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An ethnobotanical survey of medicinal plants used for diabetes treatment in Rabat, Morocco

Souad Skalli*, Rachida Hassikou, Moustapha Arahou

Microbiology and Molecular Biology Team, Center of Plant and Microbial Biotechnology, Biodiversity and Environment, Faculty of Sciences, MOHAMMED V UNIVERSITY IN RABAT, 4 Avenue Ibn Battouta PB 1014, Rabat, Morocco

* Corresponding author.
E-mail address: sophieskalli@gmail.com (S. Skalli).

Abstract

Diabetes mellitus is a major public health problem in Morocco. The value of ethnobotanical information is now increasingly acknowledged. To inventory and to provide ethnobotanical information on some of the medicinal plants used in traditional medicine to treat diabetes in Rabat (Morocco), a survey was undertaken from March 1st to April 30th 2018. This survey was conducted using a semi-structured questionnaire targeting diabetic patients from the SOS Diabetes Center. 334 diabetic patients were interviewed. Of this group, 53.6% (34 men and 145 women) use medicinal plants to control their diabetes. 47.2% have type 2 diabetes and 52.5% have type 1diabetes. Thirty plant species belonging to 18 botanical families were recorded for the treatment of diabetes. The most represented families were Lamiaceae with 8 species followed by Fabaceae with 3 species. Based on the highest number of users, the most important species were *Trigonella foenum-graecum* L. (15.4%), *Salvia officinalis* L. (13.3%) and *Olea europaea* L. (10.8%). Leaves (47.5%), seeds (20.2%) and stem (17.6%) were the parts predominantly used to prepare the formulations, which were mainly infusions (50.9%), administrated by the oral route (98.9%). Some plants were used only by type 1 diabetics while others were used by type 2 diabetics. The observed adverse events

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related to the use of medicinal plants were represented by occasional heartburn in 2.2% of diabetic patients. This study is the first to collect and document information on medicinal plants and how they are used by diabetic patients. *Calamintha alpina* L. is reported for the first time at the international level as used in traditional treatment of diabetes and seven others were reported as new medicinal plants used to treat diabetes in Morocco. This will extend the list of plants already mentioned as used for diabetes. Further research should be carried out to validate the antidiabetic uses of most of these plant species.

Keywords: Metabolism, Public health, Anthropology

1. Introduction

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Hyperglycemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, especially the nerves and blood vessels. Globally, the number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014 [1], and the disease directly caused 1.6 million deaths in 2015 [2]. In addition, it has been predicted that the number of diabetic patients will increase to 300 million by 2025 [3]. The World Health Organization (WHO) projects that diabetes will be the seventh leading cause of death in 2030 [1].

The increase in prevalence of type 2 diabetes has been greatest in low- and middle-income countries in the past few decades [2]. In Morocco, diabetes causes more than 24 000 deaths a year. Between 2011 and 2015, the number of diabetics increased from 1.5 million to over 2 million, aged 20 and over [4].

The side effects of conventional drugs are increasingly recognized and pharmacovigilance systems have been developed to detect and manage these adverse effects [5]. Even today, in the most industrialized countries, traditional health care is seen as very important due to the reduced cost compared to pharmaceutical drugs, and the perception of fewer adverse effects [6, 7]. The appropriate use of the country's medicinal plants in combination with effective conventional medicines could have a positive impact on the health and quality of life of the diabetic population [8, 9].

Nowadays, there is an increasing interest in the public for consumption of medicinal plants because patients prefer ″natural″ products and also since they are inexpensive and widely available. This is especially important as diabetes imposes a large economic burden on health care systems and national economies [2]. According to the statistics of the WHO, more than 80% of the world's population, particularly in the underdeveloped countries, obtain their primary healthcare needs from medicinal

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herbs [10]. Traditional herbal remedies are used even in highly industrialized settings because they are important pillars of culture and human socialization [11].

Medicinal plants with little toxicity and few side effects, are be important therapeutic possibilities for the treatment of diabetes [12]. Even if systematic studies on the folkloric use of medicinal plants used to combat diabetes mellitus are scanty [13], Literature data from around the world indicate that several medicinal plants have antidiabetic properties. The use of these plants has increased over time [14]. Plants can be used as a complementary and alternative therapy, particularly in metabolic diseases such as diabetes. These plants may also be of interest in the development of new pharmaceutical drugs for diabetes. The mechanisms of action of these plants on glycemia are variable. Some of them have actions similar to conventional antidiabetic drugs, for example sulfonylureas, inhibitors of hepatic neoglucogenesis, or inhibitors of glucosidase [15]. It was reported also, that combination of plants extracts or their components may have synergistic effects to better act on diabetes [16].

Since ethnobotanical surveys, including those conducted with patient interviews, are effective methods in documenting and identifying medicinal plants used in traditional knowledge systems [17], the present survey was undertaken in the SOS Diabetes Center of Rabat in Morocco in order to record medicinal plant species used in traditional medicine to treat diabetes by diabetic patients.

