Chinese Patent Traditional Medication Containing Aristolochic Acid and its Herbal Medicinal Plant, Efficacy and Harmfulness

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Abstract  The nephrotoxicity of traditional herbal medications containing aristolochial acid has attracted wide attention in China and abroad, and some countries have banned the use of traditional herbal medications containing aristolochic acid. In this study, the traditional herbal materials and patent traditional herbal medications containing aristolochic acid were statistically analyzed. Among the common traditional herbal medications containing aristolochic acid, there are 14 kinds of aristolochial plants and 10 kinds of Asarum plants, of which there are 24 kinds of herbal materials from the family of Aristolochiaceae that may contain aristolochic acid and 47 kinds of patent traditional herbal medications that have been listed that may contain aristolochic acid from the genus of Aristolochia L.. In this review, these medicinal plants were systematically analyzed. It was concluded that the renal toxicity of herbal medication containing aristolochic acid should be paid enough attentions even though Aristolochia herbs have a special significance in traditional herbal medication of China.

Keywords  Chinese patent traditional medication; Traditional herbal plant; Aristolochic acid; Aristolochia L.; Asarum L.

English Chinese glossary and their abbreviation in this paper:
Chinese Traditional Medicine: CTM，中医学
Chinese Traditional Doctor: CTD，中医生
Chinese Traditional Medicine and Herbal Medication: CTMHM，中医药或中国传统医药
Chinese Traditional Herbal Medication: CTHM，中药，中草药
Chinese Patent Traditional Herbal Medication: CPTHM，中成药
Chinese Traditional Herbal Material: CTHM，中药材
Chinese Traditional Herbal Medicinal Plant: CTHMP，中草药植物
Herbal Medication: HM，草药
Herbal Medicinal Plant: HMP，草药植物

In this paper, the commodity name of Chinese traditional herbal medication or Chinese patent traditional herbal medication is written in Chinese Pinyin; the name of Chinese traditional herbal material is written in Chinese Pinyin plus Latin scientific name in bracket, such as: Dayeqingmuxiang, written as dayeqingmuxiang (A. austroechuanica L.).

Aristolochial acids, AA, is also known as total aristolochic acids, phagogenic acids or lignoceptors, which are a type of nitrophenanthranilic acids. Aristolochial acids naturally exists in Aristolochia, such as Aristolochia and Asarum. These plants are widely used as Chinese traditional herbal medications.

In 2002, International Agency for Research on Cancer evaluated the carcinogenic risks and labelled Aristolochial acids as Class I carcinogen and found that it is carcinogenic to human (Cosyns, 2003; Gold and Slone, 2003). Europe, the United States, Taiwan and Hong Kong continuously banned the use of traditional
herbal medications containing aristolochic acids, but Mainland China did not permorphology those actions (Suborova et al., 1994; Schmeiser et al., 1996; Lord et al., 1999).

Aristolochic acids have specially meanings in the traditional medicine field. Aristolochic acids causes renal failure was reported in 2003, which altered the understanding of traditional herbal medication being toxic-free and side-effects-free. This caused people to have significantly opposite understanding of the toxicity of traditional herbal medication and the medical field began to reexamine the safety issues of traditional herbal medications.

Under the sponsor of State Administration of Traditional Chinese Medicine, the experiment on the safety of traditional herbal medications included herbal medicines that contains aristolochic acids (Guan Mu Tong, Guang Fang Ji, and Long Dan Xie Gan Wan). The conclusion was that all traditional herbal medications containing aristolochic acids should be strictly regulated or banned and replacements for the medicines should be found as soon as possible (Bai et al., 2018).

Unfortunately, in the 2005 edition of Chinese National Pharmacopoeia, only three medicines that are considered to contain higher concentrations of aristolochic acids, i.e. Guang Fang ji, Qing Mu Xiang, and Guan Mu Tong have been banned. Other traditional herbal medications containing aristolochic acids are listed as prescriptive medications, which was the way to reduce or regulate the usage of aristolochic acids’ medications.

In October 2017, a blockbuster paper of aristolochic acids was appeared on the cover of a leading medical journal of Science Translation Medicine. This research showed that traditional herbal medications containing aristolochic acids is one of the more important cause for Asian liver cancer. This report created a arguable question: should aristolochic acids be banned or restricted?

