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## From Healing to Harm: Exploring Moroccan Herbalists' Insight Into the Nephrotoxicity and Cancer Threats of Aristolochiaceae

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### ABSTRACT

The Aristolochiaceae family consists of hundreds of species. In Morocco, four species have been identified and sold under the vernacular name «Berreztem» in unregulated markets. The aim of this study is to evaluate herbalists' knowledge, particularly regarding the identification, toxicity, and side effects of Aristolochiaceae plants in eastern Morocco. An ethnobotanical survey was conducted among herbalists and plant sellers including those with fixed premises and street vendors, in the cities of Oujda and Guercif, Morocco. All herbalists were interviewed by the same person using a 30-item questionnaire. Ninety herbalists were included in the study. Men comprised nearly nine out of ten herbalists. Most of them believed that there is only one species of Aristolochia in Morocco. Only 15.6% of the herbalists mentioned that the plant can cause chronic kidney disease. Additionally, 33.3% of the interviewees prescribed Aristolochia when needed, and 77.8% continued selling it. According to the interviewed herbalists, Aristolochia is predominantly used in the treatment of cancerous diseases, followed by skin diseases and wounds, digestive disorders, and able bowel syndrome. The majority (97.8%) believes that Aristolochia can not cause cancer. Despite the documented dangers of Aristolochia, including kidney damage (nephrotoxicity) and increased cancer risk (carcinogenicity), the plant remains readily available for purchase in Moroccan herbal shops. This suggests a lack of awareness among some herbalists and/or a disregard for the severity of these health risks.

**Keywords:** Aristolochia, Herbalists, Ethnobotanical investigation, Nephrotoxicity, Carcinogenic effect.

### Introduction

The Aristolochiaceae family consists of hundreds of species, primarily distributed worldwide in tropical, subtropical, and Mediterranean regions. These plants have long been recognized for their widespread use in traditional medicine. They have been cultivated as ornamental plants and utilized for various purposes and treatments, including as abortives, emmenagogues, analgesics, diuretics, anticancer agents, anti-inflammatory agents, sedatives, muscle relaxants, antihistamines, antiallergics, anthelmintics, antimicrobials, and antimalarials. Additionally, they have been used to address digestive issues, rheumatism, skin diseases, edema, and various types of venomous bites and stings.<sup>1</sup>

The lack of knowledge about these plants exposes some users to specific kidney toxicity. Severe Chronic Kidney Disease (CKD) was reported for the first time, following the consumption of Aristolochia in Belgium in 1992, and since then, several studies have been published, establishing a strong link between the consumption of Aristolochia plants and the occurrence of End Stage Kidney Disease (ESKD).<sup>2</sup>

The use of Aristolochia is based on ancestral practices and uncontrolled ethnopharmacological knowledge, which poses a significant public health risk, particularly in developing countries.<sup>3</sup>

In Morocco, there are four native species of Aristolochia, but only two, *Aristolochia baetica* Linn. and *Aristolochia fontanesii* Boiss. & Reut., are commonly used by the local population under the vernacular name of Berreztem.<sup>4</sup>

The profession of herbalist in Morocco was legally recognized with the promulgation of the dahir (edict) on August 20, 1926. From this dahir, it was inferred that the herbalist is a person holding a certificate that entitles them to practice their profession and sell all medicinal plants, except for poisonous plants.<sup>5</sup> However, many plant sellers lack the formal training, knowledge, or skills required to successfully practice the herbalist profession.<sup>6</sup>

In Morocco, confusion and substitution are more likely to occur in the root part of the plant, as these are more difficult to identify. Misidentification and intentional substitution of medicinal plants are two of the most widespread and significant causes of toxicity.<sup>7</sup> Previous research has shown that, in northeastern Morocco, *Aristolochia fontanesii* Boiss. & Reut. has frequently been substituted by another species which is 20 to 100 times more nephrotoxic.<sup>4</sup> Therefore, the lack of training among plant sellers poses a real public health risk.

