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Ethnobotanical Study of Medicinal Plants used by Traditional Health Practitioners to Manage Diabetes Mellitus in Safi and Essaouira Provinces (Central-Western Morocco)

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ABSTRACT

The Moroccan population heavily rely on herbal remedies to control diabetes mellitus. The population of the central-western region of Morocco uses a number of anti-diabetic medicinal plants, but there is a lack of good ethnobotanical information on these plants. Thus, the present survey was conducted in the Safi and Essaouira provinces to inventory the main medicinal plants used in folk medicine to treat diabetes mellitus. Seventy-seven traditional health practitioners were interviewed face-to-face throughout different sites in the study area. The data were analyzed using relative frequency of citation (RFC), Jaccard index (JI), Jaccard distance, and Sorensen's similarity index (QS). In total, 84 plants species belonging to 41 families were reported. Lamiaceae, Fabaceae, Apiaceae, and Asteraceae were reported as the most represented families. Eight taxa were described for the first time for treating diabetes mellitus. The most frequently cited plants species were *Trigonella foenum-graecum* L., *Artemisia herba-alba* Asso, *Olea europaea* subsp. *europaea* L., *Allium sativum* L., and *Origanum compactum* Benth. Leaves and fruits were the most cited plant parts used, and decoction and infusion were the preferred modes of preparation. As for the level of similarity to other regions of Morocco, the province of Tarafaya in the south seems to be the most like the study area (JI=36.94). The current survey represents a valuable contribution that can help preserve ethnobotanical knowledge in this area as well as explore medicinal plant, phytochemical, and pharmacological potential.

Keywords: Ethnobotanical survey, Diabetes, Safi, Essaouira, Morocco.

Introduction

Diabetes mellitus describes a group of metabolic disorders. It is characterized by chronic hyperglycemia resulting from insulin deficiency or insulin resistance.[1] Type-1 diabetes, 5-10% of all diabetes worldwide, is an immune-mediated form marked by T-cell-induced destruction of the pancreatic beta cells. Meanwhile, type 2 diabetes, which accounts for about 90% of all cases, is the outcome of insulin resistance and beta-cell dysfunction. This can be strongly associated with overweight and having a sedentary lifestyle.[2, 3]
Due to a higher incidence of the risk factors, the global prevalence of diabetes and impaired glucose tolerance is on the rise in adults worldwide, which is deemed as a major threat to public health.[4] In 2017, among adults aged 20-79, there were nearly 425 million diabetic patients in the world, and the rate is expected to reach to 629 million by 2045. The annual worldwide diabetes-related health expenditure is estimated at US$ 727 billion.[4, 5] Diabetes prevalence is exacerbating in developed as well as in developing countries. In 2017, more than 1.6 million people were estimated to be diabetic in Morocco, and this is expected to increase to 2.6 million by 2030.[6,7]

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The diabetes prevalence ranges between 4.4 % and 9 % in rural and urban areas, respectively.[8]
Many complications are resulting from both types of diabetes and are considered as a leading cause of premature mortality.[9,10] Diabetic patients with prolonged uncontrolled hyperglycemia run the risk of developing macrovascular and microvascular angiopathy,[9] cancers, cardiovascular and Alzheimer's diseases.[2,11] Furthermore, untreated diabetic patients are prone to develop bladder, skin, and sexual dysfunctions.[12-14] Chronic exposure of diabetics to an irregular metabolic environment disturbs the immune system and lung physiology, aggravates inflammation, and increases virus infectivity and virulence.[15]
Diabetic patients should commit to a set of self-care behaviours, such as diets, physical activities, glycemia control, and appropriate medications.[16] Presently, the injection of exogenous insulin is still the basic treatment for type-1 diabetic patients as well as for some type-2 diabetic patients, who failed to keep their glycemia under control by other means.[3] Several antihyperglycemic agents are frequently used to manage diabetes mellitus. These include sulfonylureas, incretin mimetics, meglitinides, thiazolidinediones, biguanides, α-glucosidase inhibitors, dipeptidyl peptidase-IV inhibitors, and sodium/glucose co-transporter 2 inhibitors.[17] Though the antihyperglycemic drugs have shown promising results, they are not devoid of side effects.[18] For instance, biguanides such as metformin are known to cause anorexia, transient nausea, diarrhea, renal hypoperfusion and lactic acidosis with severe renal damage. Sulfonylureas can cause mild headaches, gastrointestinal disorders, increased food intake, weight gain, and cardiovascular mortality. Thiazolidinediones lead to anemia, insomnia, headache, dizziness, gastrointestinal disorders, weight gain, haematuria, proteinuria, impotence, and, less commonly, fatigue, vertigo and hypoglycemia.[18] In low and middle-income countries, poor quality of

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medicines, knowledge, and perceived burden may be barriers of diabetes management.[19]

Of note, developing novel, safe drugs to control diabetic disorders remains a major challenge.[18,20] Accordingly, there is a growing interest in natural products due to their low cost, easy availability, and fewer side effects compared to synthetic drugs.[2] Medicinal plants have been a primary source of many marketed drugs, such as metformin, which has been isolated from *Galega officinalis* L.[21] Note that more than 200 compounds isolated from plant extracts have shown a blood glucose-lowering effect.[22] Plants constituents such as alkaloids, steroids, flavonoids, polysaccharides, peptidoglycans, glycopeptides, triterpenoids, amino acids, carotenoids, and inorganic ions are reported to have a lowering effect on blood-glucose.[2, 23] Several alkaloids can inhibit α-glucosidase and decrease glucose transport through the intestinal epithelium.[24] Polysaccharides and steroidal glycosides increase the levels of serum insulin, reduce blood glucose levels and improve glucose tolerance.[25] Phenolic compounds and flavonoids suppress the level of glucose, decrease the plasma cholesterol and triglycerides, enhance glycogen metabolism by increasing insulin release from pancreatic islets, and improve insulin sensitivity.[26] On the other hand, several terpenes were identified as insulin-stimulating agents and as aldose reductase inhibitors. They also slow or reverse diabetes complications.[2,27]

In developing countries, the usage of medicinal plants is still popular, especially among traditional healers and elderly citizens. The information is transmitted from generation to generation, which enables the preservation and dissemination of medicinal plants usage.[28] Unfortunately, this orally communicated traditional knowledge is doomed to disappear, because it is possessed mainly by older people, and local communities undergo continuous acculturation and westernization.[29]

Morocco is one of the richest countries in Africa in terms of culture as well as plant diversity. There are more than 5000 species of vascular plants, 900 endemic plants, and more than 600 medicinal plants.[30] In Morocco, the use of plants for medical purposes has been practiced since immemorial times, and Moroccan people are more dependent on traditional medicine.[31, 32] Local folk medicine has been an important source of remedies for the treatment and/or management of various ailments, including diabetes.[33-35] Several ethnobotanical studies carried out in Morocco have stated that diabetics are still committed to folk medicine.[36-38] Of note, many plant species are threatened with local extinction due to excessive exploitation, prolonged waves of heat and drought, and deforestation, and the growth of the rural population.[39] Importantly, the documentation of the indigenous knowledge through ethnobotanical surveys may contribute to conserving and rationalizing the utilization of biological resources.[40, 41]

Nevertheless, ethnobotanical research has not been yet undertaken in the Atlantic Central-Western area of Morocco, notably in the Safi and Essaouira provinces. This region has inherited a rich traditional medicinal knowledge, along with other Moroccan regions, from Arabic, Berber, and Jewish traditions.[42] Up to our knowledge, the region remains unexplored, then this work aimed to carry out a qualitative and quantitative study of antidiabetic medicinal plants in the Safi and Essaouira provinces.

Materials and Methods

Study area

Morocco has a land area of 710.850 km^2 and is bordered by the Mediterranean Sea and the Atlantic Ocean on the north and west, respectively, as well as wide mountainous areas in the interior and the Sahara Desert in the far south. It is situated in the extreme northwest of Africa, separated from the European continent by 13 km of spanning the water. The country's climate is as varied as its diverse geography. There are three main climatic zones: the Atlantic, the mountains, and the eastern zone. Such heterogeneous ecological conditions are behind floral biodiversity throughout the country.[43]

The study was undertaken in six sites of the Safi and Essaouira provinces, two administrative divisions located along the central section of Atlantic Morocco. The study area (located between 31°50 and 32°29 N latitude and 9–10 W longitude) is limited to the north by the province of Sidi Bennour, to the south by Agadir, to the east by Youssoufia and Chichaoua provinces, and to the west by the Atlantic Ocean (Fig. 1). The survey area belongs to the semi-arid Mediterranean zone, which is characterized by important seasonal fluctuations, and is marked by warm and dry summers with cold and rainy winters.[44] Maritime trade winds are prevalent in the area, particularly in the summer.[45] Due to the oceanic influence, fog and mist are common due to the atmospheric humidity reaching 85% for many months of the year, primarily in the summer and autumn.[46] Occult precipitation is a significant factor associated with the remarkable density of vegetation. Precipitation levels range from 100 to 400 mm according to the location and the altitude, and the mean air temperature ranges from 22 to 25°C, and rarely drops below 10°C.[47]