2. Materials and methods

2.1. Study design

A survey was performed among diabetic patients of the SOS Diabetes Center in Rabat, and who use medicinal plants. The SOS Diabetes Center is a non-governmental association (NGO) for adult diabetics, founded in 1991. Patients attend this center twice a month to obtain routine analyses such as blood glucose, glycated hemoglobin test and electrocardiogram (ECG) measurements. Some patients benefit from a device to control their blood glucose at home. This survey was conducted from March 1st to April 30th 2018 and consisted of oral interviews in the Moroccan Arabic dialect.

Questionnaire

The questionnaire was composed of 15 questions which were divided into three distinct parts:

- Patient: Age; Gender; Educational level.
- Disease: Type of Diabetes; Date of diagnosis.
- Plant(s) used: vernacular name; parts used; amount or dose used; mode of preparation; mode of administration; duration of treatment; who recommended or

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prescribed the plant; selling location; medicinal plant effectiveness; possible adverse effects (AEs) observed.

In the questionnaire, treatment by medicinal plants for diabetic symptoms like frequent urination, leg sores, neuropathy etc. in patients was not included. The study related to the disease itself, not to its complications. So, it sought to obtain information on medicinal plants that are used for treating diabetes.

2.2. Study integrity

This study was exempt from review by the institutional review board that examined the questionnaire and it was confirmed that Moroccan legislation does not request this review for studies like ours. It was judged that this anonymous survey, where the questionnaire does not contain the patient's identity, does not affect patient privacy. Participation in the survey was voluntary. Each patient who was willing to participate in the study received oral information about the research and its publication for scientific purposes. Patients could at any time withdraw from the interview. Patients received no incentives or payments and all cooperated voluntarily.

For illiterate patients, the questionnaire was completed by the interviewer who reported what the patient told him orally in the Moroccan dialect.

2.3. Plant identification

Patients were asked to bring back a sample of the plants used. These plant samples were brought back to the Institut Scientifique (ISR) Mohammed V University in Rabat where the National Herbarium specimens (RAB) are tored. The plant species were identified using the Moroccan identification key ″FLORE PRATIQUE DU MAROC″ (Practical Flora of Morocco) [18, 19, 20] by the ISR botanical team. A voucher herbarium specimen code was given to the plants provided. Regarding food and exotic plants from these plant samples, they were identified through their direct translation from their local or commercial names to their scientific names using EPPO codes (https://www.eppo.int/DATABASES/GD&Codes/EPPO_Codes). An EPPO code is a core component of a database of names, both scientific and vernacular, formerly known as a Bayer code. It is an encoded identifier that is used by the European and Mediterranean Plant Protection Organization (EPPO). Such identifications were done by Professor Souad Skalli (Faculty of Science University Mohammed V in Rabat) with the help of Professor Abdelkader Taleb (Agronomic and Veterinary Institute Hassan II University, Rabat) and Professor Fatima Ezzahra El Alaoui-Faris (Faculty of Science University Mohammed V in Rabat).

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2.4. Data analysis

The data reported on the questionnaire were entered and listed on a Microsoft Excel database and analyzed to determine the proportions of different variables such as gender and age, plant parts used, and preparation methods. These results were analyzed descriptively and comparatively.

In addition, ethnobotanical data was analyzed using relative frequency of citation (RFC) to determine the well-known and most used species among diabetic patients. Relative frequency of citation shows the local importance of each species and is obtained by dividing the number of informants (diabetic patients) who mention the use of the species, also known as the Frequency Citation (FC), by the number of informants (diabetic patients) participating in the survey (N): $RFC = FC/N$ ($0 < RFC < 1$) [21].

2.5. Literature data

The use of plants from this survey was compared with other surveys of plants used traditionally in treating diabetes in Morocco and in other parts of the world. This was not done exhaustively. A single reference was enough to determine that a plant was already used for diabetes.

3. Results

3.1. Socio-demographic profile of the diabetic patients

During the period of the survey, 334 diabetic patients were interviewed. No patient declined to be surveyed. Of these, 53.6% (179/334; 34 men and 145 women) use medicinal plants. Table 1 displays the sociodemographic profile of the diabetic patients. The age of patients varied between 17 and 87 years. The diabetic patients were

Table 1. Sociodemographic characteristics of diabetic patients who used medicinal plants.

Variable	Subgroup	Number	Percentage (%)
Sex	Male	34	19
	Female	145	81
Age	<20 years	3	1.7
	20–40years	71	39.7
	40–60 years	51	28.5
	>60 years	54	30.1
Educational Level	Illiterate	82	45.8
	Primary	30	16.7
	Secondary	25	14
	University	42	23.5

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arbitrary divided into four age groups: < 20 years, 20−40years, 40−60 years and >60 years accounting for, respectively, 3, 71, 51 and 54 diabetic patients. The most represented age group was that of patients aged from 20 and 40 years with 39.7% of the patients. For the educational level, 45.8% of the diabetic patients were illiterate while 16.7% attended at least primary school. The rest were either secondary (14%) or university level (23.5%) of education.