Aristolochic acid is commonly found in traditional Chinese herbal materials, such as, Ma Dou Ling, Guan Mu Tong, Tian Xian Teng, Qing Mu Xiang, Guang Fang Ji, Han Zhong Fang Ji, Xi Xin, Zhiu Feng Teng, Xun Gu Feng, Huai Tong, Zhu Sha Lian, San Tong Guan, Du Heng, Guan Nan Xiang, Nan Mu Xiang, Teng Xiang, Bei She Shen, Jia Da Shu, Hu Die An Xiao, Bi Xue Lei, Bai Jin Guo Lan, Jin Er Huan, Wu Jin, etc. (Lu, 2002). These herbal materials mostly belong to Aristolochia and Asarum in Aristolochiaceae plant, among which there are dozens of plants, such as Ma Dou Ling, Shan Ci Gu, Du Heng, Tu Mu Xiang, Zhu Sha Lian, Xun Gu Feng, Xi Xin, Fang Ji, Mu Fang Ji, etc.. In order to have a better understanding of the biological taxonomix status and characteristics of these pants, this paper systemically analyzed the plants containing aristolochic acids, providing a fundamental reference for reasonable choosing and usage of these types of medications.

1 Chinese Patent Traditional Herbal Medications Containing Aristolochic Acids
Aristolochic acids (AA) is a type of nitrophenanthrene organic acid compound (Peng et al., 2013). Aristolochic acids naturally exist in genus Aristolochia, genus Asarum, and other plants in the Aristolochiaceae family. These plants were widely used for detoxification purposes. Moreover, the butterflies that rely on these plants as food has has aristolochic acids in their bodies. Aristolochic acid I is the most common aristolochic acid compound. It can be found in all Aristolochia plants and it is coexist with aristolactams.

Chinese National Medical Products Administration released“List of Aristolochiae herbs that may contain aristolochic acid“and“List of Chinese patent traditional herbal medications that may contain Aristolochiae herbs”, in which there are 24 herbal medicines containing aristolochic acids and there are 47 medicines on sale that contains aristolochic acids. (Table 1) (Wang Zhimin, 2002, Chinese Journal of Inmorphologyation on Traditional Chinese Medicine, 27(10): 800). According to the Chinese National Medical Products Administration, in commonly used herbal medicines containing aristolochic acids, 14 of them are Aristolochia plants used for medication and 10 of them are Asarum plants.
### Table 1: The list of Chinese patent traditional herbal medications that may contain herbal materials of genus *Aristolochia*

