Int. J. Plant Bas. Pharm. (2022) 2(2), 145-154

INTERNATIONAL JOURNAL OF PLANT BASED PHARMACEUTICALS

https://ijpbp.com

RESEARCH ARTICLE

OPEN ACCESS

Traditional medicinal plants used in the treatment of diabetes: Ethnobotanical and ethnopharmacological studies and mechanisms of action

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ARTICLE INFO

Article History:

Received: 06 January 2022
Revised: 13 February 2022
Accepted: 14 February 2022
Available online:15 February 2022

Edited by: B. Tepe

Keywords:
Diabetes
Traditional plant
Ethnopharmacological survey
Ethnobotanical survey
Antidiabetic

ABSTRACT

The use of medicinal plants for the prevention and treatment of several diseases, particularly diabetes, remains the remedy and the sustainable source for many diseases. This survey was conducted out in Bejaia province in the center of Algeria to invent the main plants used in folk medicine to treat diabetes mellitus, their availability in this region, and the mode of their use. This study was carried out in 2019 in several municipalities of the study area. Ethnobotanical information was obtained using a questionnaire through direct interviews with 323 people with diabetes. Among people with diabetes interviewed, 82% present type 2 diabetes, from which more than 60% of them use medicinal plants against 36.84% only in type 1 diabetics. Diabetes affected age groups differently; the age range most affected was 61-80 years (43.96%). A total of 43 plant species belonging to 25 families were identified and listed in this study. The most frequent species used by patients are *Artemisia herba-alba* (34.42%), *Olea europaea* (13.66%), and *Ajuga iva* (11.47%). The part of the plant used depends on the plant; the aerial part was the more used (40.9%), followed by leaves (25%) and fruits (13.63%). The other parts, such as seed, root, flower, bark, bulb, epicarp, and rhizome, were used with low frequencies. It was also interesting to indicate that decoction and infusion were the systematic preparation methods compared to others (maceration, cooking with food, and fresh). The present study clearly showed that phytotherapy is widely adopted by center Algerian society, and there is a huge diversity of medicinal plants used for the complementary treatment of diabetes. Moreover, this investigation provides researchers with important information that can be exploited to develop anti-diabetic remedies.

1. Introduction

Diabetes mellitus (DM) is a severe metabolic disease characterized by chronic hyperglycemia due to defects in insulin secretion, insulin action, or both (Arya et al., 2012). Currently, diabetes mellitus is considered one of the most common chronic diseases in nearly all countries, and its prevalence worldwide, particularly type 2 diabetes, is constantly increasing (IDF, 2013). In 1995, about 135 million people were affected by diabetes, and an increase of 300 million cases is estimated by 2025 (Vlad and Popa, 2012). More recently, some studies have estimated that by 2030, more than 552 million people will have diabetes, which represents about 9.9% of the world's population (Whiting et al., 2011).

The treatment of diabetes is based primarily on diet, physical exercise, and pharmacological agents. Regarding the therapeutic aspect, although several drugs are available for the treatment of diabetes, some antidiabetic drugs cause serious side effects, such as

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e-ISSN: 2791-7509
doi:

Please cite this article as: Belmouhoub, M., Tacherfiout, M., Boukhalfa, F., Khodja, Y.K., Bachir-Bey, M., 2022. Traditional medicinal plants used in the treatment og diabetes: Ethnobotanical and ethnopharmacological studies and mechanisms of action. International Journal of Plant Based Pharmaceuticals, 2(2), 145-154.

digestive, hepatic, and renal problems. Due to the adverse drug effects, patients are increasingly using medicinal plants as an alternative to prevent and treat diabetes. Thus, in recent decades, research has been focused on new antidiabetic molecules of plant origin with fewer toxic effects (Zhang et al., 2016). Many plant species are currently used worldwide to treat diabetes and are considered a major source of new antidiabetic agents. More than 1200 different plants have been described as a traditional diabetes treatment (Eddouks et al., 2007). Of all the plants tested *in vitro*, 80% are potentially antidiabetic, and some of them are at the origin of the development of new drugs, as in the case of metformin, which was developed from *Galega officinalis* L. (Bailey and Day, 2004). However, very little is known about the active compounds of antidiabetic plants, either their structures or actions, thus preventing them from being used in standard diabetes care (Coman et al., 2012).