3.2. Diabetes type and diagnosis

Among the diabetic patients of the survey, 47.5% (85/179) had type 2 diabetes and 52.5% (94/179) had type 1 diabetes. Diabetes was diagnosed less than one year, 1−15 years, 16−30 years and over 30 years for 14.3%; 61.2%; 22.5% and 2%, respectively.

3.3. Ethnobotanical survey data

The use of medicinal plants among the diabetics was always done in combination with their conventional treatment. This use is considered by patients as a supplement to treat their diabetes. Diabetic patients used one medicinal plant (71.2%), two plants (12.5%), or three plants (16.3%) at the same time for their diabetes.

The present survey gathered information on 30 plant species reported by the diabetic patients and belonging to 18 botanical families. These plant species have been divided into 13 Moroccan spontaneous, or wild, species (43.3%), 13 cultivated species (43.3%), 4 imported species (13.4%) and 2 undetermined mixture of powdered plants (Table 2).

The families with most plant species used for diabetes treatment, included Lamiaceae with 8 species followed by Fabaceae with 3 species and by Apiaceae, and Zingiberaceae with 2 species each. The rest of the families were represented with 1 species each (Table 2). Based on the frequency of uses, the most important species were *Trigonella foenum-graecum* L. (15.4%), *Salvia officinalis* L. (13.3%), *Olea europaea* L. (10.8%), *Artemisia herba alba* Asso and *Cinnamomum verum* J. Presl. with 8.2% each, followed by *Coriandrum sativum* L., *Thymus broussonetii* Boiss *and Origanum grosii* Pau & F.-Q. with 4.1% each. They were followed by *Rosmarinus officinalis* L. (3.1%) and the rest of plants at 2.1%.

The RFC of the encountered plant species varied from 0.17 to 0.01. The highest value of RFC ranked was for *Trigonella foenum-graecum* L. (0.17), followed by *Salvia officinalis* L. (0.15), *Olea europaea* L. *subsp. europaea var. sylvestris* (Mill.) Lehr (0.12) and *Cinnamomum verum* J. Presl. (0,10) (Table 2).

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Table 2. Medicinal plant species with their traditional uses by patients at the SOS diabetes center in Rabat and their frequency and relative frequency of citation.

Family	Botanical name (Voucher code if applicaple if not EPPO code)	Local name	Plant part used	Preparation form and dosage	Route of administration and duration of treatment	Frequency of citation	Relative frequency of citation
A- Spontaneous plants							
Asteraceae	*Artemisia herba alba* Asso (RAB43123)	Chih	Leaves and stem	Infusion (n = 6), decoction (n = 2), 1 handful (n = 8)	Orally, three times a day	8	0.05
Cucurbitaceae	*Citrullus colocynthis* L. (RAB61440)	Hdej	Fruit	1 fruit (n = 2)	Cutaneous application Once a day during three days	2	0.01
Fabaceae	*Ceratonia siliqua L.* (RAB38626)	Kharoub	Fruits	1 fruit (n = 2)	Orally once a day	2	0.01
Lamiaceae	*Calamintha alpina* L. (RAB49940)	Fliyyo diāl berr	Leaves	Decoction (n = 2), 6 to 7 leaves (n = 2),	Orally, once a day	2	0.01
	Marrubium vulgare L. (RAB47248)	Merriwet	Leaves and stem	Infusion (n = 2), 1 handful (n = 2)	Orally, once a day	2	0.01
	Mentha pulegium L. (RAB34023)	Fliyyo diāl mae	Leaves	Infusion (n = 2), 3 to 4 leaves (n = 2)	Orally, once a day on an empty stomach	2	0.01
	Origanum grosii Pau & F.-Q (RAB07156)	Zaater	Leaves	Infusion (n = 4), 3 to 4 tablespoons with water (n = 4)	Orally, twice a day (n = 6) and once a week (n = 2)	8	0.05
	Rosmarinus officinalis L. (RAB8087)	Azir	Leaves and stems	Infusion (n = 2), decoction (n = 2), maceration (n = 2), 1 handful (n = 6)	Orally once to twice a day	6	0.03
	Salvia officinalis L. (RAB61860)	Salmia	Leaves	Infusion (n = 26), 3 to 4 leaves (n = 19) or 1 handful (n = 7)	Orally, twice to thrice a day	26	0.15
	Thymus broussonetii Boiss. (RAB40439)	Zietra	Leaves and stem	Infusion (n = 4), maceration (n = 4), 1 handful (n = 8)	Orally, once a day	8	0.05

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Table 2. (*Continued*)

