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Original Research Article

Ethnobotanical Study of Potentially Toxic Plants of Fez-Meknes Region, Eastern Middle Atlas, Morocco

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ABSTRACT

Medicinal plants have been used for therapeutic purposes since ancient times. These plants are generally perceived as safe, but they could also be toxic. The present study aims to undertake a survey of the nature, mode of application, and toxic effect of medicinal plants used in Fez-Meknes region, Eastern Middle Atlas, Morocco. An ethnobotanical survey was conducted from January 2020 to August 2021. The method employed a semi-structured questionnaire with open-ended questions on the uses, mode of application, and effects of the plants. The data obtained were statistically analyzed. Parameters such as Family use value (FUV), Use value (UV), Fidelity level (FL), and Informant agreement ratio (IAR) were obtained. From the survey, 59 potentially toxic plants, distributed across 33 families were documented. Concerning the uses of these plants, 31% of the respondents claimed that the plants are for cosmetic purposes, 23% claimed they are for minor illnesses, 15% claimed they are for chronic diseases, another 15% claimed they are ineffective, while 8% each claimed that they are for acute illnesses and other uses. For the disease categories, the result showed that the IAR values ranged from 0.8 to 0.96. The disease with the highest IAR value was hair loss (IAR = 0.96), followed by rheumatism (IAR = 0.95). The findings from this study have highlighted the potentially poisonous plants in the Fez-Meknes region. Further phytochemical and pharmacological studies on acute, sub-acute, and chronic plant toxicity are needed to determine the acceptable dose (LD_{50}), the most appropriate method for optimal use.

Keywords: Poisonous plants, Medicinal plants, Ethnobotany, Ethnomedicinal use.

Introduction

Medicinal plants have been used for curative purposes since prehistoric time. Medicinal plants contain unique phytochemicals with great potential for the treatment of numerous diseases, and these phytochemicals have arose the interest of pharmaceutical industries in recent times.[1,2] According to estimates from the World Health Organization (WHO), traditional medicine serves as the major means of meeting the healthcare needs of 80% of Asian and African people[3].

Morocco has favorable climatic and edaphic conditions that support a rich and diverse endemic flora with aromatic and medicinal properties. Historically, this flora has contributed significantly to the country's traditional medicine practice.[1-3]

Furthermore, phytotherapy and herbal medicine are becoming more popular in recent years.[2,5] For example, some studies have validated the traditional use of antidiarrheal medicinal plants by investigating the biological activities such as antispasmodic effects, delay intestinal transit, suppression of gut motility, and stimulation of water adsorption or reduction of electrolyte secretion of extracts of such plants. Of the numerous phytochemicals (such as alkaloids, tannins, flavonoids, and terpenes) present in active extracts, tannins, and flavonoids are thought to be responsible for antidiarrheal activity by increasing colonic water and electrolyte reabsorption.[5-7]

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In Morocco, medicinal plants are still widely used albeit empirically. Traditional Moroccan medicine finds its roots in classical Arabic medicine, which is added innovations by the local population.[9] The Moroccan traditional therapeutic knowledge is thus organically Arab Berber in its constitution, with an African and Andalusian contribution.[9] Also, in northern Morocco, the exploitation of medicinal and aromatic plants is an important source of livelihood for a large local population. Women are generally the custodians of the knowledge of the therapeutics techniques, prospecting, harvesting, and packaging of these plants.[5]

However, according to the World Health Organization (WHO), out of the over 20000 plants used for their medicinal properties around the world, only 2000 to 3000 of these plants have been scientifically studied.[5] Medicinal plants are experiencing a significant resurgence of interest in the United States and Europe.[10] In these countries, despite the spectacular success in the use of synthetic drugs for the treatment of many disease conditions, they still possess disadvantages such as toxicity and intolerability.[11] Despite the importance of these medicinal plants in traditional medicine practices, some of these plants can cause serious toxic effects in humans. It's possible that using medicinal plants without considering their toxicity caused significant annoyance to people. Likely, early humans frequently consumed toxic herbs while foraging for food. These could cause poisoning symptoms such as diarrhea, vomiting, coma, or other toxic reactions that could eventually result in death.[12] One of the biggest obstacles to using natural preparation methods is ensuring the safety of medicinal herbs[13].

To guarantee the safety control of plants or their derivatives, comprehensive research is needed to estimate toxicity risks based on the toxicological profile. This will provide scientific information to choose doses that may be safe for humans.[3 14]

A toxic plant, or poisonous plant, is a plant species that contains in some or all of its parts substances that are toxic mainly to humans or animals. The toxic principles contained in plants are generally organic compounds, rarely minerals and toxicity is most often resulted from the

ingestion or contact with certain parts of these plants, causing significant morbidity and mortality.[15] Herbal ingredients may also be metabolically activated through phases I and II reactions in the human body, which can produce reactive intermediates and cause toxicity.[3]
The objective of this study was to carry out an ethnobotanical survey among herbalists and the local population of Fez-Meknes region, Eastern Middle Atlas, Morocco to specify the nature and the proportion of prescription of supposedly toxic plants as well as to collect data on their uses in traditional medicine.

Materials and Methods

Study area
The Region of Fez-Meknes covers an area of 40,075 km² or 5.7% of the national territory. It is bounded to the North by the region of Tangier-Tetouan-Al Hoceima; to the southwest by the region of Beni Mellal-Khénifra; to the East by the region of Oriental; and to the South by the region of Drâa-Tafilalet.
According to the General Population and Housing Census (RGPH) of 2014, the Region of Fez-Meknes has 4,236,892 inhabitants of which 60.52% are urban dwellers, a rate almost equivalent to the national rate of 60.36%, and the population density is 105.7 inhabitants per km^2, which is very high compared to the national average (47.6 inhabitants/km^2).
The Region of Fez-Meknes (Figure 1) comprises of two administrative prefectures: the Prefecture of Fez, the Prefecture of Meknes, and seven provinces of Boulemane, El Hajeb, Ifrane, Moulay Yaâcoub, Sefrou, Taounate and Taza, 194 communities consisting of 33 municipalities and 161 rural Communities.[16]

Soil types
Three main types of soil have been identified in the region: - Mineral soil, in the province of Boulemane; - The Brown soil, in the plain of Sais, which is characterized by their thick, fertile and nutrient-rich formation; - The tirs and vertisol soil of Saïss and Sefrou, with the best agricultural value (Figure 2).[16]

Climate and precipitation
The Fez-Meknes region has a Mediterranean to continental climate with winter and summer, especially in the Boulemane zone. The climate of the high areas of the Rif and Pre-Rif is mild in summer, while in winter it is cooler with frequent and strong frosts.
The continental areas are subject to the blows of the 'Chergui' which contributes to the rise in temperatures. Geographical disparities within the region result in important distinctions in the level of rainfall, which is categorized as follows:
Wetlands: These areas receive a large volume of rainfall. These are the high areas of the Middle Atlas and the Rif. The Rif is the most watered because it receives an average annual rainfall of more than 800 mm, while the Middle Atlas receives an average annual rainfall of 600 mm.
Moderately watered areas: They receive an average of 400 mm/year of rain; these are the PreRif areas and the northern flank of the region.
Dry areas: These are the alfa areas in the southeast of the region receiving an annual rainfall of less than 300 mm. They include the plains of Moyenne-Moulouya, which is practically arid, and the scarcity of water it experiences only allows vegetation of the Steppe, Alfa and Garrigue type.[16]