Drug treatment is the main method followed by people with diabetes to fight against people with diabetes. In addition to pharmacological agents, many plants are used as a complementary treatment by a significant percentage of diabetic patients (Allali et al., 2008). To conserve and enhance the Algerian heritage in medicinal plants, some ethnobotanical studies are conducted in some regions, particularly in the south and west of the country (Allali et al., 2008; Rachid et al., 2012; Telli et al., 2016). The results obtained from these studies confirm that the Algerian population is highly attached to phytotherapy and traditional treatment. Whereas, very few ethnobotanical surveys have been carried out in the center of Algeria (Boudjelal et al., 2013), especially in Bejaia province, while this region has a very diverse vegetation cover with a great large number of plants used as folk remedies. Thus, the purpose of the present investigation was to determine the antidiabetic medicinal plants mostly used by the Bejaia population, the part and mode of use, and their effects.

Table 1. Questionnaire card survey

Information about patients		Information about diabetes		Information about plants used		Plant actions
Age	....	Type of diabetes	....	Name of plants used	....	Good, normal or low therapeutic effect
Sex	....	Duration of diabetes	....			
Place of residence (city or companion)	....	Drug used	....	Used part(s)	....	
		Complications	....	Mode of use	....	

2. Materials and methods

2.1. Geographical location

The study was conducted in Bejaia province (Wilaya), called Vgayet in the local language (Kabyle). This region is situated in the central north of Algeria between latitude 36°45′21″ N and longitude 5°05′03″ E, and between 0 to 1900m of altitude. It is limited by the Mediterranean sea from the North, Jijel province from the East, Setif and Bordj-Bou-Arreridj provinces from the south, and Tizi Ouzou and Bouira provinces from the west. Bejaia covers a total area of 3223 km² (52 municipalities), with an estimated population of about 950 000 inhabitants using Kabyle as the predominant language. The density of population is estimated at 295 inhabitants/km² and the majority of which occupy urban areas (more than 80%) (ASWB, 2015).

2.2. Relief and climate

The study area is located in plain Tellian Atlas; it is marked by the importance of the mountainous land, which occupies about 75% of the total region area, crossed by the valley of Soummam and the plains located near the coast. Mediterranean climate dominates in this region, but it varies from one area to another. The coastal zone and the valley of Soummam enjoy a rainy and mild climate in winter, dry and hot in summer. However, the climate of the mountain areas is characterized by a dry and hot summer and a rainy and cold winter (Skouri, 1994). The average annual temperature is around 18 °C, while the average annual rainfall is about 700 mm (ASWB, 2015).

2.3. Forest ecosystem and vegetation cover

With about 100 km of coast, extending from west to east and about 80 km of large from sea to the continental region (from North to south), the study area is characterized by an important vegetation cover. The forest area covers a total of 122500 ha, which represents 37.57% of the total area region (Bejaia), of which 58700 ha of covered forests (about 47.91% of the total forest area) and 63800 ha (52.08%) of maquis where thousands of plant species are growing. In Gouraya National Park only, with 20.8 km² of area (less than 1/100 of total area), about 526 plant species grow, including 123 medicinal species, rare species such as *Euphorbia dendroides* L., *Bupleurum plantagineum* L., and *Lithospermum rosmarinifolium* L. and other species not mentioned in the flora of Algeria namely *Cheiranthus cheiri* L. and *Cheilanthes acrostica* (Balb.) Tod. In the rest of the region, the plant species are not completely inventoried (ASWB, 2015).

The total agricultural area represents approximately 45% of the total area of the region (129448 ha). The arboriculture is marked by the predominance of the olive tree (52800 ha), followed by fig tree (10303 ha) and citrus tree (2010 ha) (ASWB, 2015).

