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**Traditional Chinese medicine —
Processed *Aconitum carmichaelii*
lateral root**



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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 of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT), see www.iso.org/iso/foreword.html.

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

Processed *Aconitum carmichaelii* lateral root (*Aconiti Lateralis Radix*, Fuzi, 附子) has been used as a herbal medicine in traditional Chinese medicine for a very long time. It remains a highly valued herb today because of its significant effects. *Aconitum carmichaelii* lateral root is one of the most frequently used herbal medicines in traditional Chinese medicine. Of an approximate total of 80 000 traditional Chinese medicine formulas, around 7,04 % of formulations include *Aconitum carmichaelii* lateral root as an ingredient. Among 113 formulas in the *Treatise on Cold Pathogenic Diseases* (伤寒论),^[1] one of four great classics of traditional Chinese medicine, there are 23 formulations with *Aconitum carmichaelii* lateral root (occupying 20,35 %) as an ingredient. Among 202 formulas in the *Synopsis of Golden Chamber* (金匱要略),^[2] another of the four great classics of traditional Chinese medicine, there are 26 prescriptions with *Aconitum carmichaelii* lateral root as an ingredient (12,87 %). Among 148 Kampo medicines for prescription from the Ministry of Health, Labour and Welfare (MHLW) of Japan, there are 10 prescriptions with *Aconitum carmichaelii* lateral root as an ingredient (6,76 %).

Processed *Aconitum carmichaelii* lateral root contains aconitum alkaloids which have anti-inflammatory, analgesic and cardiotoxic activities. These aconitum alkaloids are irreplaceably effective for injuries, arthritis, neuropathic pain, sequelae of apoplexy, stomach pain, stomach crymodynia, menoxenia, abscesses, deep-rooted carbuncles and sores. Aconitum alkaloids are, however, a double-edged sword. At present, international trade in processed *Aconitum carmichaelii* lateral root is restricted in a number of nations due to the high natural toxicity of processed *Aconitum carmichaelii* lateral root. Also, there are sporadic cases of aconitum alkaloid poisoning reported worldwide due to misuse.

Nonetheless, the toxicity of processed *Aconitum carmichaelii* lateral root can be reduced dramatically with proper processing (such as repeated boiling or steaming), prolonged decocting and dose control. However, standards for processed *Aconitum carmichaelii* lateral root are not yet harmonized at an international level and regulatory authorities in many nations do not adequately differentiate highly toxic forms from less-toxic forms (or even non-toxic forms) of *Aconitum carmichaelii* lateral root.

The six aconite alkaloids [*Aconitine* (AC), *mesaconitine* (MA), *hypoaconitine* (HA), *benzoylaconine* (BAC), *benzoylmesaconine* (BMA) and *benzoylhypoaconine* (BHA)] are commonly used as chemical markers for quality control of processed *Aconitum carmichaelii* lateral root.^[3] AC, MA and HA are toxic diester diterpenoid alkaloids, while BAC, BMA and BHA are active monoester diterpenoid alkaloids. To guarantee safety, efficacy and quality, these six alkaloids are commonly controlled in different pharmacopoeia. Nevertheless, poisoning cases are still occasionally reported. From 1989 to 2010, 140 cases of aconitum poisoning, including one fatal case, were reported in Hong Kong.^[4] Additionally, 17 cases were reported in Taiwan from 1990 to 1999, 2017 cases were reported in China from 1989 to 2008 and 121 cases were reported in Korea from 1995 to 2007.^[5] Multiple reasons for aconitum poisoning exist, include overdoses, inadequate processing, aconitum contamination in other herbs, dispensing and management errors, and hidden risk factors. In the 17 cases reported in Hong Kong, *yunaconitine* (YAC), *crassicauline A* (CCA) and *8-deacetyl-yunaconitine* (DYA) were detected instead of AC, MA and HA in the urine samples of the aconitum poisoning patients.^[4,6] Because YAC, DYA and CCA were detected in the urine of the aconitum poisoning patients, these alkaloids are considered to be hidden risk factors and should be covered in laboratory screenings for toxic compounds.^[6] Therefore, an International Standard is required for *Aconitum carmichaelii* lateral root for quality control of the herb and its products and to ensure the safe use of these medical materials^[5].

This document provides a systematic and practical International Standard for *Aconitum carmichaelii* lateral root to control and guarantee stable quality, to ensure safe and effective use in clinics, to standardize the global market trade and to reduce cases of aconite poisoning.

As national implementation can differ, national standards bodies are invited to modify the values given in 5.2, 5.3 and 5.5 in their national standards. Examples of national and regional values are given in Annex C.

Traditional Chinese medicine — Processed *Aconitum carmichaelii* lateral root

1 Scope

This document specifies minimum requirements and test methods for processed *Aconitum carmichaelii* lateral root (lateral root of *Aconitum carmichaelii* Debx.).

This document applies to processed *Aconitum carmichaelii* lateral root that is sold and used as natural medicines in international trade, including Chinese materia medica (whole medicinal materials) and decoction pieces derived from this plant. Processing methods of *Aconitum carmichaelii* lateral root are excluded.

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

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

ISO 22217, *Traditional Chinese medicine — Storage requirements for raw materials and decoction pieces*

ISO 22258, *Traditional Chinese medicine — Determination of pesticide residues in natural products by gas chromatography*

ISO 23191, *Traditional Chinese medicine — Determination of selected Aconitum alkaloids by high-performance liquid chromatography (HPLC)*

World Health Organization *Quality control methods for herbal materials*, 2011

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

fresh *Aconitum carmichaelii* lateral root

fresh lateral root of *Aconitum carmichaelii* Debx. with the tap root, rootlet and soil removed

3.2

***Aconitum carmichaelii* lateral root**

unprocessed dried lateral root of *Aconitum carmichaelii* Debx.