contract. Users are responsible for its correct application.

© The British Standards Institution 2015. Published by BSI Standards Limited 2015

ISBN 978 0 580 82697 9

ICS 11.120.10

Compliance with a British Standard cannot confer immunity from legal obligations.

This British Standard was published under the authority of the Standards Policy and Strategy Committee on 31 July 2015.

Amendments issued since publication

Date	Text affected
------	---------------

INTERNATIONAL
STANDARD

BS ISO 18664:2015

ISO
18664

First edition
2015-08-01

**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*



Reference number
ISO 18664:2015(E)

© ISO 2015



COPYRIGHT PROTECTED DOCUMENT

© ISO 2015, Published in Switzerland

All rights reserved. Unless otherwise specified, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
Ch. de Blandonnet 8 • CP 401
CH-1214 Vernier, Geneva, Switzerland
Tel. +41 22 749 01 11
Fax +41 22 749 09 47
copyright@iso.org
www.iso.org

Contents

Page

Foreword	iv
Introduction	v
1 Scope	1
2 Normative references	1
3 Terms and definitions	2
4 Analytical methods	2
4.1 Instrumental methods	2
4.1.1 Atomic Absorption Spectrometry (AAS)	2
4.1.2 Inductively-Coupled Plasma-Atomic Emission Spectrometry (ICP-AES)	3
4.1.3 Inductively-Coupled Plasma Mass Spectrometry (ICP-MS)	3
4.2 Comparison of instrumental methods	3
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	5
Bibliography	8

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: [Foreword - Supplementary information](#)

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 throughput, 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 Cadmium 0,8 Lead 15 Mercury 300	Excellent for most elements Arsenic 1 Cadmium 0,002 Lead 0,5 Mercury 0,6	Very good for some elements Arsenic 20 Cadmium 0,1 Lead 1 Mercury 1	Excellent for most elements Arsenic < 0,05 Cadmium < 0,05 Lead < 0,05 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	/	/	/

Table A.1 (continued)

	Pb ^a	As ^a	Cd ^a	Hg ^a	Object	Analytical methods	Authority organization or regulation
Maximum MLs from different nations ^c	20	5	1	0,5	/	/	/
Calculating MLs ^d	10	4	2	3	Herbs	Colourimetric method, AAS, ICP-AES, ICP-MS	/

NOTE It would be regarded as safe when THQ is lower than 1. Since the ratio of TCM materials intake to total food each day is 13,3 % (The maximum amount of TCM materials taken by human is about 200 g per day, which of total food is around 1 500 g), so the maximum THQ of heavy metals contributed by TCM materials intake should be 0,133. After getting the safe concentration of heavy metals intake by TCM materials using THQ, it should be divided by the dissolution rate of each heavy metals in TCM materials under different medications (e.g. decoction and powder) to get the reasonable limits of heavy metals in TCM materials.

a Total chemical forms.

b Proposition 65 No Significant Risk Levels (NSRLs) and Maximum Allowable Dose Levels (MADLs) are expressed as a daily intake (µg/day) rather than as a dose (mg/kg).

c The Minimum and Maximum limits are summarized from different nations, regions and organizations above.

d Calculations using Target Hazard Quotients (THQ) given by USEPA.

$$THQ = \frac{C * EF * ED * FIR}{WAB * TA * RFD * 1000}$$

where

C is the concentration of heavy metals intake from TCM materials (mg/kg);

EF is exposure frequency (day/year), here is 30 day/year;

ED is the exposure duration, here is 30 years;

FIR is the materials of TCM ingestion rate (g/day), here is 200 g/day;

WAB is the average body weight (60 kg for adult);

TA is the average exposure time for non-carcinogens (365 days/year × 70 years);

RFD is the oral reference dose. Its value should come from USEPA. However, for arsenic, USEPA only give the *RFD* of inorganic arsenic. Hence, we use Provisional Tolerable Weekly Intake (PTWI) provided by WHO, which has similar meaning as *RFD*, to represent *RFD*. (Lead = 0,025 mg/kg·bw, Arsenic = 0,015 mg/kg·bw, Cadmium = 0,007 mg/kg·bw, Mercury = 0,005 mg/kg·bw).