2.4. Collection of information

An ethnobotanical study was conducted from June to October 2019 in several municipalities of the study area. Ethnobotanical information was obtained using a questionnaire by direct interview with 323 people with diabetes. The diabetic patients were chosen randomly in several municipalities of Bejaia province and interviewed directly face to face or by phone. The information collected from people with diabetes was divided into four parts: information concerning patients, information about diabetes, information related to plants used, and information about plant actions (Table 1).

2.5. Identification of medicinal plants used

Most of the plants used by people with diabetes were obtained from herbalists. Some plants do not grow in this region, so they are imported from other regions of the country or other countries. The growth of each plant in the study area and its common name have been confirmed by former herbalists and ancient inhabitants of this region, and their scientific names have been assigned for each plant based on various bibliographical references.

2.6. Data analysis

Microsoft Excel was used to calculate different statistical parameters and to draw graphics. The importance of each plant in the treatment of diabetes was assessed by the relative frequency of citation (RFC) calculated using the following formula (Tardío and Pardo-de-Santayana, 2008): RFC = FC/N, where "FC" is the number of people with diabetes who mention the use of the species also known as the Frequency Citation, and "N" is the total number of people with diabetes using plants (0 < RFC < 1).

3. Results and discussion

In the present investigation, 323 diabetic patients are chosen randomly, 178 men (55.10%) and 145 women (44.90%); more than 82% of patients present type 2 diabetes, and 29.72% present chronic complications (Table 2). All diabetic patients interviewed were under pharmacological treatment, but only 183 (56.65%) use antidiabetic medicinal plants, either regularly or rarely, and more than a third of them (34.97%) use more than one plant to cure diabetes.

In addition, this study shows that the use of medicinal plants is more apparent in type 2 diabetic population; more than 60% of type 2 diabetic patients use antidiabetic medicinal plants against 36.84% only in the type 1 diabetics (Table 2). It has also been observed that women use sensitively more medicinal plants than men, 59.31% and 54.49%, respectively. Moreover, our results show that the most affected age group is between 61 and 80 years with 43.96%; however, the antidiabetic medicinal plants are more used by the age group between 40 and 60 years with 61.90% (Table 3). This difference in the use of medicinal plants by diabetic groups is probably related to the type of diabetes and the severity of the disease which characterizes each group.

Table 2. Distribution of diabetics by sex, type of diabetes, and plant users

Sex	Number in percentage		Chronic complications	Diabetes type (%)		Diabetics using plants (%)	
	% of all diabetics	Using plants		T1D	T2D	T1D	T2D
Men	55.10	54.49	16.41	18.53	81.46	36.36	58.62
Women	44.90	59.31	13.31	16.55	83.44	37.5	63.63
All diabetics	-	56.65	29.72	17.64	82.35	36.84	60.90

Table 3. Distribution of diabetic plant users by categories

Age groups	20-40 years	41-60 years	61-80 years	> 80 years
% of diabetics	14.24	39	43.96	2.78
% of plant users	47.82	61.90	53.52	44.44

Concerning the use of antidiabetic plants by diabetic patients interviewed, a total of 43 medicinal plants belonging to 25 families were identified with a predominant use of Lamiaceae (18.60%) followed by Rosaceae (9.30%), Apiaceae, and Rutaceae (6.98%). The remaining plant families contribute by one or two species for each (2.33 or 4.65%).

The different plants used as antidiabetics can be divided into three origins, of which more than half (51.16%) grow in the wild, 39.53% are cultivated locally, and the rest (9.30%) are indigenous to other regions of Algeria or imported from other countries. The vernacular and binomial names of plants, used parts, preparation methods, number of citations (FC), and the relative frequency of citation of plant species (RFC) are illustrated in Table 4.