The flora in the region consists primarily of Mediterranean taxa, coexisting with tropical, Saharan, Macaronesian, and endemic taxa.[48] The main flora includes several succulent taxa and thermophilic plants, which have adapted well to the arid climate alongside many aromatic and medicinal plants. The argan tree (*Argania spinosa*) is the most remarkable of the landscape as one of the important endemic plants of the country.[49] Argan woodlands cover approximately 800,000 hectares in Morocco's west-central region. From Safi in the north to the Draa River in the south, this tree can be found in the Souss plain as well as the High and Anti-Atlas piedmonts.[50] Argan forests have multiple roles and uses. They provide a variety of ecological services, including carbon storage and sequestration, species habitat, genetic diversity protection, nutrition, water, soil fertility, and erosion prevention. Argan woodlands also constitute an important obstacle to desertification and are indispensable to the local population, which depends on vegetation for firewood and charcoal for heating and cooking, forage for livestock, and for cosmetics and medicinal purposes.[51]

The territory of the Safi province (32°29'90" N, 9°10'13" W) comprising a total area of about 3600 km^2 is marked by a relatively flat or slightly undulating topography; the highest points never exceed 500 m above sea level. The Safi province which takes its name from its capital Safi (or Asfi), one of the oldest cities in Morocco, is usually seen as an industrial province supported by fish packing plants, located midway down the Atlantic coast and by the treatment, shipping and the exportation of a huge amount of phosphates coming from the interior of the country. It is also renowned for its ceramics industry.[52] On the other hand, Essaouira province (31°50'85" N, 9°75'95" W) stretches over an area of 6355 km^2. It is a quasi-mountainous zone hilly in the south and consists of small plains interspersed with hills to the north. The highest point reaches an altitude of 1400 m. Its economy relies largely on tourism, handicrafts, agriculture, and sea fishing. Moreover, Essaouira is among the most forested provinces in Morocco. It is covered with argan trees, cedar, juniper, and other species. This gives the province exceptional biodiversity potential. Tamanar, one of the urban agglomerations in the province, is known as the capital of the argan tree in Morocco.[52]

Interviews

The data was collected from 77 local informants between November 2018 and March 2020. Respondents were made aware of the scope of the study, which was conducted based on the principle of free and prior informed consent (FPIC).[53] Interviews were conducted face-to-face in the local dialect (Moroccan Arabic "Darija" and local Amazigh "Tachelḥit"), and without time limit or pressure to allow the informants to answer questions naturally.[54] To avoid unbiased information, the informants were interviewed individually, and in the absence of other people, insofar as possible. No rewards or compensation were provided to the informants, they cooperated willingly and could withdraw from the interview at any time. The first part of the questionnaire dealt with participants' demographics, including gender, age, informant category, educational background, and residence. The second part included questions about the plants' usage: local names, general description, ecological distribution, parts used, mode of preparation, way of administration, doses, organoleptic characteristics, adverse effects, and administration frequency. Informants were selected by convenience sampling (i.e., a sampling method in which units are selected depending on accessibility or availability).[55] At the end of the meeting, the

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informant was encouraged to indicate another trusted traditional healer to participate, according to the snowball sampling procedure.[56]

Plant collection and botanical identification

Medicinal use was accepted as valid only if at least three independent interviewees mentioned it. [57] All sufficiently mentioned plants were collected. Some were acquired directly from the interviewees and others were harvested in the fields. The harvested plant samples were shown to the interviewees to authenticate them. Thereafter, the vernacular names were transliterated from Arabic and Berber into Roman syllabification using Bertrand[58] and Bellakhdar[59] methods. The botanical identification was made by a botanist (Pr Pr. A. Ennabili). Taxonomic identification follows the Moroccan identification keys;[60-62] 'Vascular Flora of Morocco, Inventory and Chorology',[63] 'Flora of North Africa',[64] 'Moroccan Plants Catalogue' and 'Flora of Sahara'[65-66] All scientific names of plant species were examined through the Plant List database (http://www.theplantlist.org). Voucher specimens of each plant were coded and deposited in the herbarium of the Faculty of Sciences, Dhar El-Mahraz, Fez.

Calculations and statistical analysis

The database containing the gathered information was developed using Microsoft Access and Microsoft Excel. The consistency of the information was tested according to the comparative data technique of El-Gharbaoui *et al.*[67] Medicinal usage information was deemed reliable when recorded at least three times by at least three separate informants. Throughout this study, only coherent information was included in our database. Quantitative data analysis was performed by computing the relative frequency of citation (RFC), Jaccard Index (JI), Jaccard Distance (JD), and Sorensen's similarity index (QS). The statistical calculations were carried out using Microsoft Excel 2016 and SPSS (Statistical Package for Social Sciences, version 25.0, SPSS Inc., Chicago, IL, USA).

Relative frequency of citation (RFC)

The Relative frequency of citation (RFC) was performed to determine the level of traditional knowledge about the use of medicinal plants in the study areas. It shows the local importance of each species.[68] The RFC is obtained by dividing the number of informants mentioning a useful species (Fc or frequency of citation), by the total number of informants in the survey (N), without considering the use-categories:

$$RFC = Fc/N \ (0<RFC<1)$$

RFC values range from 0 (nobody thinks a plant is useful) to 1. (when all the informants mentioning it as useful).[69]

Jaccard Index (JI) and Sorensen's similarity index (QS)

The Jaccard Index (JI) was determined by comparing previously published research articles from regional and national level and by calculating the percentages of cited plants species and their medicinal utilization using the formula given below:[70]

$$JI = c \times \frac{100}{(a+b-c)}$$

Where a is the number of species in the area A; b is the number of species in the area B and c is the number of species that commune to both areas A and B.

We have calculated a similarity index between our survey and other studies that have been carried out on antidiabetic plants in Morocco during the last thirty years. Accordingly, we used the JI formula (in this survey, a is the number of species in the study area; b is the number of species in another study region of Morocco; and c is the number of species common in our study area and the other areas of study. The values of the Jaccard Index were converted to the Jaccard Distance (JD), which is the complementary set of the Jaccard Index.

$$JD=1-JI$$

For the same purpose, a comparison with previously published data collected from different regions in Morocco Was carried out by evaluating percentages of the quoted species and their medicinal uses by applying Sorensen's similarity index formula.[71]

$$QS = \frac{2c}{a+b} x100$$

Where a denotes the number of species in area A, b the number of species in area B, and c the number of species shared by areas A and B.

Evidence acquisition

A systematic literature search was conducted using PubMed, Scopus, and Google Scholar databases to collect ethnobotanical and ethnopharmacological information about the inventoried plants. Various search terms, such as "diabetes," "antidiabetic," and "hypoglycemic," were used in conjunction with the name of a specific plant species reported in our survey. The documents were classified and examined for relevance. Additional articles were identified by reviewing reference lists of the papers that were retrieved.

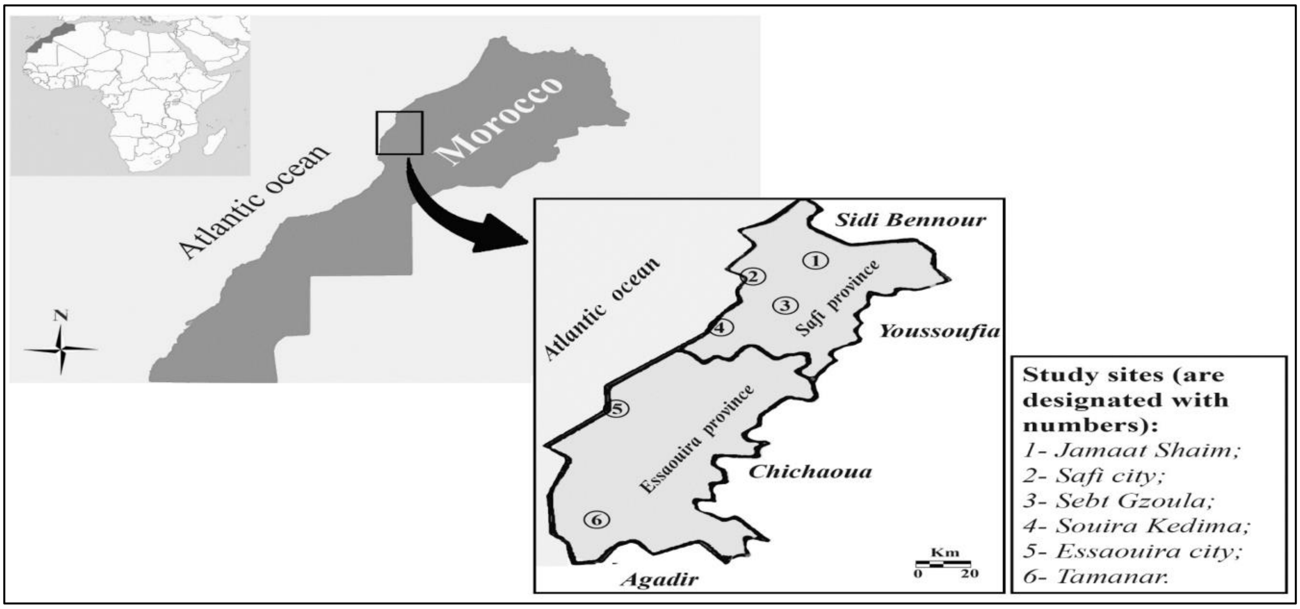

Figure 1: Geographic location of study area (Safi and Essaouira provinces) in Morocco

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Results and Discussion

Seventy-seven participants were approached, of which three were females. Forty-one (53.2%) and 36 (46.7%) respondents were in Safi and in Essaouira, respectively. The majority were herbalists (74%), followed by herbalist assistants (17%), and ambulant herb sellers (9%). Most of them were aged 51 years and above (72%) (Table 1). This age group is the most relevant insofar as ethnomedicinal knowledge is concerned. Indeed, interviews showed that the elderly were particularly skilled and knowledgeable about medicinal plants usage than young adults. For the language, 61% and 39% of the respondents spoke Arabic and Amazigh, respectively. Most of the interviewed healers had no formal education (45%), followed by those with elementary levels of education (30%), and those with secondary levels of education (18%). These findings are congruent with previous studies reporting similar demographics, especially the age and education levels of herbalists and plants users. They ascertained that elderly and illiterate participants are the main knowledge holders of antidiabetic plants usage.[34,38,72] Likewise, Kadir *et al.*[73] in Bangladesh; Kpodar *et al.*[74] in Togo and Tag *et al.*[75] in India reported that illiterates are more prevalent in using plants to alleviate diabetes mellitus. Most interviewers had learned traditional medical knowledge from family members or a competent person (a traditional healer) either orally and/or by putting their hands to work and sometimes based on their own experience and observations.