Given that the Aristolochiaceae family is among the most well-documented nephrotoxic plants, this study aims to evaluate the impact of prior research on public awareness. It specifically assesses the knowledge of herbalists in eastern Morocco regarding the identification of Aristolochiaceae species and their understanding of the associated toxicity and side effects. By addressing a region and topic largely overlooked in previous studies, this investigation provides valuable insights into the current level of awareness among local practitioners.

### Material and methods:

#### Study design

The study was conducted in two cities in eastern Morocco: Oujda and Guercif (Figure 1). These cities were selected based on their

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demographic representation, as they encompass different segments of the regional population, ensuring socio-economic and demographic diversity in the sample. Additionally, their readily accessible

geographical location and the distance of 169 Km between them facilitated efficient data collection.



**Figure 1:** The location of the study area (highlighted in green)

A face-to-face cross-sectional study was chosen, conducted from April 2021 to September 2021. The study included consenting herbalists with fixed premises or operating as street sellers. They were interviewed using a paper questionnaire in the Arabic language, containing 30 items. All interviews were conducted by Hind KHALIL, affiliated with the Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy, University Mohammed First, Oujda, Morocco. The information collected during the survey included the profiles of the herbalists interviewed (age, gender, level of education, seniority in herbalism, etc.), ethnobotanical data, such as the parts of the plants used, frequency of prescription, plant state, collection period, dosages, duration of treatments and knowledge of side effects.<sup>8</sup>

#### Ethic statement

All procedures were performed in accordance with the recommendations of the Declaration of Helsinki on biomedical research involving human subjects. This study was approved by the Ethics Committee for Biomedical Research of Oujda (CERBO), under approval number 03/2021, and consent was obtained from all participants. They were informed of the study's objectives, and data anonymity was ensured.

#### Statistical analysis

Qualitative variables were expressed as percentages, while quantitative variables were expressed as means and standard deviations. To study the factors associated with the knowledge of Aristolochia as a nephrotoxic plant leading to CKD, a Chi-square ( $\chi^2$ ) test or a Fisher's exact test were used for the comparison of qualitative variables. Data were entered and analyzed using IBM SPSS Statistics software for Windows, version 21.0.<sup>9</sup>

#### Limitations of the study

Although the use of convenience sampling yielded valuable data, it is important to note that this method can limit the representativeness of the target population, which can introduce bias and limit the generalizability of the results.

## Results and discussion

#### Descriptive study

Nephrotoxicity caused by Aristolochia plants was initially identified in a Belgian population. Numerous studies documented cases of rapidly progressing kidney damage among Belgian women who had used herbal weight loss supplements. The source of this epidemic was later traced to *Aristolochia fangchi*, which had been mistakenly substituted for *Stephania tetrandra* in the supplements.<sup>10, 11</sup>

The adulteration can be attributed to the similarity in their Chinese common names and the physical resemblance of their roots.<sup>12</sup> The interstitial fibrosis caused by exposure to Aristolochia closely resembles that seen in Balkan Endemic Nephropathy (BEN). Additionally, the detection of specific DNA adducts formed by

Aristolochic acid (AA) metabolites in the renal tissue of BEN patients firmly established the link between the consumption of Aristolochia-contaminated wheat and the onset of this disease.<sup>13, 14</sup> Nowadays Aristolochic Acid Nephropathy (AAN) refers to toxic interstitial nephropathy caused by aristolochic acids (AA), whether through ingestion of plants containing AA in traditional herbal medicines or through environmental contamination in food.<sup>15</sup>

Among the 110 herbalists visited, 90 (81.8%) agreed to participate in the survey, of which 73.3% were fixed-premises sellers and 26.7% were itinerant vendors in the weekly souks.

The average age of herbalists was  $45.52 \pm 16.15$  years, with extremes ranging from 18 to 88 years. These herbalists were grouped according to age classes. 55% of the herbalists were 45 years or younger, and 44.4% were between 46 and 88 years.