The most frequently used species by patients (used by over 5% of patients) were *Artemisia herba alba* Asso. (34.42%), *Olea europaea* L. (13.66%), *Ajuga iva* (L.) Schreb. (11.47%), *Rosmarinus officinalis* L. (8.19%), *Citrus limon* (L.) Osbeck. (7.10%), *Centaurium erythraea* Rafn. (6.01%), *Teucrium polium* L. (6.01%) and *Thymus serpyllum* L. (5.46%) (Figure 1).

The part of plants most commonly used by diabetic patients interviewed is the aerial part (Figure 2) with 40.9%, then leaf, fruit, and seed with 25%, 13.63%, and 6.81%, respectively; root, flower, bark, bulb, epicarp, and rhizome are also used but with a low percentage (2.27%).

About the preparation methods followed, the most adapted are decoction and infusion, respectively, with 79.06 and 58.13% (Figure 3). Other preparation methods such as maceration in water (11.62%) and cooking with food (4.65%) were also used. Sometimes, when it is necessary, the plant parts are taken fresh (11.62%).

We deduced in this part of the study that the preparation methods followed by diabetics are often in relation with plant part used; for example, the infusion is more used to extract active substances from soft parts such as leaves and flowers, while decoction is more used for hard parts such as roots, rhizome, and epicarp. However, fruits and vegetables are consumed fresh or cooked with other foods.

Although almost all diabetics do not have convincing scientific knowledge of the plant used, most of them are too satisfied by the antidiabetic effect obtained (Figure 4).

Many statistical studies recorded in several regions of the world reported that most diabetic patients are affected by type 2 diabetes with approximately 90% (WHO, 2016), and the most affected age group is situated between 60 and 80 years. In addition, the pharmacological treatment of diabetes is accompanied by traditional treatment in most societies of the world. However, the intensity and the manner of use of medicinal plants differ from one region to another and are always linked to the heritage of medicinal plants in societies and their attachment to traditional medicine (Jamshidi-Kia et al., 2018).

The percentage of people with diabetes using plants registered in this study is different from that reported in other regions of the country. For example, in the west of Algeria, the ethnobotanical study conducted by Allali et al. (2008) on 634 people with diabetes showed that about 62% of patients use medicinal plants. Also, in southern Algeria, the investigation realized by Telli et al. (2016) showed that among 289 diabetic patients interviewed, 60.90% use antidiabetic plants. However, only 28.30% use medicinal plants among 470 people with diabetes interviewed in southwestern and northwestern Algeria (Rachid et al., 2012). This difference may be related to the degree of availability of plants (vegetal cover) and the degree of attachment to traditional medicine by societies.

This result is in accordance with those revealed by other Algerian scientists. The results of Rachid et al. (2012) showed that more than 36% of type 2 diabetic patients used medicinal plants but only 17.16% in type 1 diabetes cases. Similarly, Allali et al. (2008) have noticed during their ethnobotanical study that more than 66% of type 2 diabetic patients used plants against 33.8% only in the type 1 diabetic population.

Table 4. List of medicinal plants used for the treatment of diabetes mellitus in the Bejaia region