Medicinal plants and floristic analysis

The present ethnobotanical survey has helped to set up an inventory of 84 medicinal plant species, belonging to 41 families and 71 genera. The collected data are arranged in the alphabetic order of the botanical family with the plant scientific name, local name, plant parts used, mode of preparation and Relative Frequency of Citation (RFC) provided for each species (Table 2).

Families with the most reported plant species were Lamiaceae (15 species and 304 use records), Fabaceae (9 species and 123 use records), Apiaceae (8 species and 101 use records) Asteraceae (4 species and 66 use records) and Oleaceae (3 species and 71 use records) (Figure 2). These findings are in line with previous reports in which these botanical families were the most represented in treating diabetes mellitus in Morocco,[34,37,76,77] in neighbouring countries like Algeria[78,79] and Spain,[80] in Iran,[81, 82] in Italy[83] and South Africa.[84] The predominance of these families could be explained by their abundance in the flora of the study area and in the flora of Morocco.[30]

The examination of the life forms of the medicinal plants used to manage diabetes in the study area revealed the prevalence of annual herbs (26.2%) followed by macrophanerophytes (trees) (22.6%), nanophanerophytes (shrubs) (19%), chamaephytes (subshrubs) (15.5%), hemicryptophytes (9.5%) and geophytes (7.1%).

Based on the value of the RFC, the most recommended species in the present survey were *Trigonella foenum-graecum* (0.60), *Artemisia herba-alba* (0.57), *Olea europaea* subsp. *europaea* (0.56), *Allium sativum* (0.55), *Origanum compactum* and *Nigella sativa* (0.53 each) followed by *Argania spinosa* (0.49), *Rosmarinus officinalis* (0.45) and *Marrubium vulgare* (0.43) (Table 2). These results seem consistent with those of other studies conducted in other areas of Morocco and elsewhere. Importantly, *Trigonella foenum-graecum* was reported as the most frequently used species to treat diabetes in different regions of Morocco, whether in the north,[85] the east,[38] or the west (36, 86). Of note, *Trigonella foenum-graecum* is also the most recommended plant for the treatment of diabetes in west Algeria[87] and the Fars area of Iran.[82]

Table 1: Sociodemographic characteristics of the participants

Characteristics	Subgroup	Number	Frequency (%)
	≤ 30	3	3.90
	31-50	18	23.38
Age	51-70	35	45.45
	71-90	21	27.27
	Total	**77**	**100**
	Male	74	96.10
Gender	Female	3	3.90
	Total	**77**	**100**
	No formal education	35	45.45
	Primary	23	29.87
Educational level	Secondary	14	18.18
	Tertiary	5	6.49
	Total	77	100
	Safi	41	53.25
Location	Essaouira	36	46.75
	Total	**77**	**100**
	Herbalist	57	74.03
Occupation	Herbalist assistant	13	16.88
	Herb seller	7	9.09
	Total	**77**	**100**
	Arabic	47	61.04
Usual languge	Amazigh	30	38.96
	Total	**77**	**100**

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Table 2: List of medicinal plants used in traditional medicine to treat diabetes mellitus in the Safi and Essaouira provinces of Morocco

Voucher	Family	Scientific name	Local name	Plant habitat	Part used	Mode of use	Citation		Other uses
							FC	RFC	
SE-123	Alliaceae	*Allium cepa* L.	**bṣel, bṣal**	Geophyte	Bu, Se	Pa, Pl, Pw, R	15	0.19	DED, MPI, TIP, USD
SE-120	Alliaceae	*Allium sativum* L.	**tūma, tiskert**	Geophyte	Bu	M, Pw, R	42	0.55	CAN, CVD, DER, ENP, RSP, TIP, USD
SE-167	Apiaceae	*Ammi visnaga* (L.) Lam.	**bū šniẖa, bešnīẖa, tabešnîẖt**	Herb	Fr, Se	D, I	9	0.12	DED, OSP, RSP, USD
SE-127	Apiaceae	*Carum carvi* L.	**karwiyâ**	Hemicryptophyte	Fr	D, I	27	0.35	DSP, RSP, USD
SE-45	Apiaceae	*Carum* spp.	**karwiyâ**	Hemicryptophyte	Fr	D, I	16	0.21	DSP, RSP
SE-207	Apiaceae	*Coriandrum sativum* L.	**Qezbūr**	Herb	Le, Se	D	7	0.09	DSP, RSD, SMP, USD
SE-203	Apiaceae	*Ferula communis* L.	**L-kelẖ, uffāl, taggwelt**	Geophyte	Fl, Fr, Ro	D, I, Pw	7	0.09	DER, DSP, TIP
SE-90	Apiaceae	*Foeniculum vulgare* Mill.	**n-nāfaɛ, âmsâ, tamsawt**	Hemicryptophyte	Ro, Se	D, I	12	0.16	DED, DSP, OSP, PNS, RSD
SE-222	Apiaceae	*Petroselinum sativum* Hoffm.	**mɛadnūs, imẓi**	Hemicryptophyte	AP, WP	D, J	12	0.16	CVD, DSP, USD
SE-253	Apiaceae	*Pimpinella anisum* L.	**ḥabbat ḥlāwa**	Herb	Se	D, Pw	11	0.14	CAN, DER, OSP
SE-41	Apocynaceae	*Nerium oleander* L.	**defla, alili**	Shrub	Le, Ro	D, Pl	7	0.09	DER, **Toxic**
SE-223	Aristolochiaceae	*Aristolochia longa* L.	**bāreẓṯem, ɛanq j-jmel**	Herb	Ro, WP	D, Pw	14	0.18	CAN, DER, DSP, **Toxic**
SE-80	Asteraceae	*Artemisia arborescens* (Vaill.) L.	**šība, šība šmaymiya**	Subshrub	AP, Le	I, Pa	11	0.14	DSP, GEH, MPI, RSD, TIP, USD
SE-121	Asteraceae	*Artemisia herba-alba* Asso	**šīḥ, îzrî**	Subshrub	AP	D, I, Pw	44	0.57	CVD, DED, DSP, ENP, MPI, RSD
SE-178	Asteraceae	*Atractylis gummifera* Salzm. ex L.	**addād, ddād, aẖfyūn,**	Hemicryptophyte	Ro	I, F	5	0.06	DED, DER, DSP, **Toxic**
SE-111	Asteraceae	*Cynara humilis* L.	**ṭimṭa, ḥekk, ẖeršūf**	Hemicryptophyte	Ro	D, Pl	6	0.08	OSP, TIP
SE-136	Berberidaceae	*Berberis vulgaris L.*	**argis, irġīs**	Shrub	Fr	D	10	0.13	DSP, EEP, ENP, OSP

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Table 2 (*Continued*)

Voucher	**Family**	**Scientific name**	**Local name**	**Plant habitat**	**Part used**	**Mode of use**	**Citation**		**Other uses**
							FC	**RFC**	
SE-122	Cactaceae	*Opuntia ficus-indica* (L.) Mill.	**hendiya, zaɛbul**	Subshrub	Fl, St	D, O, Pa, R	15	0.19	DER, RSP, TIP, USD
SE-47	Capparaceae	*Capparis spinosa* L.	**kebbār, âkkabâr, taylulut**	Subshrub	Fr, Le, Ro	D, I, Pw	15	0.19	CAN, CVD, DSP, RSD, SMP
SE-219	Caryophyllaceae	*Herniaria hirsuta* L.	**ḍaɛīfa, herrāst l-ḥjar, ḥrīša**	Herb	AP, WP	D, Pw	11	0.14	CVD, DER, TIP, USD
SE-65	Chenopodiaceae	*Chenopodium ambrosioides* L. (=*C. suffruticosum* Willd.)	**mẖīnza**	Herb	AP, WP	D	22	0.29	DSP, OSP, RSP, SMP
SE-33	Cistaceae	*Cistus salviifolius* L.	**irgel, tuzzalt**	Shrub	Le, Se	D, I, Pw	9	0.12	BNP, RSD, DSP
SE-184	Cruciferae	*Lepidium sativum* L.	**ḥabb r-ršād, l-ḥarf**	Herb	Se	I, Pl	29	0.38	CVD, DSP, RSD, RSP
SE-155	Cucurbitaceae	*Citrullus colocynthis* (L.) Schrad.	**leḥdej, ḥdej, timḥiddjit, âferzîz**	Geophyte	Fr, Se	I, Pw, Pl	9	0.12	CVD, DER, SMP, TIP, **Toxic**
SE-247	Cucurbitaceae	*Cucumis sativus* L.	**ẖyār**	Herb	Fr	J, R	9	0.12	DER, DSP, OSP
SE-187	Cupressaceae	*Tetraclinis articulata* (Vahl) Mast.	**ɛarɛār, el-ɛarɛār, 'ar'ar, âzuka**	Tree	Fr, Le	D, I, Pw, Pa	31	0.40	DER, DSP, RSP, TIP
SE-236	Ericaceae	*Arbutus unedo* L.	**el-lenj, sāsnu**	Shrub	Fr, Le, Ro	D	7	0.09	CVD, MPI, USD
SE-242	Fabaceae	*Acacia tortilis* (Forssk.) Hayne	**amrād, ṭalḥa**	Tree	Fr, Le, Ro, SB	D	6	0.08	DSP, MPI, RSP, TIP, USD
SE-214	Fabaceae	*Cassia fistula* L.	**ẖyār šambâr**	Tree	Fr	D	3	0.04	CVD, DED, DSP, RSD, SMP
SE-34	Fabaceae	*Ceratonia siliqua* L.	**l-ẖerrūb, sliġwa, îkidu**	Tree	Le	D, Pw, R	24	0.31	DSP
SE-138	Fabaceae	*Glycine max* (L.) Merr.	**Soja, A'ssoja**	Herb	Se	D, M	9	0.12	DSP, MPI, BNP
SE-195	Fabaceae	*Lupinus albus* L.	**termīs, termūs**	Herb	Se	D, Pw	11	0.14	ENP, MPI
SE-100	Fabaceae	*Lupinus angustifolius* L.	**rjel ed-djaja, kīkel, bū zġayba, semqâla**	Herb	Se	D, Pw	5	0.06	ENP
SE-158	Fabaceae	*Retama raetam* (Forssk.) Webb	**rṭem, rrtem, talggūt, alggū**	Subshrub	AP, WP	D, Pw	12	0.16	DER, SMP, TIP