Family	Botanical name (Voucher code if applicaple if not EPPO code)	Local name	Plant part used	Preparation form and dosage	Route of administration and duration of treatment	Frequency of citation	Relative frequency of citation
	Mentha suaveolens Ehr. (RAB76196)	Marseta	Leaves	Infusion (n = 2), 3 to 4 leaves (n = 2)	Orally, once a day on an empty stomach	2	0.01
Sapotaceae	*Argania spinosa* L. (RAB97392)	Argane	Almond fruits	Crushed (n = 2),1 teaspoon (n = 2)	Orally, once a day	2	0.01
Verbenaceae	*Verbena officinalis* L. (RAB33517)	Louiza	Leaves	Decoction (n = 2), 1 handful (n = 2)	Orally, once a day on an empty stomach	2	0.01
B- Cultivated plants							
Alliaceae	*Allium cepa* L. (ALLCE)	Bessela	Bulb	1 bulb (n = 2)	Orally, once a day	2	0.01
Apiaceae	*Coriandrum sativum* L. (CORSA)	Kasbour	Seeds and Leaves	Infusion (n = 2) or seeds with water (n = 6), one teaspoon (n = 8)	Orally, once a day	8	0.05
	Pimpinella anisum L. (PIMAN)	Hebbat hlaoua	Seeds	Infusion (n = 2), 1 handful (n = 2),	Orally thrice a day	2	0.01
Brassicaceae	*Lepidium sativum* L. (LEPSA)	Heb erechad/Leharf	Seeds	Ground powder with milk (n = 2), 1 teaspoon	Orally, twice a day	2	0.01
Fabaceae	*Trigonella foenum-graecum* L. (TRKFG)	Helba	Seeds	Maceration in sparkling water (n = 16), 7 seeds with milk (n = 2) or with water (n = 12); 1 to 3 tablespoons (n = 18) or 1 handful (n = 12)	Orally, one to twice a day	30	0.17
	Glycyrrhiza glabra L. (GYCGL)	Ark souss	Bark	Infusion (n = 2), 1 root piece (n = 2)	Orally, twice a day	2	0.01
	Persea americana Mill. (PEBAM)	Avocat	Fruits core	Grated and ingested with milk (n = 2), 1 core (n = 2)	Orally, twice a day	2	0.01
Liliaceae	*Allium ampeloprasum* L. (ALLAM)	Leborrou	Stem	Crushed and ingested with water (n = 2), 1 tablespoon	orally, once a day	2	0.01

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Table 2. (*Continued*)

Family	Botanical name (Voucher code if applicaple if not EPPO code)	Local name	Plant part used	Preparation form and dosage	Route of administration and duration of treatment	Frequency of citation	Relative frequency of citation
Linaceae	*Linum usitatissimum* L. (LIUUT)	Lekattan	Seeds	Ground seeds with water (n = 4), 1 teaspoon (n = 4)	Orally, once a day	4	0.02
Malvaceae	*Abelmoschus esculentus* L. (ABMES)	Mloukhia	Fruits	Maceration (n = 2), 3 fruits (n = 2)	Orally, once to twice a day	2	0.01
Oleaceae	*Olea europaea* L. *subsp. europaea var. sylvestris* (Mill.) Lehr (OLVES)	Zaytoun	Leaves	Infusion (n = 17), decoction (n = 4), 3 to 4 leaves (n = 5), 5 to 7 leaves (n = 10) or 1 handful (n = 6)	orally, twice to three times a day	21	0.12
Ranunculaceae	*Nigella sativa* L. (NIGSA)	Sanouj- Habat saouda	Seeds	Ground powder with water (n = 2), 1 teaspoon (n = 2)	Orally, once a day	2	0.1
Rosaceae	*Prunus dulcis* (Miller) D. A. Webb (PRUAM)	Louz	Fruits	3 teaspoons (n = 2)	Orally, twice a day	2	0.01
C- Imported plants							
Lauraceae	*Cinnamomum verum* J. Presl. (CINZE)	Kerfa	Bark	Infusion (n = 12), decoction (n = 2), maceration (n = 2), 2 tablespoons (n = 4) or 1 to 4 bark pieces (n = 12)	Orally, once a day	18	0.10
Myrtaceae	*Syzygium aromaticum* (L.) Merr. & Perry. (SYZAR)	Kronfel/Oud newwar	Seeds	Ground powder (n = 2), 1 teaspoon (n = 2)	Orally, twice a day	2	0.01
Zingiberaceae	*Curcuma longa* L. (CURLO)	Al-kharkoum	Rhizomes	Infusion (n = 2), 2 to 3 smithereens	Orally, once a day	2	0.01
	Zingiber officinale Roscoe (ZINOF)	Skenjbir	Rhizomes	Maceration (n = 2), 1 piece (n = 2)	Orally, twice a day	2	0.01
D- Unknown							
Undetermined mixture of powdered plants	-	-	-	Mixture with water (n = 2), 2 tablespoons (n = 2)	Orally, twice a day	2	0.01

EPPO: European and Mediterranean Plant Protection Organization; n: number of times used.