Family plant species	Arab name (Local name)	English name	Statue	Used part	Use method	FC	RFC
Asteraceae							
A. herba alba	Chih	White wormwood	Imp.	A. part	Dec.	63	0.34
C. cardunculus	Kharchouf (Thagga)	Cardoon	Cu	A. part	Cooked	2	0.01
Anacardiaceae							
Pistacia lentiscus L.	Edharou (Amadagh)	Lentisk	W	Leaves	Dec.	2	0.01
Apiaceae							
P. crispum	Bakdounes (Mâadnous)	Parsley	Cu	A. part	Dec./Inf.	3	0.02
C. sativum	Kasbara (Lkousvar)	Coriander	Cu	A. part	Dec./Inf.	1	0.005
A. graveolens	Elkarfes (Lekrafez)	Celery	Cu	A. part	Dec./Inf.	2	0.01
Brassicaceae							
Lepidium sativum	Elrechad (Guerninouche)	Garden cress	W	Seeds	Fresh	1	0.005
Cactaceae							
Opuntia ficus-indica	Attine achaouki (Akarmus)	Prickly pear cactus	Cu, W	A. part	Dec.	2	0.01
Convolvulaceae							
Convolvulus arvensis	Leblab (Merraz voukal)	Field bindweed	W	A. part	Dec./Inf.	1	0.005
Cucurbitaceae							
Citrullus colocynthis	Elhandhal (Rammane lkhechkheche)	Bitter apple	Imp.	Fruit	Mac.	1	0.005
C. pepo	Elkoussa (Corgitt)	Zucchini	Cu	Fruit	Fresh	2	0.01
Fabaceae							
Ceratonia siliqua	Elkharoub (Akharrouve)	Carob	W	Leaves	Dec.	1	0.005
P. vulgaris	Elfasoulia (Louvia)	Green beans	Cu	Fruit	Cooked	1	0.005
Gentianaceae							
C. erythraea	Elkantrioun assaghir (Qlilou)	Centaury	W	A. part	Dec./Inf./ Mac.	11	0.06
Lamiaceae							
A. iva	Chendgoura (Chkendoureth)	Bugleweed	W	A. part	Dec./Inf.	21	0.11
Marrubium vulgare	Elfrassioune (Marnuyeth)	White horehound	W	A. part	Dec./Inf.	5	0.027
R. officinalis	Iklil aldjabel (Azir, Amezir)	Rosemary	W	Leaves	Dec.	15	0.08
M. piperita	Naânaâ (Naânaâ)	Peppermint	Cu	A. part	Dec./Inf.	4	0.02
O. basilicum	Errayhane (Lehvaq)	Basil	Cu	A. part	Dec./Inf.	1	0.005
Salvia officinalis	Mrimia (Kheyatta, Swak ennebi)	Sage	W	A. part	Dec./Inf./Mac.	2	0.01
T. polium	Eldjaâda (Jaâtta)	Felty germander	W	A. part	Dec./Inf.	11	0.06