Among the 90 participants, 9 were women, making up 10% of the total. The gender distribution of traditional herbalists in our study closely mirrored that of the Casablanca study, with both showing approximately 90% male participants.<sup>16</sup> The percentage of unschooled participants was 19.3%. This suggests that nearly a fifth of herbalists lack formal education, which could affect the profession's credibility and safety due to inconsistent knowledge and practices. The motivations for pursuing the herbalist profession vary: 43.7% regard it as a family tradition, 40.2% view it as an economic livelihood, and 16.1% are driven by a strong passion for medicinal plants. These results reflect the complex interplay of tradition, economic factors, and personal interest in the practice of herbalism.

The survey findings indicate that 17.4% of herbalists had less than 5 years of experience selling medicinal plants, 32.6% had 5 to 15 years, and the majority (50.0%) had 16 to 50 years of experience. This distribution suggests that while a significant proportion of herbalists possess considerable experience, there is also a notable presence of newer practitioners. These varying experience levels underscore the importance of mentorship and continuous education to ensure the effective transfer of knowledge and uphold professional standards within the field. More than three-quarters (78.4%) of herbalists have another source of income besides selling medicinal plants. This suggests that herbalism may not be their primary livelihood, and many rely on additional economic activities to ensure financial stability. *Table 1* reports the distribution of herbalists according to socio-demographic criteria.

Three herbalists reported being unfamiliar with the Aristolochia plant. Among those who were knowledgeable about it, 51.7% acquired their knowledge from other herbalists, 27.6% through personal practice, 5.7% from books, 8% from childhood exposure, and 5.7% from other sources. These findings highlight the significant role of knowledge transmission and practical experience in herbal medicine. They also illustrate that formal sources of information, such as books, play a relatively smaller role in the learning process.

The Aristolochiaceae family includes approximately 7 genera and 400 species,<sup>17</sup> with 4 species present in Morocco. However, 87.2% of the herbalists surveyed indicated that there is only one species of Aristolochia, reflecting a limited understanding of the plant's diversity

and pointing to a potential gap in knowledge regarding the different species and their distinct characteristics.

Only 42% of herbalists recognized that the Aristolochia plant can be toxic. Among the adverse effects cited were vomiting, nephrotoxicity, hepatotoxicity, digestive disturbances, gallbladder toxicity, and the promotion of cancer progression. Furthermore, 6.7% of herbalists noted that Aristolochia could potentially lead to death, although they did not specify the cause of death.

The data indicates that only 15.6% of herbalists are aware that the Aristolochia plant can cause CKD. This is despite a significant body of research showing that Aristolochia induces nephrotoxicity, primarily through extensive interstitial fibrosis of the kidneys, which ultimately leads to CKD.<sup>18, 19</sup> The low level of awareness among herbalists suggests a need for better education regarding the risks associated with this plant. Given that the toxic effects of Aristolochia are well-established in scientific literature, improving the dissemination of such information within the herbal medicine community is essential for ensuring the safe use of herbal remedies and protecting patients from harm.

The majority (97.8%) of herbalists in this study were unaware that Aristolochia can cause cancer. Despite extensive research documenting the mutagenic effects of Aristolochia species, only two herbalists recognized its potential to cause cancer, one of whom noted that