Table 2 (*Continued*)

Voucher	Family	Scientific name	Local name	Plant habitat	Part used	Mode of use	Citation		Other uses
							FC	RFC	
SE-198	Fabaceae	*Trigonella foenum-graecum* L.	**l-ḥelba, afiḍās, tifiḍas**	Herb	Se	D, M, Pw	46	0.60	BNP, CAN, DER, RSD, TIP
SE-227	Fabaceae	*Vigna sinensis* (L.) Savi ex Hausskn.	**fūl gnāwa**	Herb	Se	M, Pw	7	0.09	DSP, SMP
SE-30	Gentianaceae	*Centaurium erythraea* Rafn	**guṣṣat l-ḥayya, merrâret l-ḥneš**	Herb	AP, Fl	D, I, Pw	6	0.08	DSP, TIP, USD
SE-164	Globulariaceae	*Globularia alypum* L.	**taselġa, aselġa, ʻayn lerneb**	Shrub	Le	D, I, Pl	30	0.39	DER, DSP, SMP, TIP
SE-230	Graminaceae	*Phalaris paradoxa* L.	**zwan, senbūlt l-fār, tigurramin**	Herb	Se	D, Pw	6	0.08	TIP
SE-202	Iridaceae	*Crocus sativus* L.	**zaɛfrān, za’afran ḥôrr**	Geophyte	Fl	D, I	7	0.09	CVD, DSP, RSD
SE-193	Juglandaceae	*Juglans regia* L.	**gergaɛ, sswāk, l-jawz**	Tree	Fl, Fr, Le, SB	D, I, R	17	0.22	DED, DER, DSP, RSD, RSP, SMP
SE-93	Lamiaceae	*Ajuga iva* (L.) Schreb.	**šendgūra, tûf ṭolba**	Hemicryptophyte	AP	D, I, Pw	7	0.09	CVD, DSP, RSP
SE-249	Lamiaceae	*Lavandula dentata* L.	**ḫūzama, ḫūzama beldiya**	Shrub	AP, Le	D, I	8	0.10	DER, PNS, RSD, RSP
SE-192	Lamiaceae	*Lavandula multifida* L.	**koḥḥayla, igīz, klila diāl ḥamīr**	Shrub	Le, St	D, I	8	0.10	DSP, MPI SMP
SE-232	Lamiaceae	*Lavandula angustifolia* Mill.(=*Lavandula officinalis* Chaix)	**ḫzāma, l-ḫzāma**	Shrub	Fl, Le	EO, I, Pw	14	0.18	DER, PNS, RSD, RSP, TIP
SE-28	Lamiaceae	*Lavandula stoechas* subsp. *Stoechas* L.	**ḥelḥāl, āmezzir**	Shrub	AP, Fl	EO, I	19	0.25	CVD, RSP, PNS, SMP,
SE-177	Lamiaceae	*Marrubium vulgare* L.	**merriūt, merrîwa, ifezzi**	Subshrub	Le	D, I, Pw	33	0.43	CVD, EEP, RSP, USD
SE-181	Lamiaceae	*Mentha pulegium L.*	**fliyyo, fliyou**	Hemicryptophyte	AP	I, Pl, EO	21	0.27	OSP, PNS, RSP
SE-61	Lamiaceae	*Ocimum basilicum* L.	**ḥbaq, laḥbaq**	Herb	AP, Le	EO, I	10	0.13	DSP, PNS, OSP, SMP

SE-77	Lamiaceae	*Origanum compactum* Benth.	**zaɛtar, za’tar, ṣa’tar**	Shrub	AP	I	41	0.53	DSP, RSD, RSP, SNP

Table 2 (*Continued*)

Voucher	Family	Scientific name	Local name	Plant habitat	Part used	Mode of use	Citation		Other uses
							FC	RFC	
SE-16	Lamiaceae	*Origanum elongatum* (Bonnet) Emb. & Maire	**zaɛtar, za’tar**	Shrub	AP	I	16	0.21	DSP, RSD, RSP
SE-14	Lamiaceae	*Rosmarinus officinalis* L.	**azīr, iklīl al-jabal**	Subshrub	AP, Le	I, M, Pw	35	0.45	DSP, RSP, SNP
SE-179	Lamiaceae	*Salvia officinalis* L.	**sālmiya, es-sâlmiya, tamejjūt**	Shrub	Le	I	25	0.32	CVD, DED, DSP, RSP
SE-103	Lamiaceae	*Thymus algeriensis* Boiss. & Reut.	**merad, merrad**	Subshrub	AP	I	15	0.19	DSP, RSP
SE-163	Lamiaceae	*Thymus vulgaris* L.	**zɛitra, tazukennit**	Subshrub	AP, Le	I	30	0.39	CAN, DED, OSP, RSP
SE-98	Lamiaceae	*Thymus zygis* L.	**zɛitra, âzukenni, tazukennit**	Subshrub	AP, Le	I	22	0.29	DED, DSP, RSP
SE-206	Lauraceae	*Cinnamomum verum* J.Presl	**lakrafā, qarfa al-ḥârra**	Tree	SB	I, Pw	24	0.31	CVD, DSP, GEH, RSD
SE-137	Linaceae	*Linum usitatissimum* L.	**kettān, zerrîɛt l-kettân**	Herb	Se	I, Pw	13	0.17	DSP, RSP, SMP, USD
SE-196	Lythraceae	*Lawsonia inermis* L.	**ḥenna, l-ḥenna**	Shrub	Le	I, Pw, Pa, Pl	19	0.25	CVD, DER, DSP, TIP
SE-50	Moraceae	*Ficus carica* L.	**kermôs, tin, îmersid**	Tree	Fr, Le	D, M, R	12	0.16	BNP, CVD, DER, DSP, PNS, TIP
SE-252	Moraceae	*Morus alba* L.	**šejrat t-tūt**	Tree	Le	I	7	0.09	GEH, DSP, SMP,
SE-250	Moraceae	*Morus nigra* L.	**šejrat t-tūt**	Tree	Le	I	7	0.09	DSP, GEH, SMP
SE-152	Myrtaceae	*Eucalyptus globulus* Labill.	**kalitûs, kalibtûs**	Tree	Le, St	D, I, Pw	27	0.35	DER, DSP, OSP, RSP
SE-8	Myrtaceae	*Myrtus communis* L.	**Rīḥān, ḥbību**	Shrub	Fl, Fr, Le	D, I, Pw	17	0.22	CVD, DED, DER, DSP, RSP, TIP

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SE-132	Oleaceae	*Fraxinus excelsior* var. *acuminata* Schur	**lsān eṭ-ṭîr, lsān l'uṣfūr, ḥebb derdār**	Tree	Fr, SB	D, I, Pw	7	0.09	CVD, DER, DSP, ENP, RSD, RSP, SMP, USD
SE-71	Oleaceae	*Olea europaea* subsp. *europaea* L.	**zitūn, z-zūtin, azemmūr**	Tree	Fr, Le	D, O	43	0.56	CVD, DED, DER, DSP, RSP

Table 2 (*Continued*)