T. serpyllum	Zaâtar (Zaâtar)	Wild thyme	W	A. part	Dec./Inf.	10	0.05
Lauraceae							
C. cassia	El korfa (Elqurfa)	Chinese cassia	Imp.	Bark	Dec./Inf./Mac.	7	0.04
L. nobilis	Elghar (Rand)	Laurel	Imp.	Leaves	Dec./Inf.	3	0.02
Liliaceae							
Allium sativum	Athoum (Thicherth, thiskerth)	Garlic	Cu	Bulb	Dec./Inf./Fresh	2	0.01
Lythraceae							
Punica granatum	Rommane (Rammane)	Pomegranate	Cu	Epicarp, Leaves	Dec.	4	0.02
Moraceae							
Ficus carica	Attine (Thanqultt)	Fig tree	Cu	Leaves	Dec.	3	0.02
Oleacea							
O. europaea	Azzitoune (Azmeour)	Olive	Cu, W	Leaves	Dec./Fresh	25	0.14
Papaveraceae							
Papaver rhoeas	Chaquaeque annouamane (Jihvudh, Wahrir)	Red poppy	W	A. part	Dec./Inf.	1	0.005
Plantaginaceae							
Globularia alypum	Alainoune (Thasselgha)	Alypoglobe daisy	W	Leaves	Dec./Inf./Mac.	7	0.04
Ranunculaceae							
Nigella sativa	Alhaba assaouda (Sinoudj)	Black cumin	W, Imp.	Seeds	Dec.	5	0.03
Rhamnaceae							
Rhamnus alaternus	Annabaq (Amliless)	Privet	W	A. part	Dec./Inf.	3	0.02
Rosaceae							
Prunus dulcis	Ellaouz (Louz)	Almond	Cu, W	Fruit	Fresh	1	0.005
P. persica	Elkhaoukhe (lkhoukhe)	Peachtree	Cu	Leaves	Dec./Inf.	5	0.03
Malus domestica	Attouffah (Teffah)	Apple	Cu	Fruit	Fresh	2	0.01
Rubus fruticosus	Attout alalliq (Inigel)	Wild brambles (Blackberry)	W	Leaves	Dec./Inf.	2	0.01
Rubiaceae							
Coffea canephora	Alboune (Lqahwa)	Coffee	Imp.	Seeds	Inf.	1	0.005
Rutaceae							
C. limon	Allaymoune (Lqares)	Lemon	Cu	Fruit	Dec./Inf./Fresh	13	0.07
Ruta graveolens	Assadhab (Awarmi)	Rue	W	Roots	Dec.	1	0.005
C. sinensis	Albortoqual (Tchina)	Orange	Cu	Flowers	Inf.	1	0.005
Theaceae							
Camellia sinensis	Achay (Tay)	Tea	Imp.	Leaves	Dec./Inf.	3	0.02
Urticaceae							
Urtica dioica	Alquarasse (Azeggduf)	Stinging nettle	W	A. part	Dec./Inf.	1	0.005
Zingiberaceae							
Z. officinale	Zindjabil (Zindjabil)	Ginger	Imp.	Rhizome	Dec./Inf.	4	0.02