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Different parts of medicinal plants such as leaves, fruits, seeds or intact plant, were used by the diabetic patients. Leaves were the most commonly used part of the plant (47.5%), followed by seeds (20.2%), stem (17.6%) and bark (7.6%) (Fig. 1).

The most common application methods were infusion (50.9%) followed by maceration (16.8%), and decoction (8.4%). In addition, some plants or parts of plants were taken fresh or dry with water (17.9%). Many plants were used in more than one method of preparation (Table 2).

The oral route of administration (98.9%) was the most used route by diabetic patients who participated in this survey. The dermal route accounted for 1.1% and this route was described for the plant *Citrullus colocynthis* L.

The duration of the treatment with the plants varied considerably according to the patients questioned ranging from a few days to several years. Indeed, 22% of diabetic patients used the plant(s) from 1 to 3 days only; 6% from 1 to 3 weeks; 26% from 1 to 3 months and 33% from 1 to several years.

Plants used by the diabetic patients were bought from herbalists in 71% of cases, from traditional markets (15%) and from other stores (14%).

The review of the available literature showed that among the 30 species of plants identified in our survey (Table 2), 29 were described as plants used by diabetic patients or studied for their diabetes interest in at least one bibliographic reference. One species namely, *Calamintha alpina* L., was reported for the first time as a plant used for the treatment of diabetes.

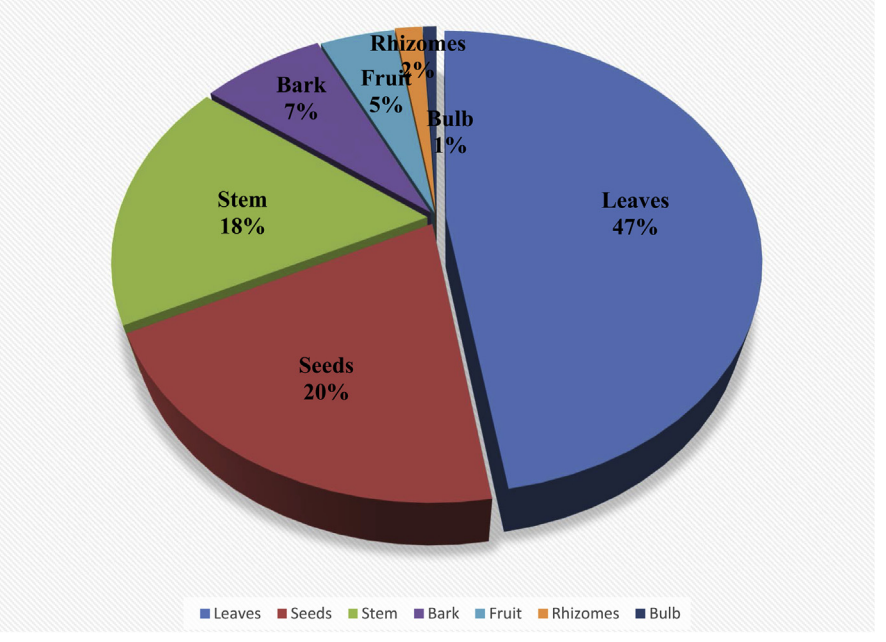

Fig. 1. Frequency of plant parts used by diabetic patients in the SOS Diabetes Center in Rabat.

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Compared to ethnobotanical studies conducted in other regions of Morocco, 22 species were already reported as plants used for diabetes: *Abelmoschus esculentus* L.; *Allium cepa* L.; *Argania spinosa* L.; *Artemisia herba alba* Asso; *Citrullus colocynthis* L.; *Coriandrum sativum* L.; *Persea americana* Mill.; *Lepidium sativum* L.; *Linum usitatissimum* L.; *Marrubium vulgare* L.; *Mentha pulegium* L.; *Mentha suaveolens* Ehr.; *Nigella sativa* L.; *Olea europaea* subsp. europaea var. sylvestris (Mill.) Lehr; *Origanum grosii* Pau & F.-Q.; *Pimpinella anisum* L.; *Rosmarinus officinalis* L.; *Salvia officinalis* L.; *Thymus broussonetii* Boiss; *Trigonella foenum-graecum* L.; *Verbena officinalis* L.; and *Zingiber officinale* Roscoe.

Seven plants have been mentioned to treat diabetes. The literature reviewed showed that these seven plants have not already been reported by other Moroccan studies. Those are *Allium ampeloprasum* L.; *Ceratonia siliqua* L., *Cinnamomum verum* J. Presl.; *Curcuma longa* L.; *Syzygium aromaticum* (L.) Merr. & Perry.; *Glycyrrhiza glabra* L.; and *Prunus dulcis* (Miller) D. A. Webb. Nevertheless, the international literature has shown that these plants have been used for diabetes in other countries.