Voucher	Family	Scientific name	Local name	Plant habitat	Part used	Mode of use	Citation		Other uses
							FC	RFC	
SE-53	Oleaceae	*Olea europaea* subsp. *maroccana* (Greuter & Burdet) P.Vargas & al.	**zitūn, zebbūj**	Tree	Fr, Le	D, O	21	0.27	CVD, DED, DSP, RSP
SE-212	Palmaceae	*Phoenix dactylifera* L.	**nḫel, tmer, tayniyût, ablūh**	Tree	Fr, Ro, Se	D, Pw, V	7	0.09	CVD, DSP, GEH, RSD, TIP
SE-231	Pedaliaceae	*Sesamum indicum L.*	**jenjlān, semsem**	Herb	Se	Pw	10	0.13	CAN, CVD, GEH, RSD
SE-25	Punicaceae	*Punica granatum L.*	**rommān, qšūr er-rommān, tarommānt**	Tree	Fr, Le	D, Pw	26	0.34	DED, DER, DSP
SE-130	Ranunculaceae	*Nigella sativa L.*	**sanūj, šanūj, l-ḥabba sawda**	Herb	Se	D, I, Pw	41	0.53	CAN, CVD, DSP, RSD, RSP, SMP, TIP
SE-112	Resedaceae	*Reseda lanceolata Lag.*	**rġūwa l-ḥrūf, islīḫ**	Herb	Le, Se	D, I, Pw	8	0.10	DSP, RSD
SE-151	Rhamnaceae	*Ziziphus lotus (L.) Lam.*	**ssder, sedra, tazuggwart, nnbeg**	Shrub	Fr, Le	D	7	0.09	DSP, OSP, RSP, USD
SE-134	Rosaceae	*Malus pumila Mill.*	**teffāḥ, l-ḥlū**	Tree	Fr	M, R, V	5	0.06	DER, DSP, ENP
SE-255	Rosaceae	*Prunus dulcis (Mill.) D.A.Webb*	**lūz lmor,tallūzt**	Tree	Se	Pw, R	7	0.09	DER
SE-241	Rutaceae	*Citrus medica L.*	**trunj, zimbwaḥ**	Tree	Fr, Le	D, J, M	8	0.10	DSP, ENP, PNS
SE-244	Rutaceae	*Ruta chalepensis* L.	**fjīla, l-fījel, āwermi**	Subshrub	AP, WP	D, Pw	3	0.04	DER, ENP, OSP, PNS, RSD, SMP

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SE-128	Sapotaceae	*Argania spinosa* (L.) Skeels	**ārġan, āwinī**	Tree	Fr, Le	D, O	38	0.49	CVD, DER, DSP, RSD
SE-246	Theaceae	*Camellia sinensis (L.) Kuntze*	**ātāy, tāy**	Shrub	Le	D	9	0.12	DED, DSP, RSP
SE-31	Thymelaeaceae	*Thymelaea hirsuta (L.) Endl.*	**l-meṯnān, ftiītiša**	Subshrub	AP	I	6	0.08	DED, DSP
SE-117	Urticaceae	*Urtica dioica L.*	**l-ḥurrayga, timezrit, bū ksās**	Herb	AP, WP	D	23	0.30	BNP, CAN, CVD, DER, DSP, RSD, SMP, USD

Table 2 (Continued)

Voucher	Family	Scientific name	Local name	Plant habitat	Part used	Mode of use	Citation		Other uses
							FC	RFC	
SE-79	Urticaceae	*Urtica membranacea* Poir. ex Savigny	**l-ḥurrayga l-malssā**	Herb	AP, Le	D, Pl	6	0.08	CAN, CVD, DER, DSP
SE-94	Zygophyllaceae	*Peganum harmala* L.	**ḥārmel, l-ḥārmel**	Geophyte	Se	I, Pw	10	0.13	CAN, CVD, DSP, PNS, RSP, SMP, **Toxic**
SE-141	Zygophyllaceae	*Zygophyllum gaetulum* Emb. & Maire	**ɛaggāya, l-ɛaggāya, tirṭa**	Shrub	Le	D, Pw, Pl	14	0.18	DER, DSP, SMP, TIP

Abbreviations:
Part used: AP: aerial parts, **Bu**: bulb, **Fl**: flowers; **Fr**: fruits; **Le**: leaves; **R**: raw; **Ro**: roots, **St**: stems, **SB**: stem bark, **Se**: seeds, **WP**: whole plant.
Citation: **FC**: frequency, **RFC**: relative frequency of citation.
Mode of use: D: decoction, **EO**: essential oils; **I**: infusion, **J**: juice, **M**: maceration, **O**: oil, **Pl**: poultice/cataplasm, **Pw**: powder, **V**: vinegar.
Other uses:
BNP: Blood and nutritional problems, **CAN**: Cancer, **CVD**: Cardiovascular diseases, **DED**: Dental and mouth disorders, **DER**: Dermatological problems and dermocosmotology, **DSP**: Digestive system problems, **EEP**: Ear, eye and nose problems, **ENP**: Endocrine problems metabolism and nutrition, **GEH**: General health, **MPI**: Microbial and parasitic infection, **OSP**: Other symptoms and poorly defined morbid states, **PNS**: Problems of the nervous system and psychiatric disorders, **RSD**: Reproductive system diseases, **RSP**: Respiratory system problems, **SMP**: Skeleton-muscular system problems, **TIP**: Traumatic injuries and poisoning, **USD**: Urinary system disorders.

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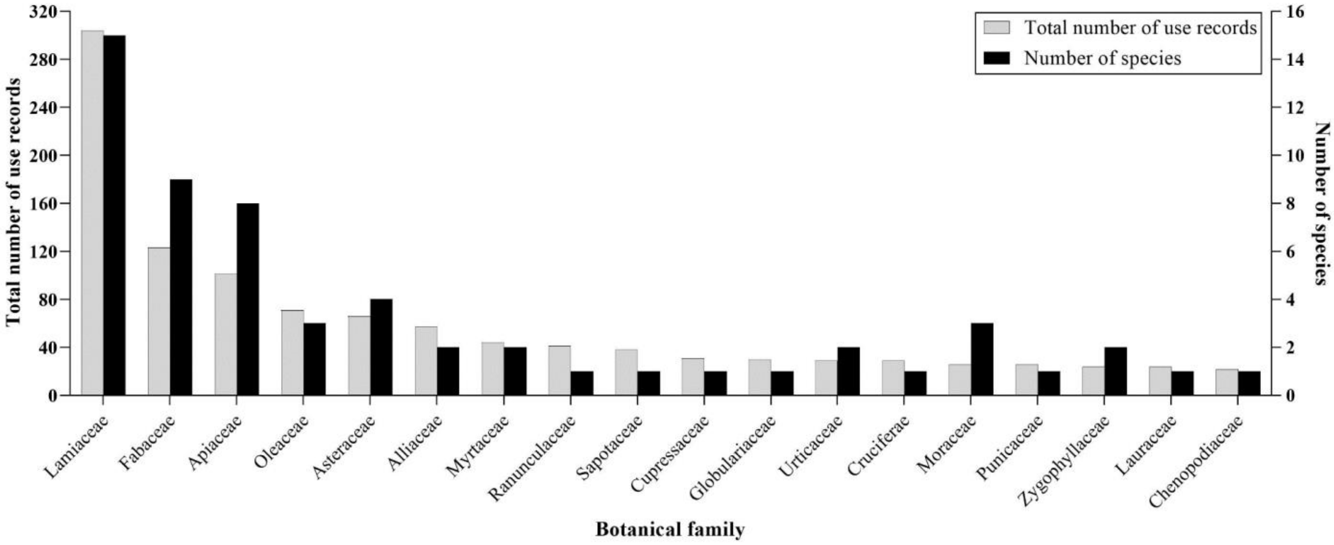

Figure 2: Distribution of the most reported medicinal plants among the botanical families.

Likewise, *Artemisia herba-alba* and *Trigonella foenum-graecum* are also documented as the most frequently used species to manage diabetes in Southeastern Algeria.[79] Furthermore, it has been reported that *Artemisia herba-alba*, *Nigella sativa* and *Rosmarinus officinalis* were reported as the most frequently used plants to manage diabetes in many Moroccan regions.[88-90]
Leaves are the most widely used part in the preparation of drugs from medicinal plants (26.1%) followed by fruits (18.1%), aerial parts (15.9%) and seeds (15.2%) (Figure 3A). On the other hand, roots were scarcely mentioned in the medicinal plants preparation to manage diabetes. The aerial plant parts play an important role in herbal medicine preparation, which is in agreement with previous research conducted in Morocco[34,35,91] and in other countries.[74,78,79, 82] The significant choice of leaves and aerial parts in herbal medicines preparation could be explained by their year-round availability, by their easy access, harvesting and manipulation and by the fact that aerial parts are the center of the photosynthetic activity.[92] On the other hand, roots and bark are not sustainable for the development of traditional medicines or for drug discovery, and the use of whole plant parts may affect strongly the species survival.[93]
The methods of preparation and prescription of the plants used included several modes, mainly decoctions (28.8 %), infusions (23.6%) and powder (20.4%) (Figure 3B). The remedies are in fact administered orally (90%). These findings are consistent with those reported in other studied areas.[94-96] This could be explained by the fact that bioactive compounds require digestive assimilation.[97] Meanwhile, plant preparations were sometimes used externally as poultices and paste, especially to treat some serious complications and external injuries like diabetic foot ulcers, or when the plants used were toxic, such as *Citrullus colocynthis* and *Nerium oleander*.
Besides their antidiabetic properties, most of the cited plants are used for the treatment of many other ailments. Indeed, 60 out of 84 species and subspecies (71.4%) are used to treat digestive and gastrointestinal disorders. Moreover, 38.1% (33 taxa), 35.7% (31 taxa), and 32.1% (28 taxa) are recommended to manage respiratory system problems, dermatological problems and cardiovascular diseases, respectively. The cited plants were recommended with a lower frequency for other diseases, mainly reproductive system disorders, traumatic injuries and poisoning, skeleton-muscular system problems, urinary system disorders, dental and mouth disorders, cancer, nervous system and psychiatric disorders and blood and nutritional problems. The use of different plants to treat various diseases shows the importance of traditional medicine, which is known as a component of daily life in many parts of Morocco, including the study area (Table 2).