A. Part: Aerial part, Dec.: Decoction, Inf.: Infusion, Mac.: Maceration, Cu: Cultivated, Imp.: Imported, W.: Wild, FC: Number of diabetics who mentioned the use of the species, RFC: relative frequency of citation (0 < RFC < 1)

This result may be due to the multifactorial nature of type 2 diabetes, where it is possible to use plant extracts as a complementary remedy to oral antidiabetic drugs. While hyperglycemia in type 1 diabetes is controlled only by taking insulin due to the absolute deficiency of this hormone in this case of diabetes.

The study realized by Allali et al. (2008) in western Algeria also showed that women use more medicinal plants than men but with different frequencies to ours, 70% of women and 30% of men. Also, in southwestern and northwestern Algeria, Rachid et al. (2012) have observed in their study that women used herbal medicine more frequently than men, with a percentage of 37.60 and 18.84, respectively. This could be related to the deep attachment of Algerian women to the traditional use of plants than men not only in the medical field but also in gastronomy and cosmetics.

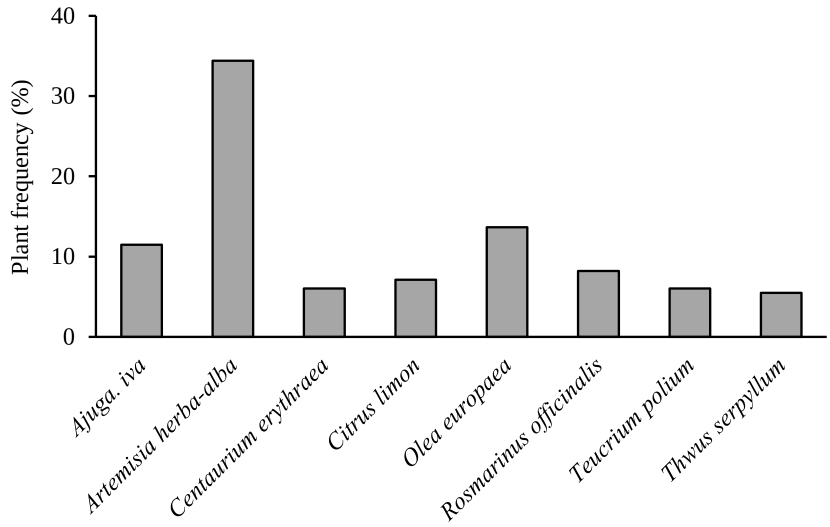

Figure 1. Frequency of more popular plants used by diabetic population

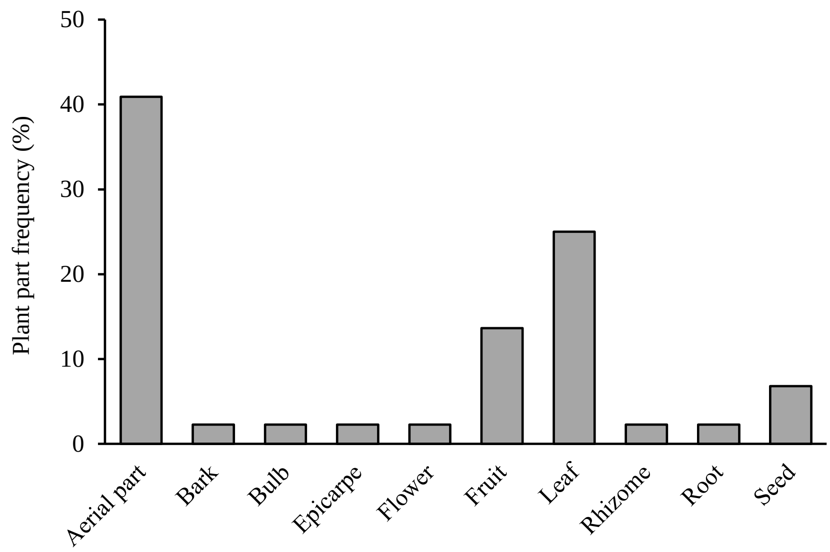

Figure 2. Frequency of plant parts used for the preparation of antidiabetic remedies

The preparation methods and the plant parts used are not based on scientific knowledge but rather on a traditional medicine heritage and social culture of people with diabetes (Rachid et al., 2012; Telli et al., 2016). They can also be recommended by herbalists' knowledge on the one hand and by the plant parts available during the year on the other hand.

The RFC of the plant used varied from 0.005 to 0.34 (Table 4). The highest value of RFC ranked was for *A. herba alba* (0.34), followed by *O. europaea* (0.14) and *A. iva* (0.11). 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 to treat diabetes. Some plants are widely cited in the bibliography as antidiabetic plants, and their antidiabetic effects have been demonstrated by several experimental studies. We have listed below the most cited plants in this survey, accompanied by some scientific studies in which they are cited.

A. herba alba (Asteraceae): It does not grow in the study area, but it is largely widespread in the highlands, the fresh semi-arid regions, and the steppes of Algeria (Jamshidi-Kia et al., 2018). It is the plant most used by diabetic using plants (34.42%). Its active compounds are extracted from the aerial part by decoction in all cases registered. In most cases, people with diabetes using this plant testifies to its satisfactory hypoglycemic action without any undesirable effect.

In fact, several experimental studies carried out in different regions of the world confirm the important antidiabetic effect of aerial part extracts of this plant (Awad et al., 2012; Boudjelal et al., 2015). Some studies demonstrated that extract of aerial part of *A. herba alba* has more anti-diabetic effect than root extract (Al-Khazraji et al., 1993).

