



PRACTITIONER ALERT

17 August 2000

Dear Practitioner Association and/or Healthcare Practitioner

The Therapeutic Goods Administration (TGA) would like to bring to your attention important safety information about botanical products containing *Aristolochia* species. We ask that you share this information with members of your professional association and other interested parties.

The TGA, along with overseas regulatory agencies, is very concerned about Traditional Chinese Medicine (TCM) herbal products that are known to contain, or suspected to contain, *Aristolochia* species. These species of herbs, and a small number of other herbs, may contain aristolochic acids which are associated with severe kidney damage (1) and urinary tract cancer (2).

Most of the herbal products found to contain aristolochic acids have been shown to be present because certain species of *Aristolochia* have been substituted for other species. These other species belong to the following genera:

Akebia, *Asarum*, *Bragantia*, *Clematis*, *Cocculus*, *Diploclisia*, *Menispermum*, *Saussurea*, *Sinomenium*, *Stephania*, *Vladimiria*.

The particular species from these genera are listed in the Attachment to this PRACTITIONER ALERT. This list is made up of three groups of herbal products as follows:

- Botanicals known or suspected to contain aristolochic acid (Group A);
- Botanicals which may be adulterated with aristolochic acid*(Group B); and
- Products which have MuTong and Fang Ji as declared ingredients (Mu Tong and Fang Ji are TCM names for products which may contain *Aristolochia* species) (Group C).

* There is unintended inclusion of *Aristolochia* in some herbal medicines because of confusion created by the fact that some herbs are very similar either in name or in appearance. There is also the possibility that certain herbal ingredients may be interchanged as part of the practice of Traditional Chinese Medicine.

While the TGA is currently testing all products on the Australian Register of Therapeutic Goods (ARTG) which may contain aristolochic acids, there are other products which are for practitioner-only use, many in the form of raw herbs, that are not regulated by the TGA.

This PRACTITIONER ALERT is to inform practitioner groups and their members of the identity of herbal products or materials which are now recognised as being at risk of containing *Aristolochia* species or the aristolochic acids. This information should be brought to the attention of all healthcare practitioners who might prescribe, dispense, administer or otherwise handle or use such herbal products or materials.

Healthcare practitioners are asked to take extreme caution in using herbal products, in raw or formulated form, if the name of any of the herb(s) appears on the attached list. If healthcare practitioners are uncertain about the identity and authenticity of any of the herbal materials or products on the attached list, they should consider discontinuing their use.

The TGA is not aware of any adverse reaction reports associated with the inadvertent administration of herbal products in Australia containing *Aristolochia* species although serious adverse events have been reported in the international literature. Healthcare practitioners are encouraged to take a thorough patient history of use of traditional and other complementary medicines and dietary supplements, especially in cases of unexplained renal pathology. Adverse reactions suspected to be associated with herbal products or preparations may be reported to the Adverse Drug Reactions Unit at the TGA on 02 6232 8381.

BACKGROUND

- All species of *Aristolochia* are prohibited for supply, sale or use in therapeutic goods in Australia under the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP). However, *Aristolochia* species are finding their way into other herbal-based TCM products, including herbs in raw form, because they are easily confused with other herbs by being very similar, either in appearance or in name, to some other TCM herbs.
- Such confusion has led to inadvertent administration of *Aristolochia*, with two very serious incidents overseas in recent years (1, 2) raising international concern and calls for greater vigilance in preventing *Aristolochia*-containing products from reaching the market.
- Following both of these incidents, one in 1993 in Belgium and the other in 1999 in the UK, the Therapeutic Goods Administration (TGA) sampled implicated products on the market and, in both cases, following the detection of *Aristolochia* in some products, withdrew those products immediately from the Australian market
- International concern remains high over trade in herbal products which are at risk of unintentionally including *Aristolochia* species or the aristolochic acids. The TGA has recently worked with overseas regulatory agencies to identify which other species and products have the greatest potential of containing the toxic aristolochic acids. The list which is attached to this PRACTITIONER ALERT has been developed on the basis of these concerns and consists of species from 11 genera, which are thought to either contain aristolochic acids or which are at risk of being adulterated with *Aristolochia* species.
- The TGA considers it important to bring the matter to the attention of practitioner associations so that they may be aware of the potential concerns.