Aristolochia is prohibited in Morocco. A study conducted by Nortier et al. demonstrated that regular consumption of powdered Chinese herbs from Aristolochia species significantly increases the risk of carcinoma in the native urinary tract of patients with ESKD, often necessitating the prophylactic removal of non-functioning, atrophic kidneys. Since all detected cases were in patients with Chinese herbal nephropathy, urothelial cancer is considered a late complication of CKD.<sup>20</sup> While in a later study, they reported a case of urothelial tract cancer related to Aristolochia without significant renal failure.<sup>21</sup> Another study conducted on histidine-deficient strains of *Salmonella typhimurium* revealed that *A. baetica* was mutagenic with strain TA-100 at concentrations starting from 0.25 mg/ml in the absence of S9 fraction (preparation of liver homogenate that contains metabolic enzymes). However, in the presence of the S9 fraction, mutagenicity was observed only at the highest dosage of 10 mg/ml. In contrast, strain TA-98 exhibited significant mutagenicity when exposed to Aristolochia, but only in the presence of the S9 fraction. Furthermore, this mutagenic effect was found to be dose-dependent.<sup>22</sup>

Among the 90 herbalists surveyed, only 4.4% declared knowing consumers had side effects after using the plant. This finding suggests that such side effects may be infrequently communicated by consumers or that there is limited awareness or monitoring of adverse effects within the herbalist community.

**Table 1:** Distribution of herbalists according to socio-demographic criteria. (N=90)

Parameters	N (%)
Mean age of herbalists <sup>1</sup>	45.52± 16.15
Age of herbalists ≤ 45 years	50 (55.6)
Male gender	81 (90.0)
<b>Level of education</b>	
Unschooling	17 (19.3)
Primary	24 (27.3)
Secondary	41 (46.6)
University	6 (6.8)
<b>The perception of profession by herbalist</b>	
Family heritage	38 (43.7)
Sources of material benefit	35 (40.2)
Passion for the trade	14 (16.1)
Mean years of experience <sup>1</sup>	19.08 ±13.75
Other professional activity: Yes	69 (78.4)

Year (mean ±SD) SD: standard deviation

According to the herbalists, the plant is obtained in fresh form (18.6%), dry form (74.3%), and both fresh and dry forms (7.1%). Regardless of its initial state of acquisition, Aristolochia is ultimately sold as a dried product, reflecting the practicality of its dried form for storage, transportation, and usage. Almost all herbalists (82.2%) reported that the Aristolochia plants were obtained from the wild, not cultivated. And the rest (17.8%) have no idea whether the plant is wild or not. This may suggest a lack of awareness or uncertainty about where the plant is obtained.

The majority of herbalists (92.2%) reported using the root of the plant, while a small percentage cited the leaves (5.2%), and one herbalist (1.3%) designed that both the root and leaves can be used. Another herbalist mentioned the stem as part used. Our results highlight the predominant use of the underground part of Aristolochia. This finding is consistent with a previous study, which also reported a high prevalence (67%) of use of the underground part.<sup>8</sup>

70% affirmed that the plant is used as a powder and 6.7% noted that it is used as an herbal tea. One herbalist out of 90 indicated that the root of Aristolochia is utilized in powdered form, while the leaves are used as herbal tea. Almost the quarter (22.2%) of the participants had no knowledge of the form of use. Therefore, our sample showed that powder is the most common mode of preparation of this plant. This finding is consistent with the study conducted in eastern Algeria (70%),<sup>23</sup> and is similar to the results of El Yahyaoui El Idrissi (57%).<sup>8</sup> Bourhia also reported the widespread use of powdered Aristolochia.<sup>16</sup>

More than half (60%) of the herbalists reported that Aristolochia was used individually with honey and 17.8% reported that Aristolochia was used mixed with other plants, mainly Barberry (*Berberis vulgaris* subsp. *australis* Boiss.), Nigella seed (*Nigella sativa* L) and Bitter orange (*Citrus aurantium* L.). Our survey found that the most common method of preparation for Aristolochia was stand-alone use, accounting for 60% of responses. This is relatively close to the findings of Yamani's study, which reported that 92% of respondents indicated that Aristolochia is used alone.<sup>4</sup> This is particularly important in light of research showing that combining Aristolochia with other plants, such as *Magnolia officinalis* - often thought to be safe - can increase its harmful effects. For example, kidney damage associated with a combination of *Aristolochia baetica* and *Magnolia officinalis* extracts was significantly higher than when these plants were used individually. This suggests that the potent combination of Aristolochia with other plants may be a key factor in the cases of Chinese Herbal Nephropathy (CHN) observed in Belgium in the 1990s.<sup>22</sup>