All patients in the survey reported that they use medicinal plants for diabetes. They do so in combination with their conventional treatment. 10% of them inform their diabetologist about this use. Plant use was recommended either by friends (69%), family (27%), mass media or herbalists (2% each).

From these thirty plant species used, three were used for diabetes type 1 only, twelve plants were used for diabetes type 2 only, and fifteen plants were used both for type 1 and type 2 diabetes (Table 3).

Regarding the question of how the patient feels that the plant used has indeed an antidiabetic effect, patients reported that this was directly observed after the first measurement of blood glucose post ingestion of the plant.

Adverse events related to the use of medicinal plants involved *Artemisia herba alba* Asso, *Syzygium aromaticum* (L.) Merr. & Perry, *Rosmarinus officinalis* L., *Glycyrrhiza glabra* L. and *Origanum grosii* Pau & F.-Q. These effects were reported by four diabetic patients (2.2%) and were restricted to occasional heartburn. These patients used these medicinal plants from 1 to 3 weeks.

4. Discussion

In our survey, the sociodemographic data of diabetic patients who used medicinal plants showed that the older population from 40 years of age and older was the most represented. This agrees with a study conducted in the Chtouka Ait Baha and Tiznit areas of Morocco where the informants' age group between 50 and 70 years old was the most represented [22]. Usually, these older individuals have gained valuable experience during their life as users of medicinal plants or have learned

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Table 3. Plants used by patients according to their type 1 or type 2 diabetes disease.

Plants	Type 1 diabetes	Type 2 diabetes
Ceratonia siliqua L.	+	-
Syzygium aromaticum (L.) Merr. & Perry.	+	-
Verbena officinalis L.	+	-
Allium ampeloprasum L.	-	+
Argania spinosa L.	-	+
Calamintha alpina L.	-	+
Citrullus colocynthis L.	-	+
Curcuma longa L.	-	+
Glycyrrhiza glabra L.	-	+
Mentha pulegium L.	-	+
Mentha suaveolens Ehr.	-	+
Nigella sativa L.	-	+
Persea americana Mill.	-	+
Pimpinella anisum L.	-	+
Prunus dulcis (Miller) D. A. Webb	-	+
Abelmoschus esculentus L.	+	+
Allium cepa L.	+	+
Artemisia herba alba Asso	+	+
Cinnamomum verum J. Presl.	+	+
Coriandrum sativum L.	+	+
Lepidium sativum L.	+	+
Linum usitatissimum L.	+	+
Marrubium vulgare L.	+	+
Olea europaea L. subsp. *europaea* var. *sylvestris* (Mill.) Lehr	+	+
Origanum grosii Pau & F.-Q	+	+
Rosmarinus officinalis L.	+	+
Salvia officinalis L.	+	+
Thymus broussonetii Boiss.	+	+
Trigonella foenum-graecum L.	+	+
Zingiber officinale Roscoe	+	+

+: used; -: not used.

from other people's experiences. It fits with a widespread belief in Morocco, as it is the case for all traditional cultures, where older people are knowledgeable in the use of medicinal plants. In comparison with men, females seem to be the more frequent users of plants for diabetes, with 81% of participants in this sex group. As in other Moroccan regions [22], Illiterate diabetic patients were predominantly represented

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with 45.8%. This study also highlights the early use of medicinal plants by patients as soon as the diagnosis of diabetes is established.

Our survey emphasized the wide-spread use of plants by diabetic patients in Rabat. 53.6% of the patients in the study used plants as a complementary treatment to that prescribed by their endocrinologist. This shows the belief and the place occupied by medicinal plants among the diabetic patients in this study.

The survey revealed at least 30 medicinal plants are used to treat diabetes and has shown similar results to those reported in other Moroccan studies [22] where *Trigonella foenum-graecum* L., *Salvia officinalis* L., and *Olea europaea* L. are the plant species most used to treat diabetes mellitus. With regard to the plants noted in our survey, the most common plant part used by the patients is the leaf. This has also been reported by other studies [23, 24, 25]. Leaves and seeds may contain or accumulate the pharmacologically active agents of plants as in the case for *Trigonella foenum-graecum* L. seeds [26, 27]. The most common preparation method was infusion. For many plants such as *Cinnamomum verum* J. Presl., the method of preparation can vary and the patients can use the same plant in the form of an infusion, a decoction, or maceration. This could be attributed to the fact that the active ingredients of these plants are heat-stable. Indeed, if the active constituents of raw medicinal plants (or parts of plants) are heat-labile and the method of extraction used is decoction, the active ingredients in these conditions are easily decomposed and subject to a loss of characteristic properties by the action of heat. However, studies to verify the optimal mode of preparation in terms of effectiveness for diabetes remains necessary.