Method of data collection
The survey was conducted from January 04, 2020, to August 27, 2021, in the region of Fez-Meknes. Data collection was done through a semi-structured questionnaire. Two hundred (200) participants consisting of herbalists and local inhabitants were administered the questionnaire and/or interviewed. The time of the interview varied from 15 to 25 minutes or more depending on the ease of understanding of the questions by the respondents. Sometimes it was filled in by the respondents themselves after explanations have been given by the interviewer.
Informed consent was sought from the respondents and the confidentiality and anonymity of the data collected were maintained.
During each interview, socio-demographic features of the respondents and information on the medicinal plants were collected. The socio-demographic features included gender, age, educational level, occupation, and place of residence in the study area. The data collected for each medicinal plant included the common/local name, scientific name, type of plant (wild/cultivated), uses, used part(s), method of preparation, route of administration, type of toxicity, and collection period.
The toxicity of medicinal plants was verified and confirmed by bibliographic summaries citing the diseases as well as the symptoms resulting from the use of medicinal plants declared toxic by the respondents.[16]

Data analysis
The results of the ethnobotanical survey were analyzed using Family Use Value (FUV), Use Value (UV), Fidelity Level (FL), and Informant Agreement Ratio (IAR). All statistical analyses were performed using the statistical package in Microsoft Excel 2010.

Family Use Value (FUV)
FUV identifies the importance of plant families. It is an index of cultural importance applied in ethnobotany to calculate a biological plant taxon value. To calculate FUV, the following formula was used:

$$FUV = \frac{\text{UVs}}{\text{NS}} \qquad 1$$

Figure 1: Provinces and Prefectures of Fez-Meknes Region.

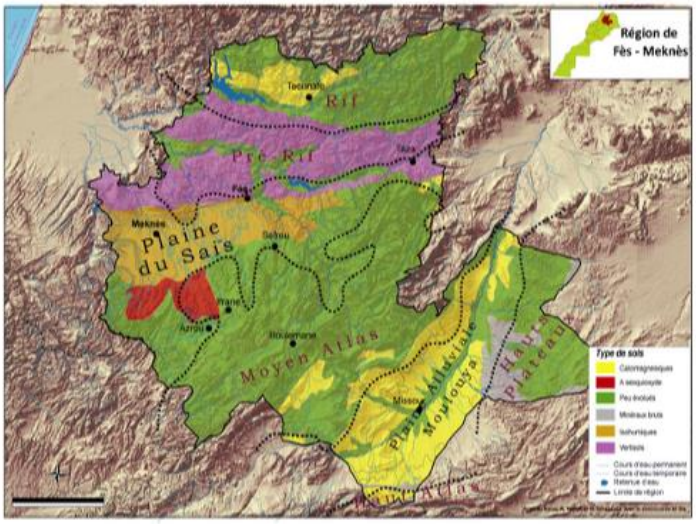

Figure 2: Soil types in Fez-Meknes Region.

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Where; UVs is the number of informants mentioning the family and NS is the total number of species in each family.[17]

Use Value (UV)

The species use value (UV), a methodical value that demonstrates the relative importance of locally known species was calculated according to the following formula:[18]

$$UV = \frac{\sum Ui}{N} \qquad 2$$

Where; Ui is the number of use reports mentioned by each informant, and N is the total number of informants interviewed for a given plant species.

Fidelity level (FL)

The level of fidelity (FL) is the percentage of informants who mentioned the use of certain plant species to treat a particular disease in the study area. The FL index is calculated using the following formula:[19,20]

$$FL(\%) = \frac{Ip}{Iu} \times 100 \qquad 3$$

Where; IP is the number of informants who independently reported the use of a species for the same disease and Iu is the total number of informants who reported the plant for any major disease.

Informant Agreement Ratio (IAR)

The IAR for each category of use was calculated using the formula:[21]

$$IAR = \frac{Nur - Nt}{Nur - 1} \qquad 4$$

Where; Nur is the number of mentions in each category and Nt is the number of taxa used in each category. The IAR is a factor whose value range from 0 to 1.

Results and Discussion

The socio-demographic features of the study population

The socio-demographic features of the respondents are presented in Table 1. The survey showed that 58% of respondents were males, and 42% of respondents were females. As for the distribution of respondents by age, it was noticed that 70% of the respondents were over 40 years old, 20% were between 20 and 40 years old, 6% were between 20 and 25 years old, while only 4% were between 10 and 20 years old. Older people possess richer and more reliable knowledge and know-how than younger people. The knowledge on the use of medicinal plants faces serious treat, because of the loss of knowledge in the course of time from older to younger population, and this is attributed to modernization and the tendency towards modern medicine as opposed to traditional medicine. The results of this study corroborated the findinds from the study conducted by Chaachouay.[22] For the distribution of respondents according to their level of education, a major proportion (38%) of the respondents were at the primary level of education, 22% had university education, while 20% of the respondents were the illiterates, and those having a secondary level of education. It was observed that the percentage of use of medicinal plants was dependent on the educational level of the respondents, this percentage decreased as the educational level increased, this observation is in agreement with the findings from previous studies.[20-22]

Figure 3 shows the percentage distribution of respondents in the provinces of the study area. According to the result, the majority (20%) of the respondents came from fez region, followed by those from the city of Taounate (17%), the region of Taza (15%), the regions of Meknes and Séfrou (12%), then 10% from the Moulay Yacoub region, and finally, 5% each from the regions of Ifran, El Hajab and Boulemane. The geographical location of Morocco gives it a climate that supports a rich biodiversity, and also makes it a prominent place among the Mediterranean countries with a good knowledge of medicinal and aromatic plants. This knowledge which is of ancestral origin are generally acquired through long experience, accumulated and transmitted from one generation to another.[23,24] Through their daily contact with plants and relationship with consumers of these plants, the people of Eastern Middle Atlas have learned to distinguish between plants with toxic effects and those that are harmless.[21]

The results obtained from the data analysis showed that a significant percentage of people who know and use medicinal plants are illiterate, and the practice cuts across all the different categories of the population. Nevertheless, there is a remarkable percentage of people who know and use toxic plants that have university education.[22]

With respect to the occupation, the majority of the respondents are professionals with the highest percentage of them being herbalists (30%), followed by traders (20%), teachers (18%), housewives (14%), farmers (10%), and the minority (8%) was students.

Table 1: Socio-demographic features of respondents in the Fez-Meknes region

Profile		Fez-Meknes Regions
Gender	Male	58%
	Female	42%
Age	10 - 20 years	4%
	20 - 25 years	6%
	20 - 40 years	20%
	Over 40 years	70%
Educational level	Illiterate	20%
	Primary	38%
	Secondary	20%
	University	22%
Occupation	Teacher	18%
	Farmers	10%
	Herbalist	30%
	Trader	20%
	Student	8%
	Housewife	14%

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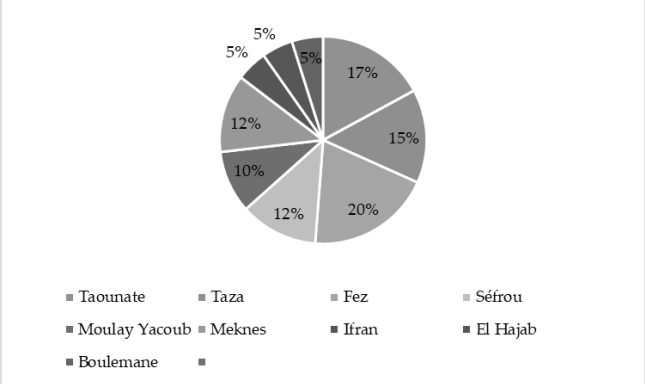

Figure 3: The percentage distribution of respondents in provinces in the study area.