The quantity of the plant to be used is not precisely defined but is estimated in small amounts, such as a spoon, half a spoon, or a dozen grams, mixed with honey and consumed over a certain period. However, a group of six herbalists emphasized that this plant should only be used dermally, not orally. The recommended doses are vague and imprecise, which could potentially lead to an overdose. This aligns with the study carried out by El Yahyaoui El Idrissi, which revealed that 94.8% of users consume the plant with unspecified doses.<sup>8</sup>

Aristolochiaceae species exhibit significant variation in AA content, which accounts for their different lethal doses (LD50) among them. For example, the LD50 for *Aristolochia albidia* Duch. is 2g/kg, *Aristolochia baetica* L. is 4g/kg, *Aristolochia indica* L. is 7.5g/kg, and *Aristolochia fontanesii* Boiss. & Reut. is 7.9g/kg.<sup>11, 24-26</sup> A study by Yamani demonstrated moderate cytotoxicity of *Aristolochia* plants, with an IC50 (half maximal inhibitory concentration) after 72 hours of 69 µg/ml for *Aristolochia Baetica* and 72 µg/ml for *Aristolochia fontanesii* Boiss. & Reut.<sup>4</sup> Despite this, doses recommended by herbalists are often imprecise and can be toxic due to insufficient knowledge of toxic thresholds. This lack of specificity poses serious risks, including CKD, which may progress to ESKD, or in severe cases, lead to UTC. Consequently, this represents a significant public health concern.

Each herbalist provided a treatment duration they deemed appropriate. Based on their recommendations, we categorized the durations into two groups, yielding the following results: 40% recommended treatment for less than 3 months, 22.2% recommended 3 months or more, and 37.8% had no clear idea about the duration. The results suggest that there is no clear standardization in the treatment durations recommended by herbalists. Some favored shorter treatment periods, others leaned towards longer ones, and a notable number were unsure about the ideal duration. This variability may point to a lack of structured knowledge or established protocols among practitioners regarding treatment timelines.

The analysis of herbalists' insights revealed that over half (52.2%) reported the plant is used for cancer treatment, with 3 specifically mentioning skin cancer. A quarter (25.6%) indicated its use for skin diseases, wounds, smallpox, and even fractures. A smaller group (11.1%) mentioned its use for diabetes. Additionally, the plant was reported to treat digestive issues (e.g., ulcer, stomach pain, etc.) by 10%, irritable bowel syndrome by 5.6%, and tuberculosis by 2.2%. Interestingly, 3.3% of herbalists suggested it for weight gain. Finally, 14.4% of herbalists identified a diverse range of other uses, including hypertension, cysts, jaundice, dandruff, and ailments such as cough, sciatica, migraines, germs, and nervousness. Consistent with these findings, *Aristolochia* is predominantly used for cancerous diseases, followed by skin conditions, diabetes, digestive disorders, and irritable bowel syndrome. This aligns with the study conducted by Benarba and Boumediene in northwestern Algeria, which similarly reported that *Aristolochia* is primarily used to treat cancer (39%), followed by skin infections (14%), diabetes (11%), and gastrointestinal diseases (9%).<sup>27</sup> Similarly, Yamani's study identified cancer as the predominant therapeutic use of *Aristolochia* (64%), with diabetes accounting for 16% of its use.<sup>28</sup> While El Yahyaoui El Idrissi expanded the plant's therapeutic profile to include kidney disease (5.1%), our research did not identify any cases of *Aristolochia* being used to treat kidney diseases among the herbalists surveyed.<sup>8</sup>

Regarding cancer treatment, a study conducted in Casablanca in 2019 found that, among the seven plant families included in the study, *Aristolochiaceae* was the most widely used for treating cancer.<sup>16</sup> Two years later, another study conducted in Algeria identified *Aristolochia fontanesii* Boiss. & Reut. as the most frequently cited plant for cancer treatment.<sup>29</sup> Although the specific ailments treated with *Aristolochia* can vary by region, most studies consistently highlight that the plant is predominantly used for treating cancer.