| S/N | Name of patent traditional herbal medications | Containing herbal materials of genus *Aristolochia* |
|-----|-----------------------------------------------|---------------------------------------------------|
| 1   | TongDiJiaoNang (通迪胶囊)                     | *Aristolochia debilis* Sieb. et Zucc. (大青木香) |
| 2   | FuFangWeiTongJiaoNang (复方胃痛胶囊)            | *Aristolochia yunnanensis* Franch. (九月生) |
| 3   | ChuanXiLingJiaoNang (喘息灵胶囊)                 | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 4   | ErShiWeiShuGanJiaoNang (二十味疏肝胶囊)        | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 5   | FeiAnPian (肺安片)                             | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 6   | FuFangSheDanChuanBeiSan (复方蛇胆川贝散)       | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 7   | JiMingWan (鸡鸣丸)                             | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 8   | JiSuWan (鸡苏丸)                               | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 9   | QiShiWeiSongShiWan (七十味松石丸)              | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 10  | QingGueZhiKeWan (青果止咳丸)                    | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 11  | RunFeiHuaTanWan (润肺化痰丸)                    | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 12  | ShiSanWeiShuGanJiaoNang (十三味疏肝胶囊)        | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 13  | ShiSiWeiShuGanJiaoNang (十四味疏肝胶囊)        | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 14  | SiSiWeiShuGanJiaoNang (四十二味疏肝胶囊)       | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 15  | WeiFuKeLi (胃福颗粒)                            | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 16  | XiaoErErKeKouFuYe (消咳平喘口服液)              | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 17  | ZhiKeHuaTanWan (止嗽化痰丸)                     | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 18  | JingZhiKeSouTanChuanWan (京制咳嗽痰喘丸)       | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 19  | XiaoKePingChuanKouFuYe (消咳平喘口服液)        | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 20  | ZhiKeHuaTanJiaoNang (止嗽化痰胶囊)               | *Aristolochia debilis* Sieb. et Zucc. (马兜铃) |
| 21  | ErShiJiuWeiNengXiaoSan (二十九味能消散)          | *Aristolochia lappa* Decne. (木香马兜铃) |
| 22  | ErShiShiWeiLvRongHaoJiaoNang (二十五味绿绒蒿胶囊) | *Aristolochia lappa* Decne. (木香马兜铃) |
| 23  | ErShiShiWeiLvRongHaoWan (二十五味绿绒蒿丸)     | *Aristolochia lappa* Decne. (木香马兜铃) |
| 24  | ErShiShiWeiSongShiWan (二十五味松石丸)         | *Aristolochia lappa* Decne. (木香马兜铃) |
| 25  | ErShiShiWeiYuGanZiWan (二十五味余甘子丸)       | *Aristolochia lappa* Decne. (木香马兜铃) |
| 26  | ErShiShiWeiLanHuangSan (二十五味竺黄散)         | *Aristolochia lappa* Decne. (木香马兜铃) |
| 27  | FengShiZhiLongJiaoNang (风湿塞隆胶囊)            | *Aristolochia lappa* Decne. (木香马兜铃) |
| 28  | FengShiZhiTongWan (风湿通痹丸)                   | *Aristolochia lappa* Decne. (木香马兜铃) |
| 29  | GanChangJiaoNang (肝畅胶囊)                      | *Aristolochia lappa* Decne. (木香马兜铃) |
| 30  | JiuWeiNiJiaoWan (九味牛黄丸)                     | *Aristolochia lappa* Decne. (木香马兜铃) |
| 31  | QiWeiHongHuaShuShengSan (七味红花舒胜散)      | *Aristolochia lappa* Decne. (木香马兜铃) |
| 32  | QiWeiHongHuaShuShengWan (七味红花舒胜丸)      | *Aristolochia lappa* Decne. (木香马兜铃) |
| 33  | QingFeiZhiKeWan (清肺止咳丸)                     | *Aristolochia lappa* Decne. (木香马兜铃) |
| 34  | SiWeiZhiXieMuTangSan (四味止泻木汤散)           | *Aristolochia lappa* Decne. (木香马兜铃) |
| 35  | WuWeiZhaXunWang (五味渣驯丸)                     | *Aristolochia lappa* Decne. (木香马兜铃) |
| 36  | HeWeiJiangNiJiaoWan (和胃降逆胶囊)               | *Aristolochia lappa* Decne. (木香马兜铃) |
| 37  | FuFangFengShiYaoJiu (复方风湿药酒)               | *Aristolochia mollissima* Hance (寻骨风) |
| 38  | FuFangQuanShenPian (复方拳参片)                  | *Aristolochia mollissima* Hance (寻骨风) |
| 39  | QuFengChaShiYaoJiu (祛风除湿药酒)                | *Aristolochia mollissima* Hance (寻骨风) |
| 40  | SanSheYaoJiu (三蛇药酒)                          | *Aristolochia mollissima* Hance (寻骨风) |
| 41  | ShenNongYaoJiu (神农药酒)                        | *Aristolochia mollissima* Hance (寻骨风) |
| 42  | YiShenJuanBiWan (益肾蠲痹丸)                     | *Aristolochia mollissima* Hance (寻骨风) |
| 43  | DuZhongZhuangGuJiaoNang (杜仲壮骨胶囊)            | *Aristolochia mollissima* Hance (寻骨风) |
| 44  | DuZhongZhuangGuWan (杜仲壮骨丸)                   | *Aristolochia mollissima* Hance (寻骨风) |
| 45  | BaoWeiJiaoNang (保胃胶囊)                         | *Aristolochia mollissima* Hance (寻骨风) |
| 46  | JinZhuZhiXiePian (金朱止泻片)                     | *Aristolochia mollissima* Hance (寻骨风) |
| 47  | ZhuShanLianJiaoNang (朱砂莲胶囊)                  | *Aristolochia mollissima* Hance (寻骨风) |

Note: These mentioned above do not include external preparations; Chinese name in brackets.
2 Aristolochia L. as Traditional Herbal Medications

There are about 500 types of Aristolochia L., which mainly distribute in tropical and temperate areas, it is a kind of rare subshrubs or small trees of herbaceous or woody vines under Aristolochiaceae. *Aristolochia debilis* L., its Chinese name came from the similarity of the fruit and the bell under the horse's neck. MaDouLing has the effect of clearing lungs, reducing coughing, clearing intestines and haemorrhoids. Its stem called TianXianTeng has the effect of regulating breathing, clearing damp, promoting blood circulation and reducing pain. Its root called QingMuXiang has the effect of promoting circulation of oxygen in the body and detumescence by detoxification.