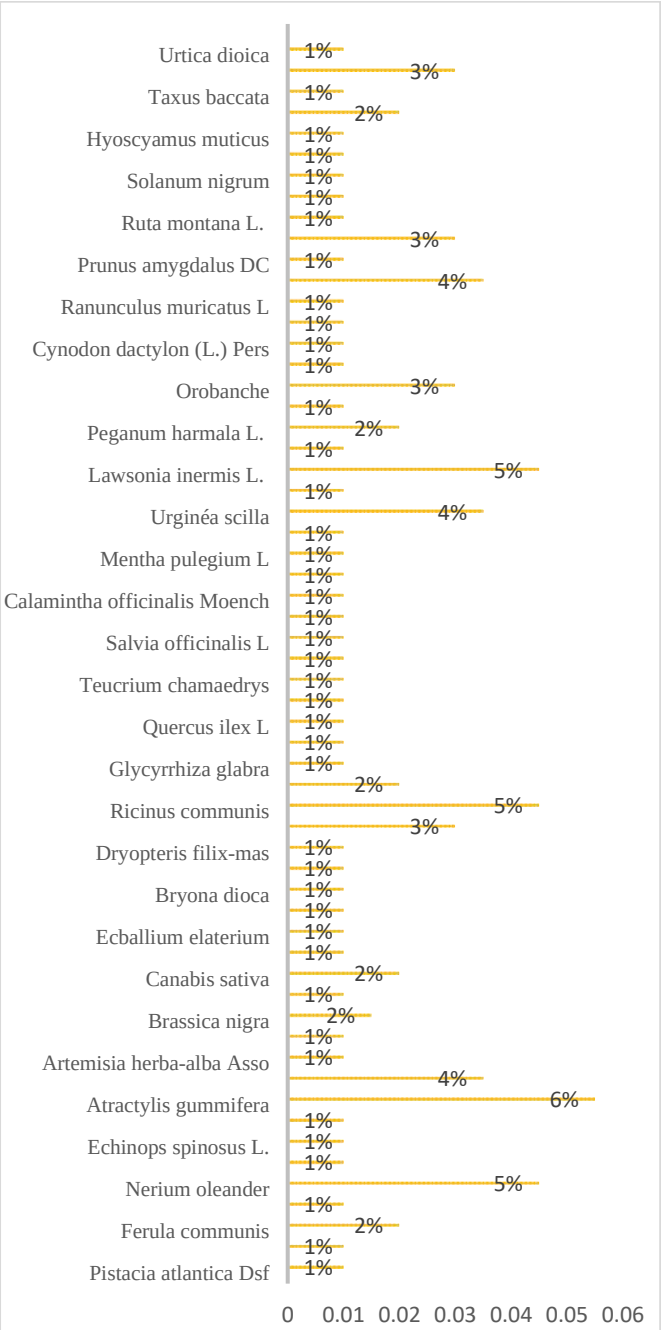

Figure 4: The percentage of toxic plants cited by the respondents in the Fez-Meknes region.

Botanical catalog of toxic plants

Following the data analysis as presented in Figure 4, the percentage of plants known by the respondents were as follows: 6% for *Atractylis sp* and *gummifera sp*, 5% for *Ricinus communis*, *Nerium oleander* and *Lawsonia inermis*, 4% for *Artemisia absinthium L*, *Urginea scilla*,. and *Nigella sp*, 3% for *Mercurialis annua* L., *Orobanche sp*, *Rubia sp*, *Datura stramonium*, and *Daphne gnidium*, 2% for *Canabis sativa*, *Eupharbia resinifera berg*, *Ferula communis* L., and *Mandragora automnalis*, and finally 1% for each of the other species.

Families of toxic plants

According to the ethnobotanical study, 59 toxic plants were documented belonging to 33 different families (Figure 5). The families represented include:

Lamiaceae (14%), Solanaceae and Asteraceae (8%), Fabaceae (7%), Ranunculaceae, Euphorbiaceae, and Cucurbitaceae (5%), Apiaceae, and Liliaceae (3%), Anacardiaceae, Apocynaceae, Asparagaceae, Aristolochiaceae, Brassicaceae, Cactacea, Cannabaceae, Chenopodiaceae, Cuperessaceae, Dryopteridaceae, Fagaceae, Lythraceae, Myrtaceae, Nitrariaceae, Oleaceae, Orobanchaceae, Papaveracaceae, Poaceae, Rosaceae, Rubiaceae, Rutaceae, Taxaceae, Urticaceae, and Thymelaeaceae (2%).

These results agrees with previous studies which showed that the Lamiaceae and the Asteraceae are the most used families in herbal medicine in the study region as well as in most Mediterranean countries, and these countries have also been shown to be a reservoir of poisonous plants.[18,25-27]

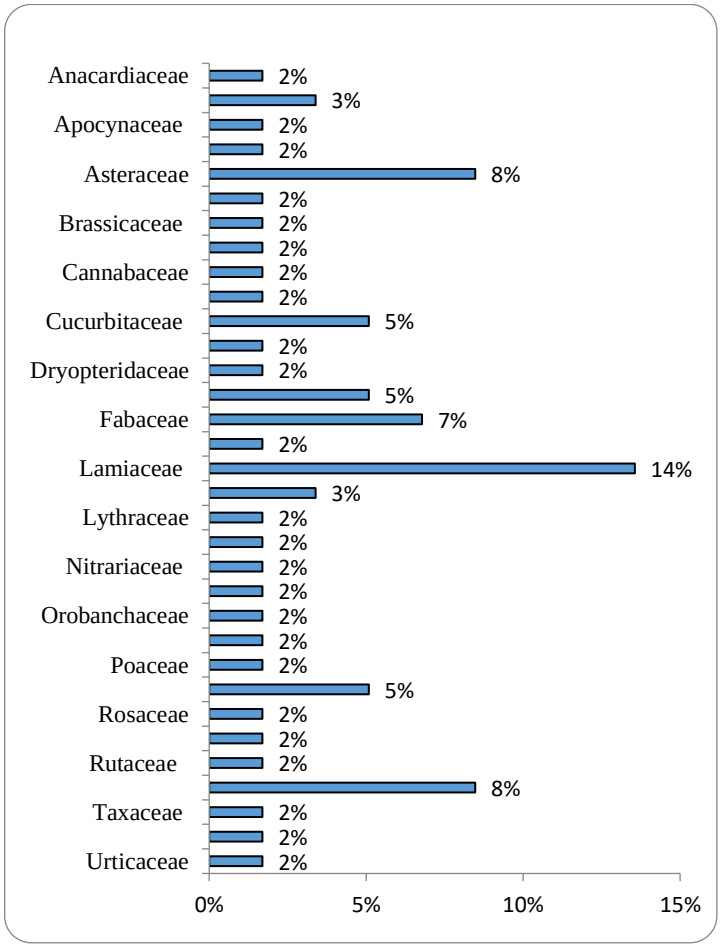

Figure 5: Distribution of the main families of poisonous plants expressed as a percentage of the total number of poisonous plants in the study area.