A limited number of herbalists still recommend its use for skin conditions, strictly as a topical poultice. A survey conducted in the Central Middle Atlas Region also reveals that *Aristolochia* is primarily used in dermatological treatments, highlighting its significant role in addressing skin-related ailments.<sup>30</sup>

Over 31% of the participants believed that the majority of people using *Aristolochia* were elderly. In contrast, roughly 14% of the participants thought that *Aristolochia* users were primarily young people. This suggests that while *Aristolochia* is primarily associated with older individuals, a smaller group perceives its use among younger people, which could reflect differing attitudes or cultural beliefs about the plant's significance, even within the same region.

Herbalists' observations on the gender distribution of *Aristolochia* users are inconclusive. Over half (52.9%) reported no gender difference, while nearly 43% believed women make up the majority, and a smaller

portion (4.3%) observed a mainly male user base. In line with El Yahyaoui El Idrissi's research,<sup>8</sup> our study also indicated that women represent the majority of users, as reported by 42.9% of the herbalists in our sample. This supports the notion that, despite some variations in observations, women tend to be the predominant users of the plant in the region.

The Covid-19 pandemic disrupted the supply chain and market demand for *Aristolochia*, with 20% of herbalists reporting difficulties in obtaining the plant, including delivery challenges. Additionally, 24.3% of herbalists stated that sales were impacted, with 21.6% experiencing a decrease and 2.7% reporting an increase. This indicates that the pandemic significantly affected both the availability and commercial demand for *Aristolochia*, primarily leading to a decline in sales.

Our survey revealed that 77.8% of herbalists reported selling *Aristolochia*, aligning with a previous study indicating that this nephrotoxic plant continues to be sold both at herbal sale sites and on cooking sites.<sup>31</sup> The data highlights the widespread availability and continued sale of *Aristolochia*, despite its known nephrotoxic effects, suggesting a persistent demand for the plant in traditional herbal practice.

33.3% of herbalists confirmed that they prescribe *Aristolochia* to people when needed. Of these, 30% often prescribe it, 20% do so occasionally, and 50% prescribe it rarely. This indicates that while *Aristolochia* is still prescribed by some herbalists, its use appears to be reserved for precise situations, possibly due to its known toxic risks.

Over half (52.9%) of herbalists' source *Aristolochia* from plant collectors, 42.9% purchase it from wholesalers, and 4.3% reported collecting the plant themselves. The data suggests that most herbalists depend on external sources, like plant collectors and wholesalers, for obtaining *Aristolochia*, with only a small percentage gathering it independently. This points to a well-organized supply chain for the plant, likely influenced by its demand.

The findings are presented in Table 2.

#### Analytic study

Itinerant plant sellers displayed a slightly higher awareness (16.7%) of the link between *Aristolochia* and CKD compared to herbalists with fixed locations (15.2%). However, this difference was statistically not significant. The lack of statistical significance suggests that the observed difference in awareness between itinerant plant sellers and herbalists with fixed locations is not substantial and may be due to random variation rather than a true disparity.

Herbalists over 45 years exhibited a significantly higher awareness of *Aristolochia*'s potential to induce CKD (25%) compared to herbalists under 45 years (8%) ( $p = 0.027$ ). The significant difference in awareness between herbalists over and under 45 years of age suggests that age may play a role in knowledge of the risks associated with *Aristolochia*.

Interestingly, gender didn't significantly impact *Aristolochia* awareness, with women showing a slightly higher awareness (22.2%) than men (14.8%) ( $p > 0.05$ ). The lack of a significant gender difference implies that factors other than gender are more influential in shaping awareness of this issue.