Aristolochia plants contain aristolochic acids, aristolactams, aristoquinolines, aristogins, and various chemical substances such as sesquiterpenes. These chemical substances grow in different environments due to different parts of the plants and types of the plants.

Many aristolochia plants can be used as medicines, such as, *A. debilis, A. contorta, A. manshuriensis*, and *A. fangchi* (Table 2). There are also different Chinese names for different parts of the plant. For example, MuTong MaDouLing's stem is called Mu Tong, MaDouLing, BeiMaDouLing, and MuXiangMaDouLing's fruit are all called MaDouLing. There stems are called TianXianTeng; together with GuangFang Ji's roots are all very common traditional herbal medications. Others such as BeiSheSheng, Er Ye MaDouLing, TongChengHu, and GuangXiMaDouLing's roots are all commonly used traditional herbal medications.

Table 2 Chinese traditional herbal materials containing aristolochic acid in the genus of Aristolochia

| Name of herbal materials | Original herbal plant |
|--------------------------|-----------------------|
| DaYeQingMuXiang (大叶青木香) | A. austrozechaunica (大叶马兜铃) |
| DaBaiJieShu (大白解) | A. chui (土木香) |
| ZhuShaLian (朱砂莲) | A. cinnabarina (四川朱砂莲), A. tuberosa (朱砂莲) |
| Ju YueSheng (九月生(朱砂莲)) | A. Tuberosa C.F. Liang et S.M.Hwang (广西朱砂莲) |
| Herba Aristolochiaceae (天仙藤 (马兜铃藤)) | A. contorta (北马兜铃), A. debilis (马兜铃) |
| Radix Stephaniae Tetrandrae (防己) | A. heterophylla (异叶马兜铃), A. austrozechaun (川南马兜铃), A. moupinensis (穆坪马兜铃) |
| Tetrandr (汉防己) | A. heterophylla (异叶马兜铃) |
| Caulis Clematidis Armandii (淮通) | A. moupinensis (穆坪马兜铃), A. lappa Decne. (木香马兜铃) |
| Radix Cocculi Trilobi (木防己 (水城木防己)) | A. lappa Decne. (木香马兜铃), A. ovatifolia (卵叶马兜铃) |
| Costustoot (木香马兜铃) | A. lappa Decne. (木香马兜铃), A. moupinensis (穆坪马兜铃), A. griffithiiYhoms ex Duchartre (藏马兜铃 (藏木通)) |
| Radix Aristolochiaceae (大青木香) | A. kwangsiensis Chun et How (广西马兜铃) |
| Mianning Radix Stephaniae Tetrandrae (冕宁防己) | A. moupinensis (穆坪马兜铃) |
| Wooly Dutchmanspipe Herb (寻骨风) | A. mollissima (绵毛马兜铃) |

Note: Chines name in brackets

3 Asarum's Function in Traditional Herbal Medications

*Asarum* L. is a genus under Aristolochiaceae. There are about 90 of them. They are also divided into two subgenus: Asarum and Dueng. They are mostly present in warm places, mainly in eastern and southern parts of Asia. Some of them grow in northern parts of Asia, Europe, and North America. There are 30 species, 4 variants, and 1 variant in China in both northern and southern parts of China, in which most are present in provinces and regions at the south of the Yangtze River. Most of the genus's chromosomes are X=12 or X=13. Some of them are X=6. Most of them are medicinal plants (Table 3), which mainly cures cold, headaches, coughing, arthralgia, toothache, or injuries from falls, fractures, contusions, and strains traumatic injury. The model species of this genus is *Asarum europaeum* L..

Due to the fact that the roots tastes spicy, therefor it got its name Xi Xin, which has the effect of dispelling wind, dispersing cold, promoting diuresis and opening the orifices. According to Chinese ancient medical book of Shennong Bencao Jing in the Qin and Han Dynasty, Xi Xin has been used as the top grade herbal medication,
which has more than 2000 years history. In Chinese ancient medical book of Shennong Bencao Jing by Zhongjing Zhang who was famous ancient Chinese traditional herbal doctor, Wumei Wan, Xiaqinglong Tang, Danggui Sinie Tang, Mahuang Fuzi Xi xin Tang, and etc. all contains commonly used prescriptions of Xi Xin. Xi Xin in traditional herbal medications is whole plant of A. heterotropoides F. Schmidt. var. mandschuricum (Maxim.) Kitagawa (Liao Xin, 辽细辛) and A. sieboldii Miq(Hua Xin, 华细辛). Liao Xin Xi's root is thin and its has a grayish yellow colour with green leaves. Its taste is spicy and pungent. In addition to the above authentic products, other species of Asarum in this genus are also used as substitutes to Xin in some places. In addition, A. forbesii Maxim. Is also used as medicine. and Du Heng (A. forbesii Maxim.) can also be used as medication.