For further details on this matter please contact the TGA or view the TGA Web-site as below:

Contact Officer: Dr John Hall, Office of Complementary Medicines Phone: 02 6232 8062
Website: www.health.gov.au/tga

Bibliography

1. Lord GM et al (1999) "Nephropathy caused by Chinese herbs in the UK". Lancet **354**: 481 – 482.
2. Nortier JL et al (2000) "Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*)". New England Journal of Medicine **342**: 1686 – 1692.

**BOTANICALS OR PRODUCTS AT RISK OF
CONTAINING ARISTOLOCHIC ACIDS**

Group A - Botanicals Known or Suspected to Contain Aristolochic Acid

Genus	Botanical Name	Common or Other Names
<i>Aristolochia</i>	<i>Aristolochia</i> spp.	Aristolochia Guan mu tong Guang mu tong
	<i>Aristolochia acuminata</i> Lam. Syn. <i>Aristolochia tagala</i> Champ.	Oval leaf Dutchman's pipe
	<i>Aristolochia argentina</i> Griseb.	
	<i>Aristolochia baetica</i> Linn. Syn. <i>Aristolochia bracteolata</i> Lam.	
	<i>Aristolochia bracteata</i> Retz.	Ukulwe
	<i>Aristolochia chilensis</i> Bridges in Lindl.	
	<i>Aristolochia cinnabarina</i> C.Y. Cheng & J.L. Wu	
	<i>Aristolochia clematitidis</i> L.	Birthwort
	<i>Aristolochia contorta</i> Bunge	Ma dou ling Tian xian teng
	<i>Aristolochia cymbifera</i> Mart. & Zucc.	Mil homens
	<i>Aristolochia debilis</i> Siebold & Zucc. Syn. <i>A. longa</i> Thunb. Syn. <i>A. recurvilabra</i> Hance Syn. <i>A. sinarum</i> Lindl.	Ma dou ling Tian xian teng Qing mu xiang Sei- mökkou (Japanese) Birthwort Long birthwort
	<i>Aristolochia elegans</i> Mast. Syn. <i>Aristolochia hassleriana</i> Chodat	
	<i>Aristolochia esperanzae</i> Kuntze	
	<i>Aristolochia fangchi</i> Y.C. Wu ex L.D. Chow & S.M. Hwang	Guang fang ji Fang ji Mokuboi (Japanese) Kwangbanggi (Korean) Fang chi Kou-boui (Japanese)
	<i>Aristolochia fimbriata</i> Cham.	
<i>Aristolochia indica</i> L.	Indian birthwort	

Group A - Botanicals Known or Suspected to Contain Aristolochic Acid (cont)

Genus	Botanical Name	Common or Other Names
<i>Aristolochia (cont)</i>	<p><i>Aristolochia kaempferi</i> Willd. Syn. <i>Aristolochia chrysops</i> (Stapf) E.H. Wilson ex Rehder Syn. <i>Aristolochia feddei</i> H. Lév. Syn. <i>Aristolochia heterophylla</i> Hemsl. Syn. <i>Aristolochia mollis</i> Dunn Syn. <i>Aristolochia setchuenensis</i> Franch. Syn. <i>Aristolochia shimadai</i> Hayata Syn. <i>Aristolochia thibetica</i> Franch. Syn. <i>Isotrema chrysops</i> Stapf Syn. <i>Isotrema heterophylla</i> (Hemsl.) Stapf Syn. <i>Isotrema lasiops</i> Stapf</p>	Yellowmouth Dutchman's pipe
	<p><i>Aristolochia kwangsiensis</i> Chun & F.C. How Syn. <i>Aristolochia austroszechuanica</i> C. B. Chien & C. Y. Cheng</p>	
	<p><i>Aristolochia macrophylla</i> Lam. Syn. <i>Aristolochia siphon</i> L'Hér.</p>	Dutchman's-pipe
	<p><i>Aristolochia manshuriensis</i> Kom. Syn. <i>Hocquartia manshuriensis</i> (Kom.) Nakai Syn. <i>Isotrema manshuriensis</i> (Kom.) H. Huber</p>	Manchurian birthwort Manchurian Dutchman's pipe Guang mu tong Kan-Mokutsu (Japanese) Mokuboi (Japanese) Kwangbanggi (Korean)
	<p><i>Aristolochia maurorum</i> L.</p>	
	<p><i>Aristolochia maxima</i> Jacq. Syn. <i>Aristolochia maxima</i> var. <i>angustifolia</i> Duchartre in DC. Syn. <i>Howardia hoffmannii</i> Klotzsch</p>	
	<p><i>Aristolochia mollissima</i> Hance</p>	
	<p><i>Aristolochia pistolochia</i> L.</p>	
	<p><i>Aristolochia rigida</i> Duch.</p>	
	<p><i>Aristolochia rotunda</i> Linn.</p>	
	<p><i>Aristolochia serpentaria</i> L. Syn. <i>Aristolochia serpentaria</i> var. <i>hastata</i> (Nutt.) Duch.</p>	Virginia snakeroot Serpentaria Virginia serpentary
	<p><i>Aristolochia watsoni</i> Wooton & Standley or <i>Aristolochia watsonii</i> Wooton & Standley Syn. <i>Aristolochia porphyrophylla</i> Pfeifer</p>	
	<p><i>Aristolochia westlandii</i> Hemsl. or <i>Aristolochia westlandi</i> Hemsl.</p>	