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Disease categories and their IAR values

The informant agreement ratio (IAR) depends on the availability in the study area of plants used for the treatment of diseases. This value is used to determine the level of prevalence of diseases in the study area, and also the effectiveness of a plant for any disease. The value of the IAR ranges from zero to one. A high IAR value indicates an agreement in the selection of taxa among informants, while a low value indicates disagreement. Recently, informant agreement ratio has been used as an important tool for the analysis of ethnobotanical data.[21] In the present study, the IAR values ranged from 0.8 to 0.96 per category of use (Table 3). Hair loss (Alopecia) was the most mentioned disease in the study area, with an IAR value of 0.96, followed by Rheumatic disorders (IAR = 0.95), Parasitic diseases (IAR = 0.94) and Dental problems (IAR = 0.92). These high IAR values indicate that the informant's knowledge of the application and effectiveness of the various medicinal plant species in the treatment of ailments is very reliable.[28] The result obtained for the treatment of rheumatism is similar to the result of the study conducted by El Khomsi M and Dandani Y .[21]

Quantitative analysis

Respondents' Knowledge of poisonous plants

Majority (60%) of the respondents claim to have knowledge of poisonous plants, while 40% claim ignorance of toxic plants (Figure 6). In addition, an ethnobotanical survey carried out among practitioners of traditional medicine in the Central Middle Atlas revealed a wealth of knowledge in medicinal and aromatic plants in the region. Analysis of the flora showed that 123 species of plants, spread over 48 families growing in the study area are prescribed for their medicinal values.[29]

The high percentage of respondents with knowledge of toxic plants can be explained by the importance of medicinal plants for the local population of the study area. Furthermore, other national studies in Morocco, have indicated that local population have extensive traditional knowledge of plants and their harmful effects, and quantitative analyses have shown that plants can have negative impact on different organs of the body, and pose a risk to human health. Despite the fact that some of the reported plants are used commonly for culinary purpose and for acute health problems, their dose is a key factor that defines whether the effect would be therapeutic or toxic. Therefore, caution should be exercised when using these plants, particularly for medicinal purposes, and adequate information on these plants including toxicity, composition, and safe doses should be obtained.[30]

The most used families and their family use values (FUV)

A total of 59 species of poisonous plants belonging to 33 families are used as medicinal plants in Fez-Meknes region. These plants are presented in alphabetical order in Table 2. For each plant presented, the scientific name, family, local name, the preparation method adopted by the local population, as well as the FUV, UV and FL are listed.

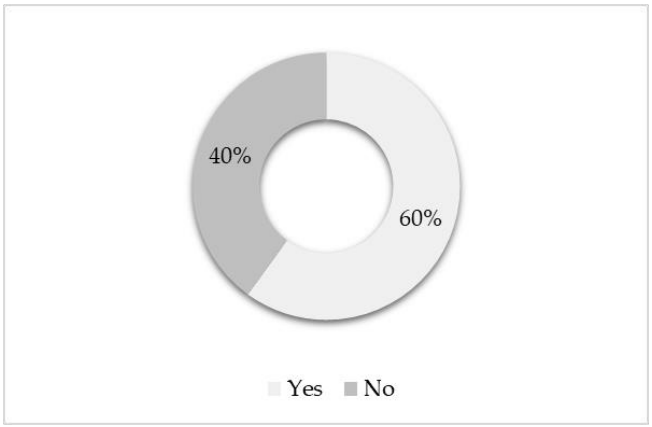

Figure 6: The percentage of respondents with knowledge of certain toxic plants

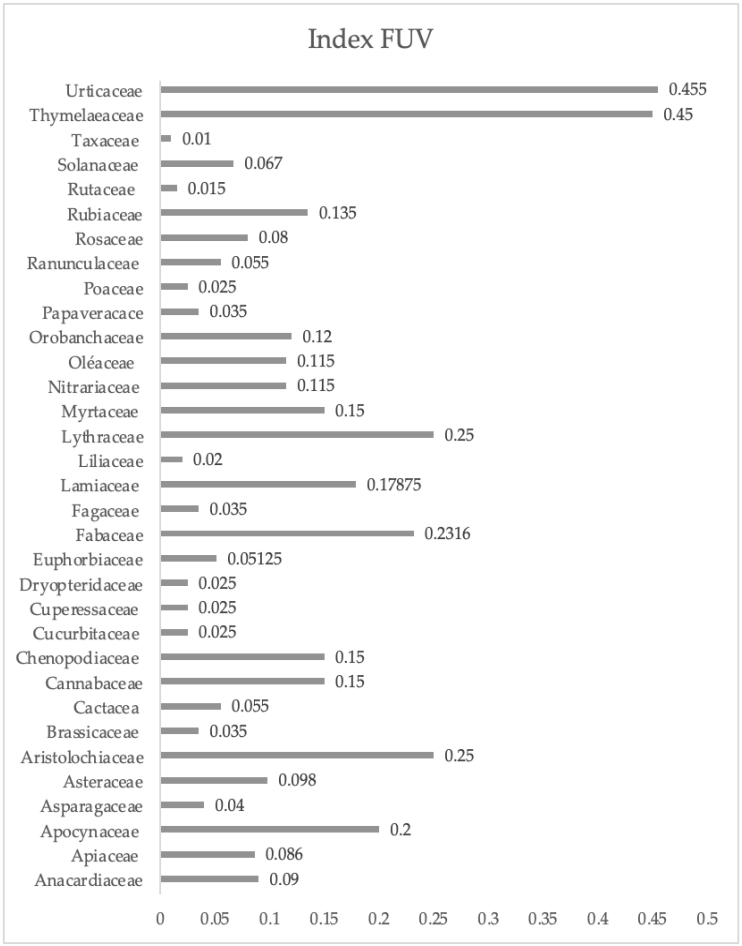

Figure 7: Family use value (FUV) of medicinal, aromatic and toxic plants.

The most representative families, in terms of the number of species, were Lamiaceae (8 species), Asteraceae and Solanaceae (5 species each), followed by Fabaceae (4 species), Ranunculaceae, Euphorbiaceae, and Cucurbitaceae (3 species each), while other families were represented by two or only one species (Figure 5).

The presence of a large percentage of these families in the study area could be explained by the availability of climatic and edaphic factors that favour the development and adaptation of most species. These results corroborated the results obtained from previous studies, which showed that Lamiaceae and the Asteraceae are the most used families of herbal medicine in the Fez-Meknes region as well as in most Mediterranean countries.[22] These observations can be explained by the fact that families with many species probably have a rich morphological and chemical diversity, and are also rich in medicinal plants as well as reservoir of poisonous plants.[31]

Based on the FUV index, the most cited families are Urticaceae (FUV = 0.455) and Thymelaeaceae (FUV = 0.45) (Figure7). This could be explained by the large representation of these families in the flora of the Fez-Meknes region due to the presence of factors which favour the development and adaptation of the majority of the species.