Table 3 Chinese traditional herbal materials containing aristolochic acid in the genus of Aristolochia

| Name of herbal materials | Original herbal plant |
|--------------------------|-----------------------|
| Tiaoyexixin (苔叶细辛) | Asarumcaudigerellum C.Y.Cheng et C.S.Yang (短尾细辛)  
AsarumcaudigerumHance (九尾花细辛)  
Asarumsplendens (Maekawa) C.Y.Cheng et C.S.Yang (青城细辛)  
Asarumcaulescens Maxim. (双叶细辛) |
| Wujinqi (乌金七) | Asarumcaulescens Maxim. (双叶细辛) |
| Forbes Wildginger Herb (杜衡) | Asarumforbesii Maxim (杜衡)  
Asarumichangense C.Y.Cheng et C.S.Yang (宜昌细辛) |
| XiangXixin (湘细辛) | Asarumforbesii Maxim (杜衡)  
Asarumichangense C.Y.Cheng & C.S.Yang (小叶马蹄香)  
Asarumichangense C.F.Liang (五岭细辛) |
| Herba Asari (细辛) | Asarumheterotropoides Fr.Schmidt var. mandschuricum (Maxim.) Kitag. (北细辛)  
Asarumhimalaeum Hook.f. et Thoms. exKlotzsch (单叶细辛)  
Asarumhimalaeum Hook.f. et Thoms. exKlotzsch (单叶细辛) |
| Gansu Herba Asari (甘肃细辛) | Asarumhimalaeum Hook.f. et Thoms. (单叶细辛) |
| Nanping Herba Asari (南坪细辛) | Asarumhimalaeum Hook.f. et Thoms. exKlotzsch (单叶细辛) |
| Mao Herba Asari (毛细辛) | Asarumhimalaeum Hook.f. et Thoms. exKlotzsch (单叶细辛) |

Note: Chines name in brackets

4 Examples of Medicinal Plant Containing Aristolochic Acids

4.1 Madouling (Aristolochia debilis L. Sieb. et Zucc)

Morphology: Perennial climbing herb, the whole plant is hairless, the root is long, the leaves have long stalks, the triangular shape is rounded to the ovate lanceolate or ovate, the base is heart-shaped, and the ears are rounded on both sides. The leaves are solitary in leaf axils, the flowers are horny, straight, base swelled into globose, stamens 6, sessate (Figure 1).

Figure 1 Flower and fruits of Madouling (Aristolochia debilis L. Sieb. et Zucc)

Other name: 臭铃铛, 葫卢罐, 水马香果, 蛇参果, 三角草, 秋木香罐

As medication: Add the dried fruit of Aristolochia debilis L. Sieb. et Zucc in medicine.

Property and flavor: Bitter, a little spicy, and cold.

Channel tropism: Lungs and large intestine.
Effects: Clears the lungs, reduce mucus, promotes blood circulation, reduces pain, and detumescence by detoxification.
Major functions: Lung heat and coughing
Dosage & Usage: Boil and drink, 3~10 g, appropriate amount for outer usage, limit usage to avoid vomiting.

4.2 Ouxixin (Asarum europaeum L.)
Morphology: Herbs perennial, roots often succulent, aromatic and spicy; rhizomes long and sessile; stems absent or short; leaves only 1-2 or 4, basal, alternate or opposite, leaves usually heart-shaped or The stalk is sessile, sessile or sessile, sessile, sessile, sessile, sessile. Quality: many seeds, elliptic or elliptical, ovate, convex on the back, flat on the ventral surface, with fleshy appendages (Figure 2).

Figure 2 Leaves and flower of Ouxixin (Asarum europaeum L.)
Other name: 细辛, 欧洲野生生姜, 榛子, 野生小穗

As medication: Add the dried stem and roots of Asarum europaeum L..
Property and flavor: Spicy and warm
Channel tropism: Heart, lungs, and kidneys
Effects: dispelling wind, dispersing cold, promoting diuresis and opening the orifices
Major functions: Cure cold, headache, toothache, stuffy nose, reduce mucus, 风湿痹痛, and coughing.
Dosage & Usage: Drink: boil, 1.5~9 g; grind, 1~3 g. Outer usage: appropriate amount, grind to put in nose, ears, navel; or boil and keep in mouth.