The oral route of administration is the most used route by diabetic patients who participated in this study with the exception of *Citrullus colocynthis* L. where the dermal route was used. This probably relates to the fact that bitter apple is a toxic plant if taken orally [28]. Colocynthis fruits have already been mentioned to reduce blood glucose in traditional systems of medicine of many countries [29, 30] and a study has showed that *C. colocynthis* fruit has a considerable effect on reduction in the mean serum level of HbA1c and fasting blood sugar in patients with the type 2 diabetes [31].

The duration of the treatment with the plants varies considerably according to the diabetic patients questioned, going from a few days to several years. This testifies to the trust that patients have in these plants and confirms their regular use as a complement to conventional treatment. Moreover, and in terms of research on new molecules with antidiabetic activity, this can be taken into consideration.

Relative RFC values obtained from the reported species indicate the degree of indigenous knowledge shared by local people regarding the use of medicinal plants for the

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treatment of diabetes. The plants having the highest RFC are, in fact, predominantly used and commonly known by the local people. These may prove important for linking and evaluating research for future drug discovery and sustainable use of medicinal plants for the treatment of diabetes.

This study has the distinction of being conducted with patients who provided important information about the plants used and how they were used regarding the quantity, the part used and the duration of use. Obtaining this information is an advantage and a positive finding in this study. Indeed, this information is valuable because it can be used for future pharmacological studies, especially with respect to the most promising plants. This information is often missing or not detailed when ethnobotanical surveys are conducted with herbalists or with traditional healers who refuse to inform about their traditional recipes. Indeed, the majority, if not all, of the ethnobotanical studies available in the literature have been conducted with herbalists or traditional healers [29, 32].

Most of the plants used are promising. *Trigonella foenum-graecum* L. has been used for numerous indications, including the hypoglycemic and antihyperlipidemic properties of the seed powder taken orally [33]. Fenugreek is also the most recommended plant for treating diabetes in the Fars region of Iran [34] and in west Algeria [35]. It has efficacy in reducing blood glucose [36], produced a significantly reduced insulin resistance [37] and improved fasting and postprandial blood glucose levels [38, 39] in diabetic patients. In our survey, fenugreek was used by diabetic patients both for type 1 and type 2 diabetes.

Salvia officinalis L., is prepared as an infusion of 4−6 g of dried leaves in two divided doses per day and is taken in Iranian traditional medicine as an antihyperglycemic agent to treat diabetes mellitus [40]. Research has shown that common sage has hypoglycemic actions [41, 42, 43, 44]. The use of this plant may be of interest in complementing conventional treatment in diabetic patients, particularly in hyperlipidemic type 2 diabetes patients [45].

Olea europaea L. leaves are well known for their effect on metabolism, and in particular as a traditional antidiabetic and antihypertensive herbal drug. They contain several potentially bioactive compounds that may have hypoglycemic properties in both human diabetic subjects and in rats [46, 47]. These bioactive compounds may explain the fact that leaves of this plant were used by diabetic patients for both type 1 and type 2 diabetes.

Artemisia herba alba (Asso), is known for its medicinal properties to treat diabetes [22, 48]. White wormwood was reported also by an ethnopharmacological survey that was performed in the Ouargla region of the Algerian Sahara [49], as a medicinal plant used for diabetes.

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Cinnamomum verum J. Presl. contains derivatives such as cinnamaldehyde and cinnamic acid that have an antidiabetic effect [50]. Cinnamon may be used in the daily care of diabetes mellitus by its dietary or supplementary use [51].

The use of *Coriandrum sativum* L. seeds in the Moroccan traditional treatment of diabetes remains to be experimentally [52] validated. The antihyperglycemic effect of coriander leaf and stem in alloxan-induced diabetic rats was shown [53]. This study indicated that the extracts could protect liver function and exhibited hypoglycemic, hypolipidemic, and antioxidant effects in diabetic rats. These studies support the traditional use of the leaves, seeds and stem of this plant by the diabetic patients taking part in our survey.

Linum usitatissimum L. seed is the richest source of the lignan secoisolariciresinol diglucoside (SDG). Metabolites of SDG may protect against cardiovascular disease and the metabolic syndrome by reducing lipid and glucose concentrations [54, 55]. Prasad and Dhar [56], suggest that SDG may have a great potential for reducing the incidence of type 1 diabetes and delaying the development of type 2 diabetes in humans. This supports the use of this plant by our diabetic patients for both type 1 and type 2 diabetes.

Rosmarinus officinalis L. is used in the traditional treatment of diabetes in others region of Morocco such as in south-eastern Morocco, Errachidia province [56]. Rosemary has been shown to lower blood glucose in *in vivo* studies [57] and exerts a hepatoprotective effect [58].

For *Allium cepa* L., the ingestion of crude red onion in type 1 and type 2 diabetic patients, caused a considerable reduction in fasting blood glucose levels in relation to insulin in type 1 and type 2 diabetic patients [59]. In our survey, *Allium cepa* L. was mentioned to be used by diabetic patients having both type 1 and type 2 diabetes.