Group A - Botanicals Known or Suspected to Contain Aristolochic Acid (cont)

Genus	Botanical Name	Common or Other Names
<i>Aristolochia (cont)</i>	<p><i>Aristolochia zollingeriana</i> Miq. Syn. <i>Aristolochia kankauensis</i> Sasaki Syn. <i>Aristolochia roxburghiana</i> subsp. <i>kankauensis</i> (Sasaki) Kitam. Syn. <i>Hocquartia kankauensis</i> (Sasaki) Nakai ex Masam. Syn. <i>Aristolochia tagala</i> var. <i>kankauensis</i> (Sasaki) T. Yamaz.</p>	
<i>Asarum</i>	<p><i>Asarum canadense</i> Linn. Syn. <i>Asarum acuminatum</i> (Ashe) E.P. Bicknell Syn. <i>Asarum ambiguum</i> (E.P. Bicknell) Daniels Syn. <i>Asarum canadense</i> var. <i>ambiguum</i> (E.P. Bicknell) Farw. Syn. <i>Asarum canadense</i> var. <i>reflexum</i> (E.P. Bicknell) B.L. Rob. Syn. <i>Asarum furcatum</i> Raf. Syn. <i>Asarum medium</i> Raf. Syn. <i>Asarum parvifolium</i> Raf. Syn. <i>Asarum reflexum</i> E.P. Bicknell Syn. <i>Asarum rubrocinctum</i> Peattie</p>	<p>Wild ginger Indian ginger Canada snakeroot False coltsfoot Colic root Heart snakeroot Vermont snakeroot Southern snakeroot</p>
<i>Asarum</i>	<p><i>Asarum himalaicum</i> Hook. f. & Thomson ex Klotzsch or <i>Asarum himalaycum</i> Hook. f. & Thomson ex Klotzsch</p>	<p>Tanyou-saishin (Japanese)</p>
	<p><i>Asarum splendens</i> (F. Maek.) C.Y. Cheng & C.S. Yang</p>	<p>Do-saishin (Japanese)</p>
<i>Bragantia</i>	<p><i>Bragantia wallichii</i> R.Br. Specimen exists at New York Botanical Gardens. Tropicos does not list this species as a synonym for any <i>Thottea</i> species. Kew Gardens Herbarium does not recognize the genera <i>Bragantia</i>. Until additional information is obtained we will use the name as cited in J.Nat. Products 45:657-666 (1982)</p>	