Level of similarity between the current survey and others undertaken in Morocco
The level of similarity between the present study and previous ones, carried out on antidiabetic plants in other Moroccan areas during the last thirty years, was assessed by calculating the Jaccard similarity (JI), Jaccard Distance (JD), and Sorensen's similarity (QS) indices (Table 3). The chosen study areas were: Alhaouz-Rhamna, Beni Mellal, Chtouka Ait Baha, and Tiznit, Errachidia, Fez-Boulemane, Fez-Meknes, Moroccan Rif, Oriental Morocco, Rabat, Rabat-Salé-Kénitra, Sidi Slimane, Tafilalet, Tarfaya, and the Central Middle Atlas.[34, 36-38, 72, 76, 77, 85, 86, 88-90, 94, 98]
The similarity indices were calculated using data from 14 published studies, which were conducted in different areas of Morocco. The highest degree of similarity in terms of medicinal plants used to manage diabetes was found in the study conducted in Tarfaya province (JI = 36.94 and JD = 0.63),[77] while the lowest level of similarity was found in the Moroccan Rif (JI = 5.34 and JD = 0.95).[88]
Concerning Sorensen's similarity index (QS), the values range between 10.31% and 53.95%. The highest values were found in studies conducted in Tarfaya province (QS = 53.95%),[77] the Fez-Meknes region (QS=52.24%),[85] and the Fez-Boulemane region (QS=52.17%).[90] The lowest QS values were found in Rabat (QS = 30.58%)[36] and the Rif region (QS=31.58%).[88]
The high degree of similarity indicates that regions share the same culture, vegetation traditions, similar environmental factors and geographical proximity, as well as a high level of intercultural exchange of ethnobotanical knowledge between communities. Whereas a low degree of similarity indicates that regions have different cultural values. In addition, traditional knowledge is often influenced by the origin of Indigenous communities.[99] Our results indicate that climatic and geographical factors appear to be of secondary importance given the low degree of medicinal species overlap between Safi and Essaouira provinces and neighbouring areas (200-300 km), namely Alhaouz-Rhamna (JI/QS=20.7/34.2%) and Chtouka Ait Baha and Tiznit (JI/QS= 25.7/40.9%). The higher levels of similarity between our study area and relatively distant regions (600-700 Km) like Tarfaya and Fes-Meknes could be explained by similarities in ethno-botanical habits and the profile of medicinal plants cultivated in these different areas.[100] Comparisons between different communities within the same area showed that there is still a massive discrepancy in terms of traditional medicinal plants even after a long fusion. Hence, the national specificity of the use of medicinal plants persists in the region and in modern society as well.[101] Besides, in the present study the respondents are exclusively herbalists or herb sellers who are used to seeking plant materials as well as knowledge far away from their local communities.

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The ethnopharmacological heritage of the different Moroccan ethnic groups is well preserved, and continues to flourish. It is handed down from one generation to another by oral tradition and through written records. The Moroccan pharmacopoeia has been developed and enriched by the knowledge provided by various ethnic groups that have migrated to Morocco from many locations, such as the Middle East (Arabs), southern Europe (Andalusians and Jews), and southern countries of Africa.[93] The study area is one of few regions in Morocco where various ethnic groups especially Arabs, Amazigh, Jews and Africans have coexisted for a long time, which favoured cultural blending and the flourish ethnomedicinal knowledge.

To our knowledge, among the total plants inventoried in this survey, eight taxa (either species or subspecies) were described for the first time for treating diabetes mellitus: *Atractylis gummifera*, *Crocus sativus*, *Cynara humilis*, *Ferula communis*, *Olea europaea* subsp. *maroccana*, *Origanum elongatum*, *Reseda lanceolata*, and *Urtica membranacea*. Note that *Cassia fistula*, *Citrus medica* and *Morus nigra* are already known as antidiabetic agents in other countries. However, these species were documented for the first time with this activity in Morocco.

Other plants were cited only in Morocco, such as *Acacia tortilis*, *Argania spinosa*, *Cistus salviifolius*, *Fraxinus excelsior*, *Herniaria hirsuta*, *Lavandula dentata*, *Lavandula multifida*, *Lupinus angustifolius*, *Petroselinum sativum*, *Phalaris paradoxa*, *Thymus algeriensis* and *Thymus zygis* Interestingly, six taxa were identified as endemic in Morocco, namely *Argania spinosa*, *Olea europaea* subsp. *maroccana*, *Origanum compactum*, *Origanum elongatum*, *Thymus zygis and Zygophyllum gaetulum*.

Despite their alleged therapeutic effects, medicinal plants are not exempt of toxicity risks.[102] Even though the Moroccan law prohibits the retail of toxic remedies, its application remains lenient towards the smugglers of poisonous plants, which are treated on a large scale.[103] This raises concerns about the use of traditional remedies when they are undermining public health. As a result, many of the 84 plants on the list are toxic, including *Aristolochia longa*,[103] *Atractylis gummifera*,[31] *Citrullus colocynthis*,[72] *Globularia alypum*, *Nerium oleander*,[104] *Nigella sativa*,[105] *Peganum harmala*,[90] *Retama raetam*.[31] Accordingly, most herbalists are aware of toxic plants. They asserted the adverse effect could be avoided when draconian measures are considered. In this line, the herbalist should be aware of the toxicity of the treaded plants, which varies according to the parts used, mode of preparation, dosage, route of administration, and interaction with other medicines.[106]

Experimental evidence and clinical implications for diabetes mellitus

The incorporation of plant-based medicines into health systems requires pre-clinical as well as clinical trials. Pre-clinical studies are primarily conducted using in vitro and in vivo disease models. Clinical validation is performed through randomized, placebo-controlled clinical trials involving human subjects. In the present study, as shown in table 4, the most frequently cited species (mentioned at least twenty times by the participants) have shown experimental *in vivo, in vitro*, and clinical anti-diabetic effects. In this light, several plants have shown positive effects in humans during clinical trials, namely *Allium sativum, Cinnamomum verum, Nigella sativa, Olea europaea* subsp. *europaea, Salvia officinalis, Trigonella foenum-graecum* and *Urtica dioica* (Table 4). Several plant species have shown significant inhibitory effect on α-amylase, while other species inhibited α-glucosidase. Some plants were found to increase glucose tolerance improvement, as it is the case for *Ceratonia siliqua* and *Mentha pulegium*. Other plants had insulinotropic and/or cytoprotective effects in pancreatic cells (e.g *Rosmarinus officinalis* and *Nigella sativa*).Thus, such medicinal plants may have additional benefits, especially for patients with type 2 diabetes who are not at the end of their pancreatic function.

The antioxidant properties of plant species identified in the present study have been experimentally established, which justifies their use to alleviate diabetes and related complications. Oxidative stress is a major hallmark for the pathogenesis of diabetes mellitus.[107] Herbal remedies primarily combat the complications of diabetes through their antioxidant properties.[108] There is an inverse association between the intake of antioxidants, derived from edible herbs and the induction of diabetes. An antioxidant can control free radical levels to counter oxidative damage.[109] There has also been a linear correlation between antioxidant capacity of plant extracts and their total phenolic contents.[110] Additionally, extracts from many cited species were found to have significant antiglycative properties. Accordingly, these modes of action were proposed as antioxidant therapy to reduce diabetes-related complications mainly due to oxidative stress and the advanced glycation products accumulation.[111]

Similarly, in vivo studies are not only essential to establish the dose within the therapeutic index range, but also help to conceive the complete effect in an intact organism. In both types of diabetes, glycemic control is a major therapeutic concern. Out of the all cited plants, more than 65% were assessed for their antidiabetic activities in an animal model. A total of 51 (60.7%) species have shown anti-diabetic properties, especially hypoglycemic and antihyperglycemic effects in an animal model.

Finally, to our knowledge, among the listed plants, eighteen (or 21.1%) have no pharmacological record. This group of plant species include *Artemisia arborescens*, *Carum* spp., *Chenopodium ambrosioides*, *Cynara humilis*, *Ferula communis*, *Herniaria hirsuta*, *Lavandula officinalis*, *Olea europaea* subsp. *maroccana*, *Origanum compactum*, *Origanum elongatum*, *Phalaris paradoxa* L., *Reseda lanceolata*, *Tetraclinis articulata*, *Thymus algeriensis*, *Thymus vulgaris*, *Thymus zygis*, *Urtica membranacea* and *Vigna sinensis*. These species may constitute potential candidates for advanced experimental investigations to probe for antidiabetic drugs.