4.3 Shancigu (Asarum sagittarioides L.)
Morphology: Perennial herb, leaves long ovate, broadly ovate or suborbicular, apex acuminate, base deeply heart-shaped or sate-like, often sessately sessately sessately pubescently pubescently pubescent Close to the eyelashes. Each flowering branch has 2 flowers, flowers purple-green; perianth tube cylindrical, glabrous, inner wall with longitudinal pleats, throat contracture, membrane ring width approx. 2 mm, perianth ovate-like kidney, base with milk Staple pleats; drug septum extending, narrowly tapered; ovary semi-inferior, style free, apically 2~lobed. The stigma is lateral. Fruit is oval (Figure 3).

Figure 3 Flower and pseudobulbs Shancigu (Asarum sagittarioides)
Other name: 金灯花, 鹿蹄草, 山茨菇, 芹姑, 毛慈姑, 人头七, 丽江山慈姑, 草贝母, 益辟坚

As medication: Pseudobulbs.
Property and flavor: Sweet, a little spicy, and cold.
Channel tropism: Liver, stomach, and belly
Effects: Clears away heat and detoxification
Major functions: Swollen sputum, sputum nucleus, lymph node tuberculosis, and snake bite.
Dosage & Usage: Drink: boil, 3–6 g; or grind as liquid; or process as pills, powder. Outer usage: appropriate amount, grind as liquid to apply; or grind as powder to apply.
4.4 Dusuanlan (Cremastra appendiculata (D. Don) Makino)
Morphology: False bulbs are ovoid or subglobose, intimate, jointed, and torn into fibrous residual sheaths. Leaves usually one, born on the top of a pseudobulb, narrowly elliptic, nearly elliptic or oblancoolate narrowly elliptic, apex acuminate, base narrowed, nearly cuneate; petiole 7~17 cm long, often lower. The remaining sheath is covered. Calyx from the upper part of the pseudobulb, erect; racemes with 5~22 flowers; calyx lanceolate to ovate-lanceolate; flowers often on one side of the inflorescence, somewhat drooping, not completely open, aroma, narrow bell-shaped, pale purple brown; bracts inverted lanceolate, from the central to the base suddenly narrowed into a narrow line shape, apex sharp or acuminate; lateral bracts slightly oblique. Petals oblancoolate or narrowly lanceolate, narrowly sessate into sate. The base has a fleshy protrusion between the two side lobes; the size of the fleshy bulge varies greatly, and there are sometimes small bulges on the top; the column is slender, the tip is slightly enlarged, and the ventral surface sometimes has very narrow wings. Capsule nearly elliptic, drooping. Flowering period from May to June, fruiting period from September to December (Figure 4).

4.5 Dusuanlan (Pleione bulbocodioides (Franch.) Rolfe)
Morphology: Semi-episophylic herb. False bulbs are ovate or ovate-conical, with a neck at the upper end and a leaf at the top. The flowering leaves are young and tender. Leaves narrowly elliptic-lanceolate or nearly oblancoolate, paper. The calyx is born in the base of the leafless pseudobulb, and the lower part is enclosed in a cylindrical sheath with 1~2 flowers at the top. The bracts are longer than the peduncle and ovary; flowers pink to lavender, with dark spots on the lips; middle bracts nearly lanceolate, lateral bracts as long as mid stellate; petal lanceolate, slightly obliquely sate, valvate, 3 micro-cracked, the base wedge shape slightly attached to the column. Capsule nearly oblong. Flowering period from April to June (Figure 5).
Channel tropism: Liver and belly.
Effects: Replenish the lungs, relieve cough and phlegm, stop bleeding and build muscle.
Major functions: treatment of silicosis, tuberculosis, whooping cough, bronchitis, gastrointestinal bleeding, carbuncles, traumatic bleeding.
Dosage & Usage: Drink: Boil, 15~25 g; or grind as powder. Outer usage: grind and apply on necessary area or grind as powder.

4.6 Duheng (Asarum forbesii Maxim.)
Morphology: Herbs perennial; rhizomes short, roots clustered, slightly fleshy, 1~2 mm in diam. Leaves broadly heart-shaped to renal heart-shaped, apex obtuse or round, base heart-shaped, leaf surface dark green, white veins on both sides of midvein, short hairs on veins and proximal margins, leaf blade lightly green; perianth lobes erect, Ovate, broad and long, nearly equal, smooth, apex-free; sulcate slightly extending; ovary semi-inferior, styles free, apically 2~lobed, stigma ovate, lateral. Flowering period from April to May (Figure 6).