Group B - Botanicals Which May Be Adulterated With Aristolochic Acid

Genus	Botanical Name	Common or Other Names
<i>Akebia</i>	<i>Akebia</i> spp.	Akebia Mu tong Ku mu tong Zi mutong Bai mu tong Mokutsu (Japanese) Mokt'ong (Korean)
	<i>Akebia quinata</i> (Houtt.) Decne. Syn. <i>Rajania quinata</i> Houtt.	Chocolate vine Fiveleaf akebia Mu tong Yu zhi zi Mokutsu (Japanese)
	<i>Akebia trifoliata</i> (Thunb.) Koidz).	Mu tong Three leaf akebia Yu zhi zi
<i>Asarum</i>	<i>Asarum forbesii</i> Maxim.	Batei-saishin (Japanese)
	<i>Asarum heterotropoides</i> F. Schmidt Syn. <i>Asarum heterotropoides</i> F. Schmidt Syn. <i>Asiasarum heterotropoides</i> (F. Schmidt) F. Maek.	Keirin-saishin (Japanese) Chinese wild ginger Manchurian wild ginger Bei xi xin Xin xin
	<i>Asarum sieboldii</i> Miq. Syn. <i>Asarum sieboldii</i> fo. <i>seoulense</i> (Nakai) C.Y. Cheng & C.S. Yang Syn. <i>Asarum sieboldii</i> var. <i>seoulensis</i> Nakai Syn. <i>Asiasarum heterotropoides</i> var. <i>seoulense</i> (Nakai) F. Maek. Syn. <i>Asiasarum sieboldii</i> (Miq.) F. Maek.	Usuba-saishin (Japanese) Chinese wild ginger Xi Xin Hua Xi Xin Manchurian wild ginger Siebold's wild ginger
<i>Clematis</i>	<i>Clematis</i> spp.	Clematis Mufangji Clematidis Ireisen (Japanese) Wojoksum (Korean)

Group B - Botanicals Which May Be Adulterated With Aristolochic Acid (cont)

Genus	Botanical Name	Common or Other Names
<i>Clematis (cont)</i>	<p><i>Clematis armandii</i> Franch. Syn. <i>Clematis armandii</i> fo. <i>farquhariana</i> (W.T. Wang) Rehder & E.H. Wilson Syn. <i>Clematis armandii</i> var. <i>biondiana</i> (Pavol.) Rehder Syn. <i>Clematis biondiana</i> Pavol. Syn. <i>Clematis ornithopus</i> Ulbr.</p>	<p>Armand's clematis Chuan mu tong (stem) Xiao mu tong Armand's virgin bower</p>
	<i>Clematis chinensis</i> Osbeck.	Chinese clematis Wei ling xian (root)
	<i>Clematis hexapetala</i> Pall.	
	<i>Clematis montana</i> Buch.-Ham. ex DC. Syn. <i>Clematis insulari-alpina</i> Hayata	
	<i>Clematis montana</i> Buch.-Ham. Ex DC.	
	<p><i>Clematis uncinata</i> Champ. ex Benth. Syn. <i>Clematis alsomitriifolia</i> Hayata Syn. <i>Clematis chinensis</i> var. <i>uncinata</i> (Champ. ex Benth.) Kuntze Syn. <i>Clematis drakeana</i> H. Lév. & Vaniot Syn. <i>Clematis floribunda</i> (Hayata) Yamam. Syn. <i>Clematis gagnepainiana</i> H. Lév. & Vaniot Syn. <i>Clematis leiocarpa</i> Oliv. Syn. <i>Clematis ovatifolia</i> T. Ito ex Maxim. Syn. <i>Clematis uncinata</i> var. <i>bitermata</i> W.T. Wang Syn. <i>Clematis uncinata</i> var. <i>coriacea</i> Pamp. Syn. <i>Clematis uncinata</i> var. <i>floribunda</i> Hayata Syn. <i>Clematis uncinata</i> var. <i>ovatifolia</i> (T. Ito ex Maxim.) Ohwi ex Tamura Syn. <i>Clematis uncinata</i> var. <i>taitongensis</i> Y.C. Liu & C.H. Ou</p>	
<i>Cocculus</i>	<i>Cocculus</i> spp.	Cocculus
	<p><i>Cocculus carolinus</i> (L.) DC. Syn. <i>Cebatha carolina</i> Britton Syn. <i>Epibaterium carolinum</i> (L.) Britton Syn. <i>Menispermum carolinum</i> L.</p>	
	<p><i>Cocculus diversifolius</i> DC. Syn. <i>Cocculus madagascariensis</i> Diels</p>	
	<p><i>Cocculus hirsutus</i> (L.) Diels Syn. <i>Cocculus villosus</i> DC. Syn. <i>Menispermum hirsutum</i> L.</p>	
	<p><i>Cocculus indicus</i> Royle Syn. <i>Anamirta paniculata</i> Colebr.</p>	Indian cockle
	<p><i>Cocculus laurifolius</i> DC. Syn. <i>Cinnamomum esquirolii</i> H. Lév.</p>	
	<i>Cocculus leaebe</i> DC.	