Bibliography

- [1] ISO 6633, *Fruits, vegetables and derived products — Determination of lead content — Flameless atomic absorption spectrometric method*
- [2] ISO 6637, *Fruits, vegetables and derived products — Determination of mercury content — Flameless atomic absorption method*
- [3] *2007 WHO guidelines for assessing quality of herbal medicines with reference to contaminants and residues Annex 3: Determination of arsenic and toxic metals*
- [4] *The American Herbal Products Association (AHPA), Heavy Metals: Analysis and Limits in Herbal Dietary Supplements. AHPA, US, 2009*

British Standards Institution (BSI)

BSI is the national body responsible for preparing British Standards and other standards-related publications, information and services.

BSI is incorporated by Royal Charter. British Standards and other standardization products are published by BSI Standards Limited.

About us

We bring together business, industry, government, consumers, innovators and others to shape their combined experience and expertise into standards-based solutions.

The knowledge embodied in our standards has been carefully assembled in a dependable format and refined through our open consultation process. Organizations of all sizes and across all sectors choose standards to help them achieve their goals.

Information on standards

We can provide you with the knowledge that your organization needs to succeed. Find out more about British Standards by visiting our website at bsigroup.com/standards or contacting our Customer Services team or Knowledge Centre.

Buying standards

You can buy and download PDF versions of BSI publications, including British and adopted European and international standards, through our website at bsigroup.com/shop, where hard copies can also be purchased.

If you need international and foreign standards from other Standards Development Organizations, hard copies can be ordered from our Customer Services team.

Subscriptions

Our range of subscription services are designed to make using standards easier for you. For further information on our subscription products go to bsigroup.com/subscriptions.

With **British Standards Online (BSOL)** you'll have instant access to over 55,000 British and adopted European and international standards from your desktop. It's available 24/7 and is refreshed daily so you'll always be up to date.

You can keep in touch with standards developments and receive substantial discounts on the purchase price of standards, both in single copy and subscription format, by becoming a **BSI Subscribing Member**.

PLUS is an updating service exclusive to BSI Subscribing Members. You will automatically receive the latest hard copy of your standards when they're revised or replaced.

To find out more about becoming a BSI Subscribing Member and the benefits of membership, please visit bsigroup.com/shop.

With a **Multi-User Network Licence (MUNL)** you are able to host standards publications on your intranet. Licences can cover as few or as many users as you wish. With updates supplied as soon as they're available, you can be sure your documentation is current. For further information, email bsmusales@bsigroup.com.

BSI Group Headquarters

389 Chiswick High Road London W4 4AL UK

Revisions

Our British Standards and other publications are updated by amendment or revision.

We continually improve the quality of our products and services to benefit your business. If you find an inaccuracy or ambiguity within a British Standard or other BSI publication please inform the Knowledge Centre.

Copyright

All the data, software and documentation set out in all British Standards and other BSI publications are the property of and copyrighted by BSI, or some person or entity that owns copyright in the information used (such as the international standardization bodies) and has formally licensed such information to BSI for commercial publication and use. Except as permitted under the Copyright, Designs and Patents Act 1988 no extract may be reproduced, stored in a retrieval system or transmitted in any form or by any means – electronic, photocopying, recording or otherwise – without prior written permission from BSI. Details and advice can be obtained from the Copyright & Licensing Department.

Useful Contacts:

Customer Services

Tel: +44 845 086 9001

Email (orders): orders@bsigroup.com

Email (enquiries): cservices@bsigroup.com

Subscriptions

Tel: +44 845 086 9001

Email: subscriptions@bsigroup.com

Knowledge Centre

Tel: +44 20 8996 7004

Email: knowledgecentre@bsigroup.com

Copyright & Licensing

Tel: +44 20 8996 7070

Email: copyright@bsigroup.com



...making excellence a habit.™