Diversity of medicinal plants and their use values (UV)

Use value assesses the relative importance of the reported use of poisonous plants used as medicinal plants. The use values were calculated based on the information obtained from informants used in the study area. The UV ranged from 0.005 to 0.4 (Table 2). The results of this study showed that *Mentha pulegium* L., exhibited the highest UV of 0.45, followed by *Origanum compactum Benth* (UV = 0.4), *Trigonella foenum graecu* (UV = 0.3), and *Aristolochia longa* L (UV = 0.25). The lowest UV was shown by *Teucrium chamaedrys* (UV = 0.005).

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Table 2: List of toxic plants cited by respondents and their uses in traditional medicine in the Fez-Meknes region

Scientific name	Local name	Type of plant	Toxicity	Therapeutic Use	Plant condition	Method of preparation	Mode of administration	Type of toxicity	FUV	UV	FL
Anacardiaceae *Pistacia atlantica Dsf*	Lebtem	Wild	YES [36]	Cavities, Stomach burns	Gum	Decoction	Rinsing	Irritating	0.09	0.09	33.33
Apiaceae *Ammi visnaga (L) Lam*	Bachnikha	Wild	Yes [36]	Dental care, Diabetes	Dry/Fresh	Decoction/ Brute	Gargle/oral/ fumigation	Irritating	0.086	0.15	43.33
Apiaceae *Ferula communis L.*	Bouble, Lkalkh	Wild	Currently, interest in *F. communis* focuses on the presence of two chemotypes in the wild. One chemotype is poisonous to animals, whereas the other chemotype is non-poisonous.[45]	Rheumatism, Dermatological disorder, Trauma, Diabetes	Dry/Fresh	Decoction/ Poultice	Oral	Irritating/ Deadly		0.085	58.82
Apiaceae *Foeniculum vulgare*	Bessbass	Wild	Yes [36]	Gastrointestinal pain, Asthma	Dry/Fresh	Decoction	Oral	Irritating		0.025	40
Apocynaceae *Nerium oleander*	Defla	Cultivated	The potential toxic effects of all parts of the shrub either fresh or dried on animal and human body were documented [37].	Parasitic diseases, Fever, Mouth rinsing, Rheumatoid arthritis	Dry/Fresh	Decoction/ Poultice	Rinsing/ Fumigation	Irritating	0.2	0.2	75
Asparagaceae *Asparagus officinalis L.*	Seckoum	Wild	Yes [38]	Intestinal pain, Cancer, Rheumatism	Dry/Fresh	Infusion// Decoction	Oral	Irritating	0.04	0.04	50
Asteraceae *Echinops spinosus L*	Tasekra, Echinops	Wild/ Cultivated	It is a toxic plant that causes neuro-vegetative disorders and exciting effects and convulsion[39].	Dermatological disorder, Gastric disorder	Dry/Fresh	Decoction	Fumigation/ Rinsing	Irritating	0.098	0.01	50

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Asteraceae *Anacyclus pyrethrum*	Ouda latlass	Wild	Yes [36]	Rheumatism, Sciatica	Fresh	Decoction	Oral	Irritating/ Deadly	0.01	50
Asteraceae *Atractylis gummifera*	Addâd	Wild	Atractylis gummifera is a toxic plant widely used in Mediterranean traditional medicine[40]	Parasitic diseases, Cosmetic use	Dry/Fresh	Poultice/Cui	Fumigation/ Rinsing	Irritating/ Deadly	0.15	60
Asteraceae *Artemisia absinthium L.*	Chiba	Wild/ Cultivated	Toxicity tests of wild wormwood essential oils were performed using the brine shrimp (*Artemia sp*.) test. Nauplii lethality (LC_{50}) ranged from 15.7-31.9 µg/mL, depending on oil composition. The most toxic *A. absinthium* oils were found to be those containing an appreciable amount of trans-sabinyl acetate (45.2%) and (cis+trans) thujones (12.3%), while other samples with equivalent amounts of sabinyl acetate, but without thujones were found to be less toxic.[46]	Stomach pain, Heart problem	Dry/Fresh	Infusion	Oral	Irritating	0.2	50
Asteraceae *Artemisia herba-alba Asso*	Chih	Wild/ Cultivated	Yes [36]	fever, Gastric pain	Dry/Fresh	Decoction	Oral	Irritating	0.12	50
Aristolochiaceae *Aristolochia longa L.*	Berztem	Wild	The ingestion of this herb is associated with development of a syndrome indicating	Kidney problem, Digestive tract disorder,	Dry	Decoction/ Raw Powder	Oral	Irritating	0.25	0.25	20

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			aristolochic acid nephropathy (NAA)[41]	Cancers							
Brassicaceae *Brassica nigra*	Lkhardl	Wild	Several species of the Brassica genus (Brassica napus and Brassica rapa) contain thioglucosides, the progoitrins, which, under the action of a myrosinase, produce oxalidine thiones with a goitrogenic action in non-ruminants.[42]	Hair loss, Constipation, Rheumatism	Dry	Poultice	Ointment	Irritating/ Deadly	0.035	0.035	42.85
Cactacea *Opuntia ficus-indica (L.)*	Hendiya	Cultivated	The current study has shown low toxicity of *Opuntia ficus*.[47]	Stomach pain, Kidney stones	Dry/Fresh	Powder/ Decoction	Oral	Irritating	0.055	0.055	36.36
Cannabaceae *Canabis sativa*	leKif	Cultivated	Neurotoxicity is common after acute cannabis exposures[43].	Hair loss, Drug addiction	Dry/Fresh	Crushed	Smoking	Irritating	0.15	0.15	50
Chenopodiaceae *Chenopodium ambrosioides L.*	Mkhinza	Wild/ Cultivated	The aqueous extract from C. ambrosioides leaves produce slight hepatotoxic lesions in rats[44].	Headache, Fever	Dry/Fresh	Brute	Poultice	Irritating	0.15	0.15	66.66
Cucurbitaceae *Ecballium elaterium*	Fkoss lhmar	Wild	Ecbalium elaterium has a very violent effect on the body and has little use in modern herbalism[45].	Dermatological disorders	Dry/Fresh	Infusion	Fumigation	Irritating/ Deadly	0.025	0.01	100
Cucurbitaceae *Citrullus colocynthis*	Hdej; hantel	Wild/ Cultivated	The functioning of the rats' kidney, bone marrow, and liver were all negatively impacted by the extract of ripe Citrullus colocynthis fruit[46].	Stress, Rheumatism	Dry/Fresh	Crushed.	Poultice	Irritating		0.04	50