4.7 Tumuxiang (Inula helenium L.)
Morphology: Perennial herb, up to 1.8 meters, the whole plant is densely pubescent. Basal leaves stalk, broad, broadly elliptic, apex acute, sessately sessately sessately sessately sessately sessately sessate sessectate With irregular teeth. Inflorescences axillary, yellow. The apex is slightly pointed, the margin is purple; the receptacle is bald and has a sputum; the stellate stellate female, apex 3-toothed; central tubular flowers bisexual, apex 5-lobed. Achenes are long, with 4 to 5 ribs on the surface and more crowns. Flowering period from June to July (Figure 7).

As medication: Use the dried root of Inula helenium L. or Inula racemosa Hook.f.. Dig up in fall, remove mud and sand, then dry under the sun.
Property and flavor: Spicy, bitter, warm.
Channel tropism: Liver and belly.
Effects: Strengthen the spleen and stomach, regulate qi and relieve phlegm, and relieve pain and fetus.
Major functions: For chest flank, abdominal pain, vomiting and diarrhea, chest contusion, suffocation, fetal movement.
Dosage & Usage: Drink: boil 3~9 g; or process as pills or powder.

4.8 Zhushalian (Aristolochia cinnabarina C.Y.Cheng et J.L.Wu.)
Morphology: Perennial vine. The roots are blocky, traversing, and 1 to 3 are connected. The stem has 7 longitudinal lines, and the young and young leaves are pilose. Leaves alternate, ovoid, entire, apex pubescent, base sately sately sately sately sately sately sately. Short racemes axillary, flowers drooping; calyx tuberculace, base swelled into globose, stellate. Veins, apex obtuse or dimpled; stamens 6, combined with style; style 6 lobed, stigma not conspicuous, ovate long column-like, 6 ribs, lower, 6 locule. Flowering period from February to March (Figure 8).

Figure 8 Leave and fruits and root-like stems of Zhushalian (Aristolochia cinnabarina C.Y.Cheng et J.L.Wu.)
Other name: 辟水雷，雷见怕，牛血莲，背蛇生，躲蛇生

As medication: Use root and stem as medicine. Get root and stem in spring or fall, before growth or after growth, remove damaged stem and root, wash, and let dry under the sun.
Property and flavor: Bitter, spicy, cold. A little poisonous.
Channel tropism: Heart, lungs, liver.
Effects: Clearing away heat and detoxification, qi and pain.
Major functions: For enteritis, dysentery, tail, duodenal ulcer, sore throat, poisonous snake bite, swollen poison, traumatic bleeding.
Dosage & Usage: Drink: Boil, 5~10 g, can use more if fresh; or grind, 0.5~1 g per does, 2 times per day. Outer usage: appropriate amount, grind as powder, mix with alcohol or vinegar to apply on necessary areas.

4.9 Xungufeng (Aristolochia mollissima Hance)
Morphology: Perennial entwined herb, the whole plant is densely white-yellow wool. The stem is slender and has several longitudinal grooves. Leaves alternate, ovoid or ovoid-shaped, apex acute or sessate, base sateate, entire, sately pubescently pubescently pubescent. Flowers solitary in leaf axils; sepals 1, ovoid. Capsule elliptic obovate, cytoplasmic. The seeds are flat. Flowering period from June to August; fruiting period from September to October (Figure 9).

Figure 9 Fruits and roots of Xungufeng (Aristolochia mollissima Hance)
Other name: 清骨风，猫耳朵，穿地节，毛香，白毛藤，地丁香，黄木香，白面风，兔子耳
As medication: Use the whole plant.
Property and flavor: Spicy, bitter, natural.
Channel tropism: Liver and stomach.
Effects: Hurricane dehumidification, promoting blood circulation and relieving pain.
Major functions: Main rheumatic pain; limb numbness; tendons and tendons; abdominal pain; bruises; traumatic bleeding; chyle and a variety of purulent infections.
Dosage & Usage: Drink: boil, 10~20 g; or mix with alcohol.