Unschooling herbalists also had a marginally higher awareness (16.7%) than schooled herbalists (15.7%), but this difference was not statistically significant ( $p > 0.05$ ). The slight increase in awareness among unschooled herbalists may suggest that factors other than formal education could influence their knowledge of *Aristolochia*. However, the lack of statistical significance indicates that this difference is not substantial enough to conclude a meaningful relationship between education level and awareness. Similarly, experience didn't significantly influence *Aristolochia* awareness, with herbalists having more than 5 years of experience exhibiting a slightly higher awareness (18.3%) compared to those with less than 5 years (6.7%) ( $p > 0.05$ ). While herbalists with more than 5 years of experience demonstrated a higher level of awareness, the lack of statistical significance suggests that experience alone may not be a strong determinant of knowledge regarding *Aristolochia*'s risks. In the same way, herbalists whose sole source of income is the sale of medicinal plants (21.1%), are more aware compared to those who have another source of income (14.5%); however, this difference is statistically not significant.

**Table 2:** Knowledge and habits of herbalists concerning *Aristolochia* plants. (N=90)

Parameters	N (%)
Knowledge of <i>Aristolochia</i> plants, yes	87 (96.7)
<b>Species of <i>Aristolochia</i></b>	
Only one	75 (87.2)
Two	8 (9.3)
No idea	3 (3.5)
Idea about the toxicity of the plant, yes	34 (42.0)
<b>Type of toxicity</b>	
Vomiting	2 (2.2)
Nephrotoxicity	4 (4.4)
Hepatotoxicity	5 (5.6)
Gallbladder	7 (7.8)
Toxicity of the digestive system	4 (4.4)
Promotion of cancer	1 (1.1)
Death	6 (6.7)
<b><i>Aristolochia</i> is used as</b>	
Powder	63 (70.0)
Herbal tea	6 (6.7)
No idea	20 (22.2)
<b><i>Aristolochia</i> is used</b>	
Alone	54 (60.0)
Mixed with other plants	16 (17.8)
No idea	20 (22.2)
<b>Period of collection of the plant</b>	
autumn	1 (1.1)
Winter	3 (3.3)
Spring and/or Summer	52 (57.8)
No idea	34 (37.7)
<b><i>Aristolochia</i> is used for</b>	
<3 months	36 (40.0)
>3 months	20 (22.2)
No idea	34 (37.8)
Use of <i>Aristolochia</i> for cancer	47 (52.2)
Use for skin diseases, wounds and variola	23 (25.6)
Use of <i>Aristolochia</i> for diabetes	10 (11.1)
Digestives disorders	9 (10)
Use for irritable bowel syndrome	5 (5.6)
Use for weight gain	3 (3.3)
Other diseases	13 (14.4)
<b>Sale of <i>Aristolochia</i>, yes</b>	70 (77.8)
Always	1 (1.4)
Often	13 (18.6)
Sometimes	17 (24.3)
Rarely	39 (55.7)
Prescription of the plant, yes	30 (33.3)

Herbalists dependent on medicinal plant sales tend to have greater awareness than those with other income sources. However, this difference lacks statistical significance, suggesting no conclusive impact.

In addition, there was no significant difference observed in awareness of the associated risk of CKD from *Aristolochia* between herbalists who learned about the plant from sources such as the internet, books, or practical experience (19%) and those who acquired this knowledge from other herbalists (13.3%). Awareness of CKD risks from *Aristolochia* did not differ significantly between herbalists who learned from different resources and those who learned from other herbalists. This suggests the source of information does not influence awareness. Herbalists recommending shorter durations (22.2%) tended to be more aware of the link between *Aristolochia* and CKD compared to those recommending long durations (15%), however, this difference was not statistically significant. More importantly, herbalist sales showed a clear distinction. Informed herbalists, aware of CKD risks, sold *Aristolochia* at a much lower rate (11.4%) compared to uninformed

herbalists (30%), however the difference was not statistically significant. Although informed herbalists tended to sell *Aristolochia* at a lower rate, the lack of statistical significance suggests that awareness of CKD risks may not be the sole factor influencing their decision to sell the plant.