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Cucurbitaceae *Bryona dioca*	Lwaya	Wild	Mice exposed to acute toxicity conditions were shown to be toxic when given an aqueous extract of B. dioica roots at a dose more than 250 mg/kg via oral administration[12].	The grains are used for flushing the bodies	Dry/Fresh	Infusion	Oral	Irritating		0.025	100
Cuperessaceae *Tetraclinis articulata*	Ar'âr, Thuya de Berbérie	Wild/ Cultivated	Numerous studies have documented the neurotoxic effects of extremely low concentrations of EO chemicals.[47]	Hair loss, Eczema	Dry/Fresh	Decoction	Powder/ Poultice	Irritating		0.075	46.66
Dryopteridaceae *Dryopteris filix-mas*	Sarkhass	Wild/ Cultivated	The leaf extract of Dryopteris filix-mas may be nephrotoxic following 6 months exposure.[48]	Kidney problems	Dry/Fresh	Decoction	Oral	Irritating	0.025	0.025	100
Euphorbiaceae *Mercurialis annua L*	Harrigua melsa,	Wild/ Cultivated	The extract was found to have a cytotoxic effect on two cell lines: colorectal (HRT-18) and breast cancer (T47D).[49]	Back pain, Gastrointestinal disorders.	Dry/Fresh	Infusion	Oral	Irritating	0.051 25	0.045	44.44
Euphorbiaceae *Ricinus communis*	Krenk/ lkharwaa	Wild	Numerous components of Ricinus communis have been isolated and determined to be poisonous.[50]	Hair loss, Parasitic diseases, Prostatitis	Dry/Fresh	Brute/ Poultice	Massage/Oral/ Inhalation	Irritating		0.09	50
Euphorbiaceae *Euphorbia resinifera berg.*	Lfarbyon	Wild	latex presents frequent intoxications.[51]	Cyst, Diabetes, Cosmetic use	Dry/Fresh	Decoction	Poultice/Oral	Irritating		0.025	40
Fabaceae *Glycyrrhiza glabra*	Irk soss	Wild/ Cultivated	Numerous earlier research have documented the toxicological effects of the Glycyrrhiza radix[52].	Headache, Asthma, Rheumatism.	Fresh	Decoction	Oral	Irritating	0.231 6	0.095	36.84

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ISSN 2616-0692 (Electronic)

Fabaceae *Trigonella foenum graecu*	El-halba	Cultivated	Additionally, mounting data points to the possibility of neurodevelopmental, neurobehavioral, and neuropathological adverse effects from fenugreek.[53].	Loss of Appetites, Common cold, Heamatological disorders, Obesity	Dry/Fresh	Maceration, Decoction	Oral	Irritating		0.3	50
Fabaceae *Trifolium*	Nafla	Wild	This plant is generally non-toxic in colder climates, but could be toxic in warmer climates.[49]	Parasitic diseases	Dry	Decoction	Fumigation	Irritating/ Deadly		0.03	100
Fagaceae *Quercus ilex L*	Korrich	Wild	At a dosage of 2000 mg/kg, all of the mice die and their weight significantly decreases.[54]	Stomach pain.	Dry/Fresh	Decoction	Oral	Irritating	0.035	0.035	100
Lamiaceae *Teucrium chamaedrys*	Jaaydya	Wild	The usage of germander preparations is nevertheless prevalent despite their toxicity[55].	Dermatological disrders	Dry/Fresh	Decoction	Poultice	Irritating	0.178 75	0.005	100
Lamiaceae *Ocimum basilicum L*	Basil; Lahbaq	Wild/ Cultivated	As the leaf extract of R. officinaliand O. basilicumis a highly toxic even at low doses, these plants may eventually prove to be useful as a larvicide[56]	Hair loss.	Dry/Fresh	Decoction	Rinsing	Irritating		0.01	50
Lamiaceae *Salvia officinalis L*	Salmiya	Wild/ Cultivated	50% of the rats die after receiving 3000 mg/kg of S. officinalis essential oil, along with various clinical symptoms of poisoning such as paralysis, sleepiness, shaking, and asphyxiation.[57]	Heart disease	Dry/Fresh	Decoction	Oral	Irritating		0.25	100

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ISSN 2616-0692 (Electronic)

Lamiaceae *Origanum compactum Benth*	Za'tar,	Wild	The current study's findings imply that at greater concentrations, O. compactum essential oil demonstrated genotoxic action. [58]	Influenza, Hypoglycemia	Dry/Fresh	Infusion, Decoction, Gargle, Inhalation	Oral	Irritating		0.4	87.5
Lamiaceae *Calamintha officinalis Moench*	Manta	Wild/ Cultivated	The EOs of C. nepeta, T. mastichina, and O. virens had oral fatal toxicity doses (LD50) ranging from 1000 to more than 2000 mg/kg.[59]	Fever, Flu	Dry/Fresh	Infusion	Oral	Irritating		0.01	50
Lamiaceae *Marrubium vulgare L.*	Merrîwa	Wild/ Cultivated	This plant contain toxic chemical compounds and photosensitizers such as psoralen, polyphenols, and coumarins.[51]	Fever, Flu	Dry/Fresh	Decoction	Poultice	Irritating		0.105	76.19
Lamiaceae *Mentha pulegium L*	Fliyo	Wild/ Cultivated	The essential oil of *M. pulegium* is toxic.[50]	Fever, Common cold, Flu	Dry/Fresh	Infusion/ Decoction	Oral/Poultice/ inhalation	Irritating		0.45	55.55
Lamiaceae *Lavandula angustifolia Mill.*	Khzama	Wild/ Cultivated	Adults' fat, protein, and carbohydrate contents decrease when exposed to L. angustifolia essential oil.[60]	Cough, Asthma	Dry/Fresh	Decoction	Oral	Irritating		0.2	75
Liliaceae *Urginea scilla*	Lansla	Wild	pathological alterations in the heart, brain, and sciatic nerve were discovered when compared to control groups[61].	Trauma	Dry	Crushed	Poultice	Irritating	0.02	0.025	60
Liliaceae *Colchicum autumnale*	Katil lklab	Wild	Colchicine poisoning can result in gastroenterocolitis followed by multi-organ dysfunction syndrome [62]	Parasitic diseases	Dry/Fresh	Decoction	Fumigation	Irritating		0.015	100

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Lythraceae *Lawsonia inermis L.*	Henna	Cultivated	Mildly harmful[63].	Hair loss	Dry/Fresh	Decoction	Poultice	Irritating	0.25	0.25	100
Myrtaceae *Myrtus communis L*	Rayhan	Wild	The ethanolic extract is not as harmful as the aqueous extract, which is far more toxic.[64]	Stomach pain, Fever, Pain	Dry/Fresh	Decoction	Oral	Irritating	0.15	0.15	56.66
Nitrariaceae *Peganum harmala L*	Harmel	Wild	Additionally, we noticed that exposure to PHS may have a harmful effect on body length, brood size, and movement patterns.[65]	Eczema	Dry	Decoction	Poultice	Irritating	0.115	0.115	100
Oleaaceae *Olea europeae L.*	Zitoun	Wild/ Cultivated	The olive leaves extract should be handle with care[66]	High blood pressure	Dry/Fresh	Infusion	Oral	Irritating	0.12	0.12	100
Orobanchaceae *Orobanche*	Chwal lkhrof	Wild/ Cultivated	The traditional usage could not be properly explained by the pharmacological tests done with extracts produced from Orobanche spp.[67]	Used with the *Malva pazvifloza* plant in preparing (lkhobiza)	Fresh	Maceration/ Decoction	Oral	Irritating	0.035	0.035	85.71
Papaveracace *Chelidonium majus*	Mamiran	Wild/ Cultivated	Ten cases of acute hepatitis caused by larger celandine (Chelidonium majus) preparations have been reported to us[68].	Drug addiction	Dry	Infusion, Decoction	Oral	Irritating	0.025	0.025	100
Poaceae *Cynodon dactylon (L.) Pers.*	Njem, Quackgrass	Wild	It contains some hydrocyanic acid and can be toxic to livestock if eaten in excess.[52]	Kidney problems.	Dry/Fresh	Decoction	Oral	Irritating		0.03	100
Ranunculaceae *Delphinium staphysagria L*	Habbat râss	Wild/ Cultivated	Their primary components, diterpenoid alkaloids, appear to be in charge of both their	Hair loss, Diarrhea	Dry/Fresh	Decoction	Poultice	Irritating		0.14	64.28