The scientific literature on *Curcuma longa* L. shows that curcumin possesses antidiabetic effects [60] and possibly constitutes an important therapeutic possibility for the treatment of type 2 diabetes [61]. This coincides with the result of our survey where the use of *Curcuma longa* L. was used by diabetic patients with type 2 diabetes only.

Ceratonia siliqua L. inhibits intestinal glucose absorption, improves glucose tolerance and protects against alloxan-induced diabetes in rats. These properties may be useful for diabetes treatment [62]. In our survey, immature carob beans were used in diabetics type 1 only.

This study distinguishes between the plants used by patients with type 1 diabetes, those used by patients with type 2 diabetes and those used for both types of diabetes. This distribution is supported by the mechanisms of action of the medicinal plants in

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some cases. Some plants reported by patients as antidiabetic agents are mentioned in the literature as protectors from diabetes complications. This is the case of *Glycyrrhiza glabra* L. [63]. This comparison to determine the mechanisms of action of these plants would have been very beneficial. Unfortunately, the diabetic patients didn't specify all diabetes-related problems for which the medicinal plants were used. More studies are still needed in this respect.

Seven plants were mentioned for the first time through this survey, to treat diabetes in Morocco. These medicinal plants were already reported to be used for diabetes by other international studies: *Allium ampeloprasum* L. [64]; *Cinnamomum verum* J. Presl. [50]; *Curcuma longa* L. [61]; *Syzygium aromaticum* (L.) Merr. & Perry. [65]; *Glycyrrhiza glabra* L. [63]; *Prunus dulcis* (Miller) D. A. Webb [66]. This finding is an important contribution of this survey to the indigenous knowledge of medicinal plant use in Morocco. On the other hand, *Calamintha alpina* L., was reported for the first time internationally as a plant used for diabetes.

As the pathogenesis of diabetes involves oxidative stress, antioxidant therapies may have potential value in its treatment. Medicinal plants with antioxidant activities have been shown to be protective in diabetic rats [67, 68]. Medicinal plants with high antioxidant content have been recommended [69]. Indeed, it has been shown that under stressful conditions free radicals are over-produced, resulting in oxidative stress. Oxidative stress occurs when there is an inbalance between free radical formation and antioxidant defense capacity [70]. This oxidative stress usually causes or exacerbates chronic hard diseases such as diabetes [71]. Our study has shown that the majority of medicinal plants used by diabetic patients have this antioxidant property. This is true for plants such as *Allium cepa* L., Zingiber offinale, *Olea europaea* L., *Trigonella foenum-graecum* L., *Rosmarinus officinalis* L., *Cinnamomum verum* J. Presl or *Nigella sativa* L.

Minor adverse events, mainly occasional heartburn, have been reported. Only *Glycyrrhiza glabra* L. is known to have side effects such as prolongation of gastrointestinal transit time [72] and that could explain the heartburn adverse reactions. Among the medicinal plants identified in this survey, the main toxic plant is *Citrullus colocynthis* L. [28]. But it seems that diabetic patients are aware of this toxicity as colocynth was not noted in the AEs reported. For diabetic patients, we noted that the plants can be used for several years without showing any toxicity. This is important to exploit in clinical studies in the search for promising new herbal drugs. However, as with all medicines, medicinal plants have been shown to have adverse effects, which are related to a variety of causes, including adulteration, mistaken use of the wrong species or misidentification, incorrect dosing, errors in use and contamination (toxic metal, microbes, microbial toxins, environmental pollutants. Some medicinal plants affect the pharmacokinetic and pharmacodynamic properties of conventional drugs and thus cause herb−drug interactions [73]. But the nature of

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the adverse effects reported in the study, have not allowed to show in a concrete way this type of interaction. These potential interactions remain important to take into account when the patient takes both plants and conventional drugs simultaneously.

5. Conclusions

This survey is one of the few studies to focus on ethnopharmacological knowledge among the users of antidiabetic plants. The patients surveyed in this study provided in detail how the plants were used. The wide variety of medicinal plants that are used to treat diabetes and the frequency of this use among diabetic patients support the important role of plants in the primary healthcare system of Moroccans. This unveiled a significant diversity of medicinal plants with potential anti-diabetic properties and an ethnobotanical knowledge of these plants. This study has also the advantage of specifying for each plant the type of diabetes for which it has been used. In addition, and to our knowledge, one plant was reported for the first time at an international level as being used in the traditional treatment of diabetes and eleven plants were reported by patients as new medicinal plants to treat diabetes in Morocco. Therefore, this documented information on the medicinal plants used in Rabat may be used as baseline data for future pharmacological and phytochemical studies.

Declarations

Author contribution statement

Souad Skalli: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Rachida Hassikou, Moustapha Arahou: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

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