Finally, a non-significant difference was observed between herbalists who were aware of the risk associated with *Aristolochia* and prescribed it (13.3%) versus those who did not prescribe it (16.7%). The lack of significant difference suggests that awareness of *Aristolochia*'s risks may not strongly impact herbalists' prescribing decisions. Table 3 summarizes these findings.

As clarified in the Dahir, an herbalist must hold a specific certificate to sell medicinal plants. While herbal shop owners generally possess this certification, the same cannot be said for their employees or itinerant vendors. This disparity creates a concerning grey area, compromising both the quality of advice provided on medicinal plants and the safety of the public. This issue requires thorough discussion and the development of effective solutions.

**Table 3:** Factors associated with knowledge of Aristolochia as a nephrotoxic plant.

Kind of Knowledge about Aristolochia plants	Group 1 Aristolochia is nephrotoxic No N = 76	Group 2 Aristolochia is nephrotoxic Yes N= 14	P-Value
<b>Age range</b>			0.027
≤ 45 years	46 (92.0)	4 (8.0)	
> 45 years	30 (75.0)	10 (27.0)	
<b>Gender</b>			0.424
Female	7(77.8)	2(22.2)	
Male	69 (82.4)	12 (14.8)	
<b>Level of study</b>			0.538
Schooled	60 (84.5)	11 (15.5)	
Unschoolled	14 (82.4)	3 (17.6)	
<b>Experience</b>			0.245
≤ 5 years	14 (93.3)	1 (6.7)	
> 5 years	58 (81.7)	13 (18.3)	
<b>Service Modalities</b>			0.546
Fixed premises	56 (84.8)	10 (15.2)	
Itinerant plants sellers	20 (83.3)	4 (16.7)	
<b>Other sources of income</b>			0.353
No	15 (78.9)	4 (21.1)	
Yes	59 (85.5)	10 (14.5)	
<b>Origin of plant knowledge</b>			0.332
Herbalists	39 (86.7)	6 (13.3)	
Others	34 (81.0)	8 (19.0)	
<b>Prescription of Aristolochia</b>			0.469
No	50 (83.3)	10 (16.7)	
Yes	26 (86.7)	4 (13.3)	
<b>Sale of Aristolochia</b>			0.053
No	14 (70.0)	6 (30.0)	
Yes	62 (88.6)	8 (11.4)	
<b>The use of Aristolochia</b>			1.000
Alone	45 (83.3)	9 (16.7)	
Mixed	13 (81.3)	3 (18.8)	
<b>Recommended duration</b>			0.728
< 3 months	28 (77.8)	8 (22.2)	
≥ 3 months	17 (85.0)	3 (15.0)	

## Conclusion

Despite the investigations carried out in general, and in Morocco in particular, about the Aristolochia species plant and its harmful effects on health, this plant is still available over the counter in herbalists' shops. Most herbalists view it as a healing plant and believe it is toxic only when abused. On the other hand, the minority of herbalists who are aware of the toxicity of the plant, consider it safe in the case of external use or poultices. This highlights a significant gap in knowledge and regulation that could compromise public health. Therefore, future research should focus on evaluating the effectiveness of current regulations regarding the sale of Aristolochia and other toxic plants in herbalist shops, proposing stricter controls to ensure safety. Additionally, research should explore public awareness campaigns aimed at educating both herbalists and the general public about the risks associated with certain plants, while investigating safer practices for using medicinal plants. Addressing these issues is essential to prevent harm and safeguard the health of the population.

## Conflict of Interest

The authors declare no conflict of interest.

## Authors' Declaration

The authors hereby declare that the work presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

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