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ISSN 2616-0692 (Electronic)

			poisonous and therapeutic qualities.[69]								
Ranunculaceae *Ranunculus muricatus L*	Ouden lhalouf	Wild	It is determined that the plant Ranunculus muricatus L. may be both phytotoxic and cytotoxic.[70]	Dermatological disorders, Rheumatism	Dry/Fresh	Vintage, Cui	Brushing/Oral	Irritating		0.03	50
Ranunculaceae *Nigella sp.*	Sanoj	Wild	Our data indicated that NSO has protective effects against ethanol-induced hepato toxicity and renal toxicity through attenuating lipid peroxidation.[71]	Flu, Asthma, Rheumatism	Dry/Fresh	Decoction/ Crushed/ Powder	Oral	Irritating		0.025	60
Rosaceae *Prunus amygdalus Stokes var amara DC*	Louz lhar	Wild	Leaves, seed, and bark are toxic.[53]	Stomach- - The allergy	Dry /Fresh	Decoction/ Infusion	Oral/ Powder	Irritating	0.08	0.08	56.25
Rubiaceae *Rubia*	Al'Fouwa	Wild/ Cultivated	The methanolic extract of Rubia roots yields phytoalexins (AQs) and cyclopeptides (RAs) of the Rubiaceae type, such as RAXXIII, RA-XXIV, and RA-VII, which can be cytotoxic.[72]	Hair loss, Anemia	Dry/Fresh	Decoction	Oral	Irritating	0.135	0.135	55.55
Rutaceae *Ruta montana L.*	Fijel,	Wild/ Cultivated	The plant to be classified as moderately toxic.[73]	Stomach pain	Dry	Decoction	Fumigation	Irritating	0.015	0.015	100
Solanaceae *Datura stramonium*	Chdaqjemal	Wild	Compared to methanolic extract, the Datura stramonium aqueous extract seemed to contain potentially harmful components.[74]	Drug addiction	Dry/Fresh	Brute	Oral	Irritating	0.067	0.13	69.23

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ISSN 2616-0692 (Electronic)

Solanaceae *Solanum nigrum*	Bkninat	Wild/ Cultivated	Some parts of this plant can be very toxic to livestock and humans.[75]	Diabetes	Dry/Fresh	Decoction	Oral	Irritating		0.005	100
Solanaceae *Hyosciamus niger*	Bonj	Wild/ Cultivated	Yes[36]	Ear disorders	Dry/Fresh	Decoction	Rinsing	Irritating		0.025	60
Solanacaea *Hyoscyamus muticus*	Gangit	Wild/ Cultivated	Yes [36]	Hair loss	Dry/Fresh	Infusion	Rinsing	Irritating		0.045	100
Solanaceae *Mandragora autumnalis*	Bidelghoul	Wild/ Cultivated	Mandragora autumnalis has varying concentrations of tropane alkaloids, which have anticholinergic effects and elicit characteristic, sometimes severe atropine-like symptoms, and solanum alkaloids, which irritate the gastrointestinal tract.[76]	Cancer	Dry/Fresh	Badigeonnage	Poultice, Cui	Irritating		0.13	65.38
Taxaceae *Taxus baccata*	Tagh	Wild/ Cultivated	The stem (TXA-1,2,3) extract has greater harmful activity than the leaf (TXB-1,2,3) extract, according to an LD50 analysis[77].	Cancer	Dry/Fresh	Decoction	Tablets	Irritating	0.01	0.01	100
Thymelaeaceae *Daphne gnidium*	Lezzâz	Wild	Yes[36]	Hair loss	Dry/Fresh	Crushed	Rinsing	Irritating	0.45	0.45	100
Urticaceae *Urtica dioica*	Lhorika	Wild	Yes [36]	Rheumatism, Cosmetic use	Dry/Fresh	Infusion	Maceration/ Poultice/ basting	Irritating	0.455	0.455	44.44

Table 3: IAR values by categories for the treatment of diseases.

Categories	List of plant species used and number of uses	Nt	Nur	IAR
The teeth	*Pistacia atlantica Dsf* (7), *Ammi visnaga* (L.) (7)	2	14	0.92
The cancer	*Asparagus officinalis L* (5), *Mandragora automnalis* (4) *Taxus baccata* (2)	3	11	0.8
The hair	*Brassica nigra* (3) *Canabis sativa* (10) *Tetraclinis articulata (Vahl) Mast*. (13) *Ricinus communis* (12) *Ocimum basilicum L* (2) *Lawsonia inermis L* (50), *Delphinium staphysagria L* (24) *Rubia* (20) *Daphne gnidium* (90) *Urtica dioica* (30)	10	256	0.96
Diabetes	*Ammi visnaga* (L.) *Lam* (9) *Eupharbia resinifera berg* (3) *Solanum nigrum* (1) *Peganum harmala* (8)	4	21	0.85
Fumigation	*Nerium oleander* (30) *Atractylis gummifera* (18) *Ecballium elaterium* (2) *Trifolium* (8)	4	58	0.94
Rheumatism	*Nerium oleander* (7) *Asparagus officinalis L* (3) *Anacyclus pyrethrum* (1) *Artemisia herba-alba Asso* (12) *Citrullus colocynthis* (2) *Glycyrrhiza glabra* (5) *Trigonella foenum graecu* (10) *Mentha pulegium L* (50) *Nigella sp* (2) *Urtica dioica* (40) *Peganum harmala* (4)	7	136	0.95

An ethnobotanical study carried out in the region of Moulay Yacoub, which is part of our study area reported that *Origanum compactum Benth* was the second most cited species with UV of 0.135.[21] Plant species that have a high UV should be conserved because their overexploitation may pose a risk of extinction.[20] Furthermore, pharmacological studies are needed to validate their ethnopharmacological use and also to determine the molecules responsible for their effects.[18]

Fidelity Level (FL)

The fidelity level is an important index used to determine the most effective condition of a particular species. In this study, the FL values ranged from 15% to 100%. The survey documented 19 plant species with 100% FL (*Ecballium elaterium*, *Bryona dioca*, *Dryopteris filix-mas*, *Trifolium*, *Quercus ilex* L., *Teucrium chamaedrys*, *Salvia officinalis* L., *Colchicum autumnale, Lawsonia inermis* L., *Peganum harmala* L., *Olea europeae* L., *Orobanche, Chelidonium majus*, *Cynodon dactylon* L. Pers., *Ruta montana* L., *Solanum nigrum*, *Hyoscyamus muticus*, *Taxus baccata*, and *Daphne gnidium* (Table 2). In general, an FL of 100% for a specific plant indicates that all use reports mentioned the same method of using the plant for treatment. These data reveal that respondents in the study area tended to rely on a particular plant type for the treatment of one type of illness than for several illnesses. Therefore, plants with high fidelity level should be preserved and the knowledge transmitted to future generation so that they do not become extinct.[22] Previous studies reported that the plants with a high percentage of FL are considered bio-pharmacological[32] and should be the object of conservation and phytopharmacological studies.[33-35]

Condition of plants

According to the population of the study area, the highest percentage of remedies (53%) was prepared from fresh materials, while 47% of remedies were prepared from dry materials (Figure 8). This can be explained on the one hand by the ease of preparing remedies from fresh materials rather than from dry materials, and on the other hand by the effectiveness of fresh materials because its content of active principle is still intact, whereas dry materials might have lost its active constituents.