Group B - Botanicals which may be Adulterated with Aristolochic Acid (cont)

Genus	Botanical Name	Common or Other Names
<i>Cocculus (cont)</i>	<i>Cocculus madagascariensis</i> Diels Syn. <i>Cocculus diversifolius</i> DC.	
	<i>Cocculus orbiculatus</i> DC. Syn. <i>Cissampelos pareira</i> Linn.	
	<i>Cocculus orbiculatus</i> (L.) DC. Syn. <i>Cocculus cuneatus</i> Benth. Syn. <i>Cocculus sarmentosus</i> (Lour.) Diels Syn. <i>Cocculus sarmentosus</i> var. <i>linearis</i> Yamam. Syn. <i>Cocculus sarmentosus</i> var. <i>pauciflorus</i> Y.C. Wu Syn. <i>Cocculus sarmentosus</i> var. <i>stenophyllus</i> Merr. Syn. <i>Cocculus thunbergii</i> DC. Syn. <i>Cocculus trilobus</i> (Thunb.) DC. Syn. <i>Menispermum orbiculatus</i> L. Syn. <i>Menispermum trilobum</i> Thunb. Syn. <i>Nephroia sarmentosa</i> Lour.	Moku-boui (Japanese)
	<i>Cocculus palmatus</i> (Lam.) DC.	Columba Columbo
	<i>Cocculus pendulus</i> Diels Syn. <i>Cebatha pendula</i> (J.R. & C. Forst.) Kuntze Syn. <i>Epibaterium pendulus</i> Forst. f. Syn. <i>Cocculus Epibaterium</i> DC.	
	<i>Cocculus pendulus</i> (Forst. & Forst.) Diels	
	<i>Cocculus palmatus</i> Hook. Syn. <i>Jateorhiza Miersii</i> Oliver	Colombo
	<i>Cocculus thunbergii</i> DC.	
	<i>Diploclisia</i>	<i>Diploclisia affinis</i> (Oliv.) Diels Syn. <i>Diploclisia chinensis</i> Merr. Syn. <i>Cocculus affinis</i> Oliv.
<i>Diploclisia chinensis</i> Merrill		Xiangfangchi
<i>Menispermum</i>	<i>Menispermum dauricum</i>	
<i>Saussurea</i>	<i>Saussurea lappa</i> (Decne.) Sch. Bip.	Mokkou (Japanese)
<i>Sinomenium</i>	<i>Sinomenium acutum</i> (Thunb.) Rehder & E.H. Wilson Syn. <i>Cocculus diversifolius</i> var. <i>cinereus</i> Diels Syn. <i>Cocculus heterophyllus</i> Hemsl. & E.H. Wilson Syn. <i>Menispermum acutum</i> Thunb. Syn. <i>Sinomenium acutum</i> (Thunb.) Rehder & E.H. Wilson var. <i>cinereum</i> (Diels) Rehder & E.H. Wilson Syn. <i>Sinomenium diversifolium</i> (Diels) Diels	Orientvine Xunfengteng Dafengteng Daqingmuxinag Zhuigusan Da ye qingshener Mufangji Hanfangji Tuteng Zhuigufeng Maofangji

Group B - Botanicals Which May Be Adulterated With Aristolochic Acid (cont)

Genus	Botanical Name	Common or Other Names
<i>Stephania</i>	<i>Stephania</i> spp.	Stephania
	<i>Stephania tetrandra</i> S. Moore	Fen fang ji , fang ji Fang ji (root) Han fang ji Kanboi (Japanese) Hanbanggi (Korean) Fun-boui (Japanese)
<i>Vladimiria</i>	<i>Vladimiria souliei</i> (Franch.) Ling	Sen-mokkou

Group C – Products Which Have Mu Tong And Fang Ji As Declared Ingredients

Ba Zheng Wan
 Chun Yang Zheng Ji Wan
 Da Huang Qing Wei Wan
 Dang Gui Si Ni Wan
 Dao Chi Wan
 Dieda Wan
 Fu Ke Fen Qing Wan
 Guan Xin Su He Wan
 Ji Sheng Ju He Wan
 Kat Kit Wan
 Long Dan Xie Gan Wan
 Quell Fire
 Shi Xiang Fan Shen Wan
 Xin Yi Wan