

## Saussurea lappa and the Risk of Confusion with Aristolochia debilis: A Short Toxicological communication is Necessary

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### Abstract

If aristolochic acid is now banned in many countries such as France, the United States or Taiwan. It remains present on the market of phytotherapy through parallel circuits. Responsible for toxic nephropathies associated with cancer of the urinary tract, its global scale remains difficult to evaluate in the long term. *Saussurea lappa* is a plant introduced in the European pharmacopoeia recently because of its use in traditional Chinese medicine. This can be confused with *Aristolochia debilis* which is a plant that contains aristolochic acid. This risk of confusion is compounded by the use of Chinese herbal preparations containing aristolochic acid plants, which made a great noise in Belgium in the 1990s. Recall that *Saussurea lappa* does not contain aristolochic acid. but its potential confusion leads us to anticipate and increase our vigilance in the face of this risk of confusion. This is an opportunity to raise awareness and inform people directly or indirectly in contact with these plants by proposing solutions and by making a pharmaco-chemical acid-pharmacological booster.

**Keywords:** Aristolochic Acid; *Saussurea lappa*; *Aristolochia debilis*; Aristolochic Acid Nephropathy

### Abbreviations

AA: Aristolochic Acid; AAN: Aristolochic Acid Nephropathy

### Introduction

*Saussurea lappa* is a plant that is increasingly present in the European market of medicinal plants. The concern is that it is often confused with *Aristolochia debilis* which contains aristolochic acid (AA). This alkaloid is a potent cytotoxin and food carcinogen, as well as an etiological agent establishing severe human nephropathies and associated upper urinary tract urothelial cancers, collectively referred to as aristolochic acid nephropathy (AAN). This article aims at first to highlight this problem of confusion and think about ways to remedy it. Then, in a second step, to sensitize the reader by reminding the effects of the AA on the health of the Man.

### A case of confusion with an aristolochic acid plant

The roots of *Saussurea lappa* have been used for millennia in traditional Chinese medicine, Ayurvedic and Arab-Muslim. His entry into the European Pharmacopoeia is recent. It is absent from Western traditional herbal medicine however it is widely used in Europe through complementary and alternative medicines. It is a plant that has so far not shown any adverse effects and even has a promising future thanks to its virtues more and more studied. This plant is nevertheless easily confused with *Aristolochia debilis* which is a nephrotoxic plant. The stakes are high because the use of *Saussurea lappa* is so far absent from the circuit of conventional medicine. The lack of

knowledge of this plant, the risk of confusion with *Aristolochia debilis* as well as the effects of AA is palpable and carries with it a risk of missing the origin of an NAA when a clinical case of this kind is presented to the medical profession. Consumers, wholesalers and other intermediaries trading or consuming *Saussurea lappa* do not have a way of checking whether their product is pure or blended, cut or even replaced by *Aristolochia debilis*. The physicochemical analysis of this plant is expensive. A wholesaler or reseller who is not concerned with the quality of his product or who is unaware of the possibility of confusion is unaware of his involvement in the exposure of AA's risk to the health of men.

Solutions can be put in place and that in each protagonist in contact with this plant. This could be to sensitize all actors and that up to the consumer on the impact of AA on public health. But also, strengthen quality controls at wholesalers and resellers. Finally, to raise awareness about the criterion of selection of the supplier: To impose on him a certificate of analysis which shows a lack of AA in his product.

#### Reminder of the effects of aristolochic acid on health.

*Aristolochia* species contain a variety of AA and aristolactams in varying amounts depending on the species, plant part and the geographic location [1]. AA are nitrophenanthrene carboxylic acids. It is assumed that they arise from the oxidative opening of an aporphine (alkaloid) [2].

The principal metabolites of aristolochic acids are aristolactams, which are excreted in the urine and feces. The activation of the metabolite of aristolochic acid I (aristolactam I) by peroxidase causes the formation of the major adducts associated with the development of urothelial carcinoma following the administration of aristolochic acid-containing herbs. The cytochrome P450 isoenzymes, CYP1A1, CYP1A2 and possibly other CYP450 isoenzymes activate aristolochic acids to cyclic reactive nitrenium ions that form covalent DNA adducts on guanine and adenosine. The oral administration of aristolochic acid to female rats causes renal lesions similar to the cases of Aristolochic acid nephropathy, manifest by renal tubular necrosis, proteinuria, glucosuria and azotemia [1].

Furthermore, aristolochic acid nephropathy (AAN), a progressive renal interstitial fibrosis frequently associated with urothelial malignancies, was initially reported following an "epidemic" of renal insufficiency occurring in patients followed in a Brussels medical office specializing in slimming treatments. This disease has been attributed to the aristolochic acids contained in some plants used in traditional Chinese medicine. Similar cases are now reported around the world. For example, the use of *Aristolochia* in traditional medicine may explain the particularly high frequency of chronic interstitial nephritis in the Indian population. In terms of physiology and biology, aristolochic acids open new avenues for experimental exploration of fibrogenesis and tumorigenesis whose interest in human pathology is now evident. Finally, the identification of particularly serious complications (terminal uremia, urinary tract cancers) secondary to treatments with medicinal plants raises serious questions in terms of public health [3,4].

#### Conclusion

The health consequences linked to AA are far from harmless, especially since the toxicity may appear years after exposure to this molecule. In the face of this public health problem, it is necessary to make the whole medical profession aware of the problem of so-called natural medicinal prescriptions which are regarded as innocuous. But also to provoke the reflex of linking a symptomatology similar to that cited in the article and an investigation directed towards plants, herbal preparations or food supplements likely to contain AA or whose components can be confused or cut with plants containing AA.

#### Conflict of Interest

I don't know because PHYCACARE commercialized food supplements contains *Saussurea lappa*.

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