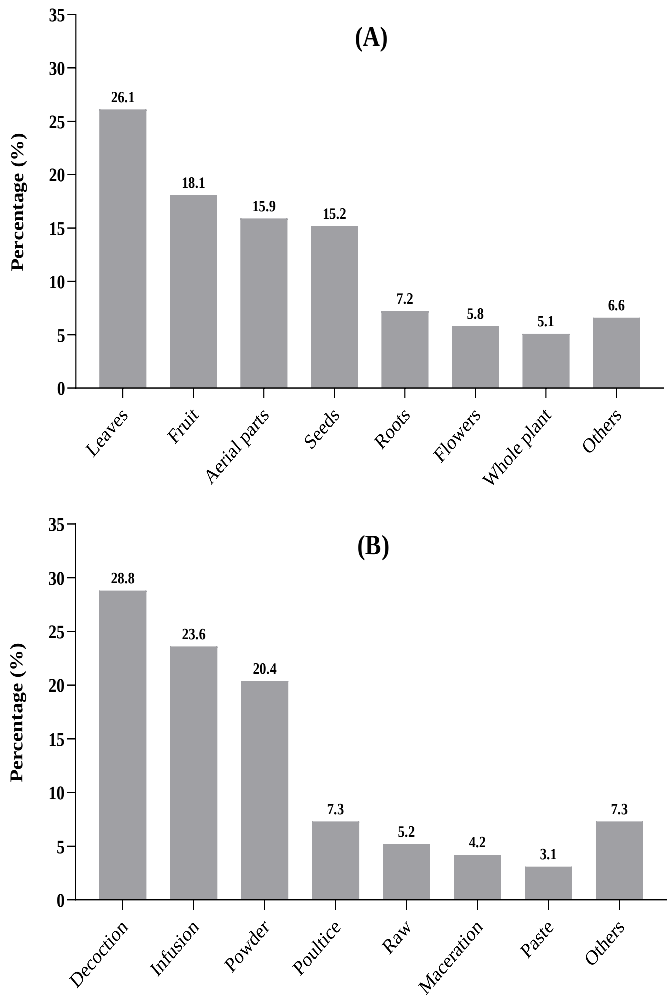

Figure 3: Plant part (A) and modes of preparation (B) used by traditional healers in Safi and Essaouira provinces.

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Table 3: Jaccard similarity index was used to compare the similarity of plant species used to treat diabetes mellitus in the Safi and Essaouira provinces to those in other regions of Morocco

Study area	**Year**	**Citation**	**Sample (N)**	**A**	**B**	**C**	**JI (%)**	**JD**	**QS (%)**
Alhaouz-Rhamna	2014	Benkhnigue et al., 2014	Local population (1700)	84	27	19	20.65	0.79	34.23
Beni Mellal region	2019	Mrabti et al., 2019	Herbalists, villagers and traditional healers (400)	84	45	30	30.30	0.70	46.51
Chtouka Ait Baha and Tiznit	2017	Barkaoui et al., 2017	Local population (380)	84	48	27	25.71	0.74	40.91
Errachidia province	2007	Tahraoui et al., 2007	Patients and traditional healers (400)	84	47	34	35.05	0.65	51.91
Fez-Boulemane	2001	Jouad et al., 2001	Diabetic patients (1095)	84	54	36	35.29	0.65	52.17
Fez-Meknes Region	2020	Mechchate et al., 2020	Diabetic patients (422)	84	50	35	35.35	0.65	52.24
Moroccan Rif	2019	Chaachouay et al., 2019	Traditional healers (582)	84	13	5	5.43	0.95	10.31
Oriental Morocco	1997	Ziyyat et al., 1997	Hypertensive and /or diabetic patients (626)	84	38	29	31.18	0.69	47.54
Rabat	2019	Skalli et al., 2019	Diabetic patients (334)	84	30	18	18.75	0.81	31.58
Rabat-Salé-Kénitra region	2020	El Hachlafi et al., 2020	Traditional herbalists and patients suffering from chronic diseases (581)	84	53	32	30.48	0.70	46.72
Sidi Slimane	2017	Laadim et al., 2017	Diabetic patients (700)	84	59	37	34.91	0.65	51.75
Tafilalet	2002	Eddouks et al., 2002	Patients and traditional healers (700)	84	36	29	31.87	0.68	48.33
Tarfaya province	2020	Idm’hand et al., 2020	Local populaion (150)	84	68	41	36.94	0.63	53.95
The Central Middle Atlas Region	2016	Hachi et al., 2016	Local population (1560)	84	77	40	33.06	0.67	49.69

A: the number of species in the present area of study (Safi and Essaouira provinces), **B**: the number of species of the area of similarity (in Morocco), **C**: the number of species shared by both the study area and the area of comparison, **JI**: Jaccard index, **JD**: Jaccard Distance, **N**: Sample size, **QS**: Sorensen's similarity index.

Table 4: Ethnobotanical report and scientific validation of the most cited medicinal plants used by traditional healers in Safi and Essaouira provinces for diabetes management.

Family	Scientific name	Recorded use for diabetes (Location reference)		Proven effects and pharmacological evidences	
		In Morocco	**In other countries**	**Model reference**	**Effects reference**
Alliaceae	*Allium sativum* L.	AR,[94] BM,[98] CM,[76] CT,[34] DT,[93] FM,[85] RS,[89] SS,[86] TF,[77] TL[72]	BD,[112] BR,[113] CD,[114] DZ,[115] GH,[116] IN,[117] IR,[118] JO,[119] KE,[120] MU,[21] NG,[3] PK,[121] SN,[122] SEA,[123] ZA[124]	*In vitro* enzymatic assays[125, 126]	α-amylase and α-glucosidase inhibition[126] Antiglycating activity[125]
				HFD-fed male C57BL/6J mice[127]	Anti-obesity effect[127]
				Human endothelial cells[127]	Antioxidant Activity[127]
				Patients with type 2 diabetes mellitus (Clinical study)[128]	Diabetic retinopathy protection[127] Hypolipidemic and hypoglycaemic effects[128]
				STZ-induced male Wistar rats[129]	Insulin- mimetic property[129]
Apiaceae	*Carum carvi* L.	AR,[94] BM,[98] CT,[34] ER,[37] FM,[85] OR,[91] RS,[89] TA,[33] TL,[72] TN[42]	DZ[115], IR[118]	*In vitro* enzymatic assays[130]	α-amylase and α-glucosidase inhibition[130] Antioxidant effects[130]
				STZ-induced diabetic rats[131]	Hypoglycemic effects[131]
				Normal and STZ-induced diabetic rats[131, 132]	Hypotriglyceridemic and hypocholesterolemic activities[131, 132]
Asteraceae	*Artemisia herba-alba* Asso	AR,[94] BM,[98] CM,[76] CT,[34] DT,[93] ER,[37] FB,[90] FM,[85] OM,[38] OR,[91] RA,[36] RS,[89] TF,[77] TL[72]	JO,[119] DZ[115]	Alloxan-induced in diabetic rats[133]	Alleviated oxidative damage[133]
				Diabetic rabbits[134]	
				HFD-induced type 2 diabetes in C57BL/6J mice[135]	Antiglycative effects[134] Hypoglycemic, antihyperglycemic, antihyperlipidemic and hypoliposis effects[135] Insulin resistance improvement[135]
Chenopodiaceae	*Chenopodium ambrosioides L. (=C. suffruticosum Willd.)*	BM,[98] CM,[76] FB,[90] FM,[85] OM,[38] SS[86]	GT[136]	**Not found**	**Not found**

Table 4 (*Continued*)

Family	Scientific name	Recorded use for diabetes (Location reference)	Proven effects and pharmacological evidences

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		In Morocco	**In other countries**	**Model [reference]**	**Effects [reference]**
Cruciferae	*Lepidium sativum* L.	AR,[94] BM,[98] ER,[37] FB,[90] FM,[85] RA,[36] RS,[89] TF,[77] TL[72]	DZ[115]	HFD-fed rats[137] Low-dose STZ with HFD-induced diabetic mice[138] Alloxan-induced diabetic male rats[139]	Anti-inflammatory effects[137] Improved insulin sensitivity[137] Improved insulin signalling[137] Antioxidant activities[139] Hypoglycemic effect[139] Improved lipids and glucose metabolism[138]
Cupressaceae	*Tetraclinis articulata* (Vahl) Mast.	AR,[94] BM,[98] CM,[76] ER,[37] FB,[90] OM,[38] SS,[86] TF,[77] TL[72]	DZ[115]	**Not found**	**Not found**
Fabaceae	*Ceratonia siliqua* L.	AR,[94] BM,[98] CT,[34] FM,[85] RA,[36] SS,[86] TF[77]	JO,[119] TR[140]	STZ-induced diabetic rats[141] Glycation model (serum bovine albumin)[142] In vitro enzymatic assays[143] Alloxan-induced diabetic rats[144]	α-amylase and α-glucosidase inhibition[141] Antiglycative effects[142] Antioxidant activity[143] Glucose tolerance improvement[144] Reduced intestinal glucose absorption[144]
Fabaceae	*Trigonella foenum-graecum* L.	AR,[94] BM,[98] CM,[76] CT,[34] DT,[93] ER,[37] FB,[90] FM,[85] OM,[38] OR,[91] RA,[36] RS,[89] SS,[86] TA,[86] TF,[77] TL,[72] TN[42]	BD,[112] DZ,[115] IN,[117] IR,[145] JO,[119] MU,[21] PK,[121] SEA,[123] SN[122]	Alloxan-induced diabetic rats[146] STZ-induced diabetic rats[147] Normal and alloxan-induced diabetic rats[148] *In vitro* enzymatic assays[149] Protein-protein interaction analysis using STRING 3.0[150] Type 2 diabetic patients (Clinical study)[151]	Anti-inflammatory and antioxidant properties[146] Attenuation of diabetic nephropathy[147] Hypoglycemic ant antihyperglycemic effect[148] Improvement of mitochondrial enzymes activities[149] Insulin signaling improvement[150] Insulin sensitivity enhancement Lipid profile improvement[151]
Globulariaceae	*Globularia alypum* L.	AR,[94] CM,[76] FB,[90] KL,[104] OM,[38] OR,[91] TA,[33] TL[72]	DZ[115]	Normal and hyperglycemic rats[152]	Hypoglycemic activity Insulin level increase[152]

Table 4 (*Continued*)

Family	**Scientific name**	**Recorded use for diabetes (Location [reference])**	**Proven effects and pharmacological evidences**

