Herbs and Hazards
Risk of Aristolochic Acid Nephropathy in Iran

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Herbs are usually considered as inherently harmless products. Nonetheless, various renal injuries have been reported in association with several herbs. The best-known herb-induced chronic kidney disease is aristolochic acid nephropathy. Aristolochic acid is found in Chinese slim herbs. Balkan endemic nephropathy is nowadays considered as an aristolochic acid nephropathy. Plants of Aristolochiaceae (also known as birthwort, dutchman’s pipe, and somersworth) is named zaravand or chupoghak in Persian and it grows in different mountainous and rural areas of Iran. The fruit and the steam of the Aristolochiaceae are named zaravand gerd (nokhod alvand) and zaravand dearaz, respectively, and have different usage in Iranian traditional such as treatment of headache, back pain, and anxiety. Some patients with end-stage renal disease and bilateral small kidneys have a history of exposure to some herbal remedies. We need to consider the possibility of environmental toxins and even Aristolochia nephrotoxicity as a potential danger in Iran.

INTRODUCTION
Herbal therapy is usually considered as inherently harmless. Nonetheless, various renal injuries have been reported in association with several herbs. Tubular necrosis, acute interstitial nephritis, Fanconi syndrome, hypokalemia or hyperkalemia, hypertension, papillary necrosis, chronic interstitial nephritis, nephrolithiasis, and urinary retention all have been reported in association with herbal products. Taiwan has the highest incidence of chronic kidney disease (CKD) and also has the highest rate of herbal medicine use. There are also a tendency among CKD patients to adhere to this type of medicine. Herbal remedies often are prepared by herbalists with no training, not tested for the content, and can be adulterated or contaminated with toxic chemicals, heavy metals, and pesticides. Confusing terminology, errors in identification, and substitution with a toxic substance all could happen and make it difficult to trace the exposure to a specific herb.

The best-known herb-induced CKD is aristolochic acid nephropathy (AAN). The toxicity of the family of Aristolochiaceae has been known in different aspects. In goats, intoxication with Aristolochia bracteata presents with loss of hair, increase in aspartate aminotransferase, ammonia and urea, and hemorrhage in the lungs, heart, and kidneys. The condition first came under notice in humans when an unusual increased number of patients with interstitial nephritis were reported in Belgium, for which aristolochic acid in Chinese slim herb was found to be responsible. The condition was therefore named “Chinese herb nephropathy.” This nomination should not denigrate the system of Chinese herbal medicine as many useful compounds has entered modern medicine from Chinese medicine. Aristolochic acid nephropathy is characterized by small kidneys, tubular proteinuria, extensive interstitial fibrosis, and tubular atrophy. Urothelial malignancy sometimes develops in some of these patients. Aristolochic acid-induced
Fanconi syndrome and acute kidney failure have also been reported.4,11,12 Balkan endemic nephropathy was first recognized in the 1950s along the Danube River and its tributaries in the Balkans, stretching into Romania, Bulgaria, Croatia, Serbia, and Bosnia Herzegovina. Aristolochic acid hypothesis in Balkan endemic nephropathy was initially proposed by Ivic in 1970; he suggested a possible chronic dietary intoxication by wheat flour contaminated with seeds of Aristolochia clematidis.13

ARISTOLOCHIA GENUS IN IRAN

Plants of Aristolochiaceae (birthwort, dutchman’s pipe; also known as zaravand and chopoghak in Persian), grows in mountainous areas and agricultural fields. In Iran, they are distributed in Mazandaran, Azerbaijan, Kurdistan, Kermanshah, Ilam, Lorestan, Isfahan, Khuzestan, and Tehran provinces. Perennial shrub of this genus grows to a height of 10 cm to 60 cm. It has reniform leaves and yellowish green flowers. The fruit is a globoid. Three herbaceous of Aristolochia are endemic to Iran. These include Aristolochia bottae Jaub & Spach (Aristolochia Maurorum), which is known as zaravand, chopoghak, kalaghak in Persian (Figure 1); Aristolochia hyrcana Davis (Aristolochia iberica Fisch & Mey), which is known as chopoghak-e-rudbari or khazari in Persian (Figure 2); and Aristolochia olivieri Collengo (Aristolochia bruguieri Jau & Spach), which is known as chopoghak-e-zaghrosi in Persian and also wild eggplant in Khorasan province (Figure 3). Aristolochia bracteata (kharbuzeh abujahl) have also been detected in the Alborz mountains.14,15

Figure 1. Aristolochia bottae (Persian name: chopoghak or zaravand). Adapted with permission.16

Figure 2. Aristolochia hyrcana Davis (Persian name: zaravand, chopoghak-e-Rudbari, or Khazari). Adapted with permission.16

Figure 3. Aristolochia olivieri Collengo (Persian name: zaravand, chopoghak-e-zaghrosi). Adapted with permission.16
ARISTOLOCHIA IN IRANIAN TRADITIONAL MEDICINE

Medicinal use of species of Aristolochia has been mentioned by the Greek scholar Dioscorides. It is an important medicinal plant in Indian-Ayurvedic and Iranian traditional medicine. Its roots had been recommended as lithotripter, diuretic, menstruator, anthelmintic, expectorant, and carminative. It has been recommended for scorpion and insect bites and induction of abortion. The steam of Aristolochia longa vulgaris is named zaravand deraz in Iranian traditional medicine.16

Herbal products have many useful effects but raising the public awareness about the potential danger of herbal products is an emergent task.17,18 Nowadays, there is a great vigor to propagate the absolute usefulness of herbal medicine herbal products. Sellers often are unscrupulous mediator who are not aware about the potential toxicity of herbs.19,20 We have visited some herbal shops in different cities of Iran including Tabriz, Tehran, Isfahan, and Mashhad, and observed that the shop keepers are familiar with zaravand, selling of Aristolochia fruit for about 200 g for US $ 1. It is often named round zaravand or zaravand modahraj, or nokhod alvand (Figures 4 and 5). In one instance the seller instructed us as follows: “Grind 2 or 3 or 4 of those beans each time and mix it with honey and repeat it twice daily. It is useful for headache, back pain, and anxiety, and generally it detoxify all of your body.”

CONFLICT OF INTEREST
None declared.

REFERENCES


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