4.10 Mufangji (Stephania tetrandra S. Moore)
Morphology: Perennial winding vines. The roots are cylindrical, sometimes in a block shape, and the outer skin is light brown or tan. Stems flexible, cylindrical, sometimes slightly twisted, with fine streaks, branches smooth and glabrous, base tips reddish. Leaves alternate, thin and soft, petiole shield-like, long and blade equal; blade shape nearly circular, with 3 to 5 angles, apex acute, base truncate or slightly heart-shaped, entire, both sides are short. The pilose, green above, grayish green below. Flowers small, sessile, apically cymose, female flowers of calyx, petals and male flowers of the same number, without degenerate stamens, carpels 1, 3 styles. Drupe spherical, red when cooked. Flowering period from April to May. Fruit period from May to June (Figure 10).

Figure 10 Fruits and root chip of Mufangji (Stephania tetrandra S. Moore)

Other name: 粉防己, 粉寸己, 汉防己, 土防己, 石蟾蜍, 蝌蜍薯, 倒地拱, 白木香

As medication: Use dried root as medicine.
Property and flavor: Bitter and cold.
Channel tropism: Bladder, belly, and kidneys.
Effects: Relief water swelling, hurricane pain.
Major functions: For edema athlete's foot, urinary adverse, eczema sore, rheumatic pain, high blood pressure.
Dosage & Usage: Drink: boil, 7.5~15 g; or process as pills or powder.

5 Alternative to Medicinal Plants of Aristolochiae
In 2004, the State Food and Drug Administration replaced Guang Fang Ji (dried roots of Aristolochia fangchi Y.’C .Wu ex L .D. Chou et S .M .Hwang) with Fang Ji (dried roots of Stephanie tetranda S .Moor); Qing Mu Xiang (dried roots of Aristolochia eblis Sieb .et Zucc .) with Tu Mu Xiang (only replaced by dried roots of Inula helenium L.). The State Food and Drug Administration has restored the regulation on Mu Tong as early as 2001. There are many reports about Guan Mu Tong causes renal failure and there has been research on Mu Tong replacing Guan Mu Tong (Chen Wen, 2001; Wang Ningsheng, 2001, Traditional Chinese Drug Research and Clinical Pharmacology, 12(6): 394-395).

Moreover, if Aristolochia is used to reduce mucus, and relief coughing, Platycodon grandiflorus (Jacq.)A.Dc., Semen Armeniacae Amarum., Peucedanum praeruptorum Dunn, Fritillaria cirrhosa D. Don, Trichosanthes kirilowii Maxim all have the same effects. If Aristolochia is used for promoting blood circulation, Curcuma rcenyujin Y and Faeces Trogopterori as the same effect.

6 Conclusions
There is an old saying in China that called "all medicines possess a little toxic", meaning that that no matter what drug, there are some toxicity or side effects. Aristolochia plants was used as long term traditional herbal medication, which was the choice of ancient Chinese people. During the era without antibiotics and artificial chemical compounds, people choose aristolochia plants to disinfect and relief pain (Zeng et al., 1995,
Traditional Chinese Drug Research and Clinical Pharmacology, 2: 48-50; Liang et al., 2004).

Even though Aristolochia herbal medications have special meaning in the traditional Chinese medicine field, its renal toxicity should be given abundant attention. Today, with the development of science, under the condition that European countries have insufficient knowledge of the toxic and side effects caused by improper use of traditional herbs and the United States uses traditional herbs as food rather than medicine, it is understandable to have such a killing action against traditional herbs containing aristolochic acid, but aristolochia in traditional herbal medications are used and regulated as medication in China. As a type of medicine, side effects exist. There are also many western medicines that have major side effects on liver and kidneys, but they are still okay to use after labeling matters and announcements (Gao et al., 2005; Jiang and Chen, 2008).

In addition, traditional herbal material is not a chemical monomer, and the chemical components in traditional herbal medication are not the same as traditional herbal material itself, so the animal toxicity experiment results of single component aristolochic acid can not be equated with traditional herbal medication containing aristolochic acid, and its safety and technical standards can never be copied according to the western medicine model (Mei et al., 2006). Chinese Traditional medicine never uses only one ingredient to cure and it also barley uses just one herbal material to cure. Therefore, according to the theory of Chinese traditional medicine and the relevant evaluation methods of Western medicine, we should establish a set of scientific evaluation methods recognized by the world, scientifically carry out the clinical and experimental research on the toxicity of Chinese herbal medications containing aristolochic acid, and gradually establish a development evaluation system with the characteristics of Chinese traditional medicine while keeping its originality, In this case, traditional Chinese medicine and Traditional herbal medication can truly be understood by the world.

Authors’ contribution
Dr. Fang Xuanjun conceived the paper, collected the literature and wrote, revised and finalized the first draft. The authors read and agreed to the final text.

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