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		In Morocco	**In other countries**	**Model reference**	**Effects reference**
Lamiaceae	*Marrubium vulgare* L.	AR,[94] BM,[98] CM,[76] CT,[34] DT,[93] ER,[37] FB,[90] FM,[85] OM,[38] RA,[36] RS,[89] SS,[86] TA,[33] TF,[77] TL[72]	DZ[115]	Alloxan-induced diabetic Wistar rats[153] HSC-T6 and HepG2 cells[154]	Hypoglycemic and hypolipidemic effects[153] PPARγ activation[154]
	Mentha pulegium L.	AR,[94] CM,[76] DT,[93] ER,[37] FB,[90] FM,[85] OM,[38] RA,[36] RS,[89] SS,[86] TF,[77] TL[72]	DZ,[115] TR[140]	STZ-induced diabetic rats[155]	Hepatoprotective Effects Glucose tolerance improvement Hypoglycemic effect[155]
Lamiaceae	*Origanum compactum* Benth.	AR,[94] CM,[76] FB,[90] FM,[85] OM,[38] OR,[91] RS,[89] TF,[77] TL[72]	DZ[115]	**Not found**	**Not found**
Lamiaceae	*Rosmarinus officinalis* L.	DT,[93] ER,[37] FB,[90] FM,[85] MR,[88] OM,[38] RA,[36] RS,[89] TF,[77] TL[72]	DZ[115], TR[156]	Alloxan-induced diabetic rabbits[157]	Antioxidant effects Insulinotropic effects Hypolipidemic effects[157]
	Salvia officinalis L.	AR,[94] BM,[98] CM,[76] CT,[34] DT,[93] ER,[37] FM,[85] RA,[36] RS,[89] SS,[86] TA,[33] TF[77]	BR,[113] DZ,[115] IR,[145] JO[158]	*In vitro* enzymatic assays[159-161] Type 2 diabetic patients (Clinical study)[162] HFD-fed C57BL/6 mice[163] Glycation model (*In vitro* glycation of proteins: BSA-glucose assay)[164]	α-amylase inhibition[159] α-glucosidase inhibition[161] Antioxidant effect[161] PPARγ activation[160] Hypoglycemic and hypolipidemic effects[162] Improved insulin sensitivity[163] Inhibition of Protein Glycation[164]
	Thymus vulgaris L.	AR,[94] CM,[76] FM,[85] RS,[89] SS[86]	DZ,[115] SN[122]	**Not found**	**Not found**
	Thymus zygis L.	CM[76]	**Not found**	**Not found**	**Not found**
Lauraceae	*Cinnamomum verum* J.Presl	FM,[85] RA,[36] RS[89]	BR,[113] DZ,[115] IR,[82] MU[21]	*In vitro* enzymatic assays[165] Type 2 diabetic patients (Clinical study)[166]	α-amylase inhibitory activity[165] Antihyperglycemic and hypolipidemic properties[166]

Table 4 (*Continued*)

Family	**Scientific name**	**Recorded use for diabetes (Location reference)**		**Proven effects and pharmacological evidences**	
		In Morocco	**In other countries**	**Model reference**	**Effects reference**

Myrtaceae	*Eucalyptus globulus* Labill	AR,[94] BM,[98] CM,[76] FB,[90] FM,[85] OM,[38] SS,[86] TF[77]	BR,[113] DZ,[115] GT,[136] IN,[117] IR,[82] JO,[119] MU[21]	STZ-induced diabetic rats[167]	Oxidative stress reduction[167]
				Normoglycemic and STZ-induced diabetic male Wistar rats[168]	Pancreatic islets volume increase[168]
				STZ-induced diabetic mice[169]	Reduced hyperglycemia and associated weight loss[169]
Oleaceae	*Olea europaea* L. subsp. *europaea*	AR,[94] BM,[98] CM,[76] CT,[34] DT,[93] ER,[37] FB,[90] FM,[85] OM,[38] OR,[91] RA,[36] RS,[89] SS,[86] TA,[33] TF,[77] TL[72]	DZ,[115] IR,[118] JO,[119] KE,[120] MU,[21] PK,[170] SN,[122] TR[140]	Low-dose STZ with HFD-induced diabetic male Wistar rats[171]	Anti-inflammatory and antioxidant activities[171] Body weight loss[171]
				Type 2 diabetic patients (Clinical study)[172]	HbA1c reduction[172] Hypoglycemic effects[172]
				Middle-aged overweight men (Clinical study)[173]	Improved β-cell responsiveness[173] Improved insulin sensitivity[173]
				STZ-induced diabetic rat[174]	Prevention of high glucose-induced apoptosis[174]
				STZ-induced diabetes in susceptible C57BL/6 and CBA/H mice[175]	Prevention of islet-directed autoimmunity[175]
	Olea europaea subsp. *maroccana* (Greuter & Burdet) P.Vargas & al.	**Not found**	**Not found**	**Not found**	**Not found**
Ranunculaceae	*Nigella sativa* L.	AR,[94] CM,[76] DT,[93] ER,[37] FB,[90] FM,[85] KL,[104] OM,[38] RA,[36] RS,[89] SS,[86] TF,[77] TL,[72] TN[42]	DZ,[115] IR,[118] JO,[119] PK[170]	Type 2 diabetic patients (Clinical study)[176, 177]	Antiglycative effects[177] Glucose and lipids homeostasis improvement[177] Fasting blood glucose and postprandial hyperglycaemia reduction[176, 177] Insulin resistance improvement[177]
				Overweight and obese women (Clinical study)[178, 179]	Insulinotropic effects[177] Anti-obesity effects[178]
				In vitro enzymatic assays[180]	Antioxidant and Anti-Inflammatory properties[180] PPARγ gene induction[179]

Table 4 (*Continued*)

Family	Scientific name	Recorded use for diabetes (Location reference)		Proven effects and pharmacological evidences	
		In Morocco	**In other countries**	**Model reference**	**Effects reference**
Sapotaceae	*Argania spinosa* (L.) Skeels	AR,[94] CM,[76] CT,[34] RA,[36] RS,[89] SS,[86] TA,[33] TF[77]	Not found	STZ-induced diabetic rats[181] Normal and STZ-induced diabetic rats[182] HTC hepatoma cell line[183]	Antioxidant activity[181] Hypoglycemic and hypolipidemic effects[182] Insulin-sensitizing activity[183]
Urticaceae	*Urtica dioica* L.	AR,[94] BM,[98] CT,[34] FB,[90] OM,[38] OR[91]	DZ,[115] IR,[145] JO[119]	*In vitro* enzymatic assays[184] STZ-induced diabetic Swiss albino mice[185] Patients with advanced type 2 diabetes mellitus (Clinical study) [186] STZ-induced diabetic male Wistar rats[187] STZ-induced diabetic Sprague-Dawley male rats[188]	α-amylase inhibition[184] Antioxidant effects[185] HbA1c reduction[186] Hypoglycemic effects[186] Hepatoprotective effects[187] Insulinotropic effects[188]

Abbreviations:
Locations in Morocco: (**AR**) Al Haouz-Rhamna region, (**BM**) Beni Mellal region, (**CM**) Central Middle Atlas region, (**CT**) Chtouka Ait Baha and Tiznit, (**DT**) Daraa-Tafilalet region, (**ER**) Errachidia province, (**FB**) Fez-Boulemane (North centre region of Morocco), (**FM**) Fez-Meknes region, (**KL**) Ksar Lakbir district, (**MR**) Moroccan Rif, (**OM**) Oriental Morocco, (**OR**) Oriental region, (**RA**) Rabat city, (**RS**) Rabat-Sale-Kenitra region, (**SS**) Sidi Slimane city, (**TA**) Tata Province, (**TF**) Tarfaya province, (**TL**)Tafilalet (South-east region of Morocco), (**TN**) Taounate province.
Alpha codes for other countries: (**BD**) Bangladesh, (**BR**) Brazil, (**CD**) Democratic Republic of Congo, (**DZ**) Algeria, (**GH**) Ghana, (**GT**) Guatemala, (**IN**) India, (**IR**) Iran, (**JO**) Jordan, (**KE**) Kenya, (**MR**) Mauritania, (**MU**) Mauritius, (**NG**) Nigeria, (**PK**) Pakistan, (**SEA**) South East Asian Countries (India, Pakistan & Sri Lanka), (**SN**) Senegal, (**TR**) Turkey, (**ZA**) South Africa.
Other abbreviations: (**HbA1c**) Glycated hemoglobin A1c, (**PPAR**) Peroxisome Proliferator-Activated Receptors, (**STZ**) Streptozotocin.

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Conclusion

In contrast to most ethnobotanical studies undertaken in Morocco, especially those targeting both traditional healers and ordinary people in rural areas, this survey mainly focused on traditional healers in the coastal areas of west-central Morocco. Hence, these findings can bring to light the differences with previous studies in other regions. It seems that the study area offers a large biodiversity of medicinal and aromatic plants, requiring further exploration. Such biodiversity enriches the culture of traditional medicine, which can be considered an inexhaustible source of research for affordable medicines.
The transmission of ethno-medicinal knowledge across generations is not taken for granted and is endangered by the continuous westernization of indigenous cultures. Indeed, the present study strives to compile as much useful data as possible, which may hopefully contribute to the preservation of knowledge regarding the use of medicinal plants in Central-Western Morocco. In this light, the interviewed healers provided valuable information about diabetes management using medicinal plants, which may henceforth play a pivotal role in sustaining the primary health care system.

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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