Types of diseases treated

As presented in Figure 9, among the individuals surveyed, 31% claimed that toxic plants are useful for cosmetic purpose, 23% think that they are useful for minor illnesses, 15% believe they are for chronic illnesses, and another 15% believe that toxic plants are not useful as remedies, and finally, 8% each believed that they are effective for acute illnesses, and for other uses.

For the mode of preparation, we found out that the method mostly used and best known by the populace is decoction (44%). This finding confirms the results of other studies where the most common method of preparation of herbal remedies was decoction.[36,37] The use of decoction in water, tea or milk, for 15 to 20 minutes, depending on the hardness of the organ used, is common in several cold regions of Morocco, as is the case with the Central Middle Atlas region. This method remains the most effective means which allows the extraction and assimilation of the active ingredients while warming the body and disinfecting the plant; however, it could destroy certain active principles of the species used.[38]

It, therefore, appears that in the central Middle Atlas as in several other Moroccan regions and elsewhere in many developing countries in Asia, Africa and Latin America, large populations, especially the rural ones, depend on phytotherapy; this is due to the accessibility of this type of therapy given its affordability, benefits and availability, and also to the difficulty of access to modern medicines.[39]

The duration of use, the mode of preparation, and the mode of administration are all key parameters, which, if they are not understood and adhered to, can cause harmful effects even for a seemingly innocuous medicinal plant. The dose of herbal preparations is often imprecisely recommended (e.g., handful, spoonful or pinch), hence, the user could be intoxicated inadvertently due to an overdose.[30]

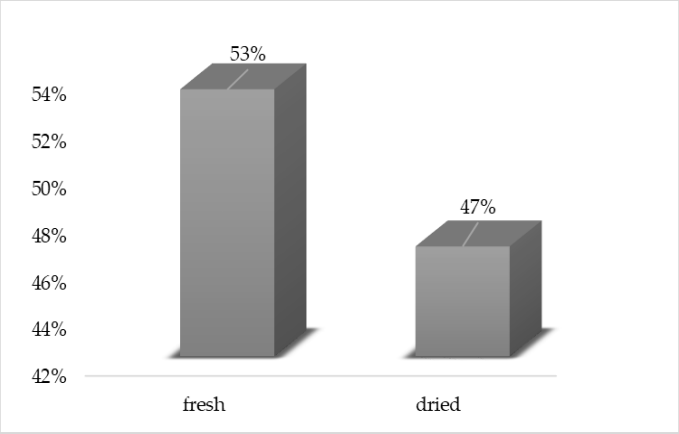

Figure 8: Percentage distribution of conditions of toxic plants used as medicinal plants.

The results from this study as presented in Table 2 showed that medicinal plants could be toxic, and the toxicity of some of these plants has been confirmed by several laboratory studies, and that certain plants like *Chelidonium majus* become toxic at high doses.

Analysis of several articles relating to laboratory research, the results of observations and clinical trials as well as the consultation of certain summary works have confirmed and documented the toxicity of 22 plants. Their impact on both humans and animals is diverse. They cause allergic reactions, skin reactions such as photosensitization and dermatoses and affect different organs and systems such as the gastrointestinal tract, liver, kidneys, heart, and the central nervous system.[30,40]

Plants that have been known to cause serious dermatitis are *Ruta montana* L., *Nerium Oleander* L., *Euphorbia helioscopia* L., *Urginea maritima* L., *Baker*, and *Ruta montana* L.[40]

There are also certain plants that are photosensitizing,[35] for example, *Ruta montana* (L.), photosensitization being the increase in the sensitivity of the skin to solar radiation, particularly to ultraviolet radiation, occurs after ingestion or contact with this type of plants. These plants contain phototoxic substances such as acetylene derivatives, beta-carboline alkaloids, furochromones, lignans and furanocoumarins.[40]

Plants such as *Atractylis gummifera* L. has been associated with several cases of poisoning in Morocco. In fact, 16 cases collected in the pediatric department in five years have been reported,[41] in addition to 240 cases declared to the Centre Anti Poison Maroc (CAPM) toxicovigilance unit between 1981 and 2004, and 72% of the victims were children under the age of 16 years.[42]

The most dangerous of the phytochemicals responsible for plant toxicity are the alkaloids, cardiotonic glycosides, terpenoids of essential oils, followed by the quinones, saponosides, furanocoumarins, glucosinolates, polyenes and calcium oxalates.[43] Poisoning by medicinal plants is a real public health problem in Morocco; they are often the cause of significant morbidity and mortality for all age groups in accidental or voluntary intoxication. The extensive use of these plants can lead to their depletion; hence, the preservation of traditional medicinal heritage and control of their economic use is imperative. Therefore, a program for the management and conservation of aromatic and medicinal plants must be considered in order to avoid their depletion and extinction.[44]

The findings from the present study will serve as a data bank of medicinal plants declared toxic. Overall, to properly exploit medicinal plants without risk, it is important to seek the services of specialists in the field as well as to encourage research on medicinal plants in order to properly understand their pharmacological effects and provide more information on the safe use of medicinal plants. Finally, it is important to make traditional medicine practitioners aware of the different risks associated with the indiscriminate use of medicinal plants.

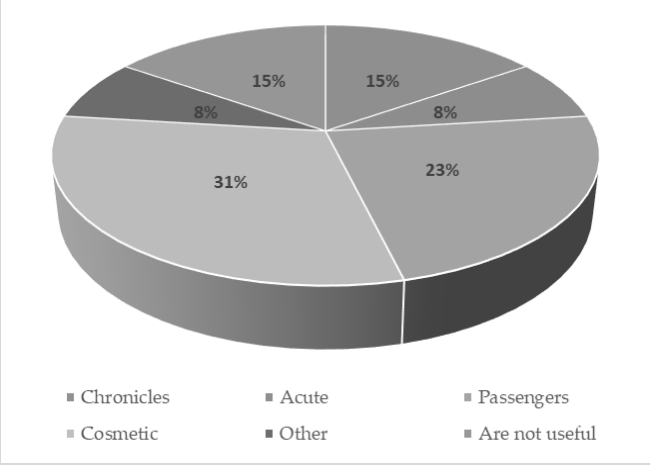

Figure 9: Percentage distribution of the use of toxic plants used as medicinal plants according to the group of diseases treated.

Conclusion

To know the toxic plants in the region of Fez-Meknes, Middle Atlas, Morocco, an ethnobotanical survey was conducted among the different categories of inhabitants. After thorough analysis of data obtained from the survey, about 59 medicinal plants suspected to be toxic, distributed across 33 families were documented. The ethnobotanical study also showed that toxic plants are widely used as aromatic medicinal plants in traditional medicine. The plants are most commonly prepared as infusion and decoction. Many of the respondents who practice traditional medicine do not have precise knowledge of the doses at which the plants become toxic. This ignorance can pose significant health risks to consumers of these plants.

To reduce the risk of toxicity by medicinal plants, more *in vitro* and *in vivo* studies by specialists in phytotherapy and pharmacology are needed to determine the precise doses as well as the mode of use of medicinal plants used in traditional medicine.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

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

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