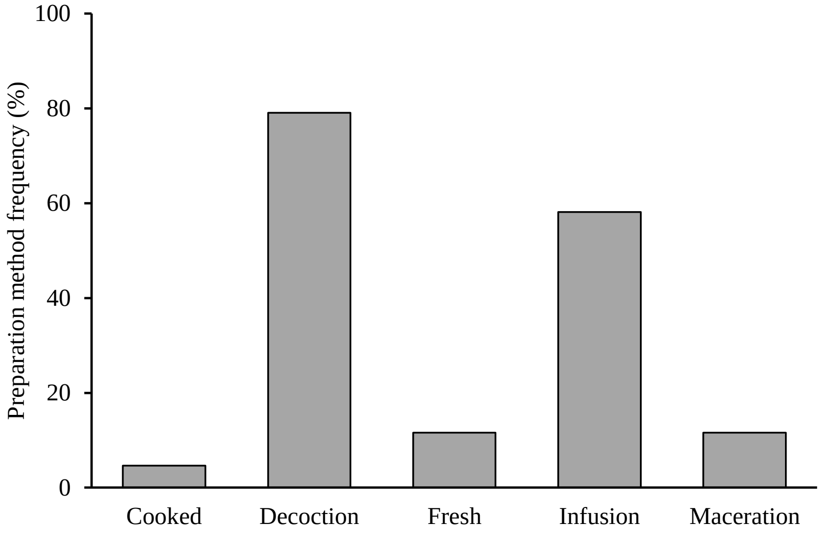

Figure 3. Preparation methods followed by diabetics to extract active substances

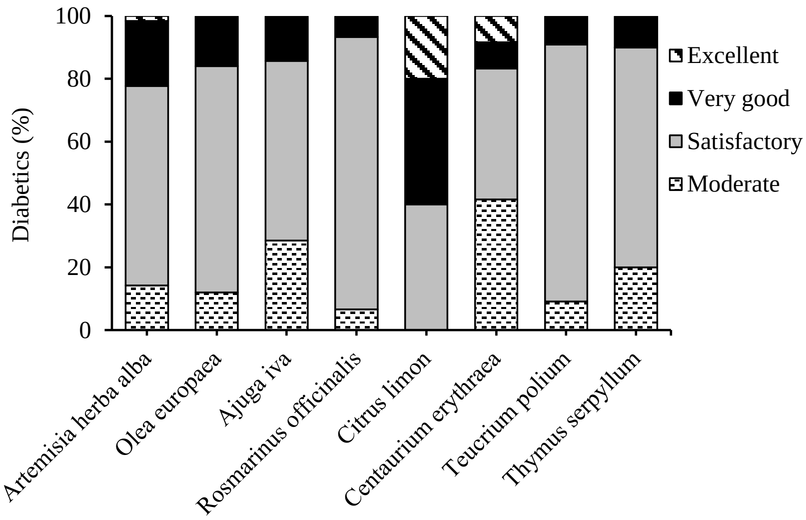

Figure 4. Testimony of diabetics about the anti-diabetic effect of plants used

Furthermore, many mechanisms of action have been suggested, such as the increase of peripheral glucose utilization (Taştekin et al., 2006), increasing insulin secretion (Awad et al., 2012), insulin-like action (Iriadam et al., 2006), and inhibition of the proximal tubular reabsorption for glucose in the kidneys (Mansi et al., 2007). The main components that may be responsible for these actions are flavonoids such as apigenin (flavones) (Awad et al., 2012) and volatile oil (Mahmoud et al., 2015).

O. europaea (Oleaceae): Largely abundant in the study area, about 3 929 418 trees with 63 varieties (ASWB, 2015). It is the second plant most used by people with diabetes (13.66%); the decoction of leaves is the method of use most adopted. However, some patients use fresh leaves by chewing.

Many experimental studies conducted in animals demonstrated that olive leaves extract possesses a potent antidiabetic action (Al-Attar and Alsalmi, 2019) without causing any toxicity (Clewell et al., 2016; Guex et al., 2018). The hypoglycemic effect has been attributed to phenolic compounds, especially: phenolic secoiridoids such as oleuropein (Annunziata et al., 2018), tannins (Wainstein et al., 2012), and flavonoids (Benhabyles et al., 2015).

The study conducted by Sato et al. (2007) showed that oleanolic acid (triterpene) extracted from olive leaves is an agonist for TGR5, a member of G-protein coupled receptor activated by bile acids and which implicated in glucose homeostasis.

Other studies showed that the potent antioxidant effect of oleuropein and other phenolic compounds of *O. europaea* could prevent diabetes and these complications by protecting body cells destruction (Al-Attar and Alsalmi, 2019; Büyükbalci and El, 2008; Guex et al., 2019; Jemai et al., 2009). Other mechanisms of action excreted by bioactive molecules of *O. europaea* leaves have been demonstrated, such as the increasing levels of liver insulin receptor substrate 1 (IRS1) and insulin receptor A (IRA) (Al-Attar and Alsalmi, 2019), the ameliorating effect of insulin secretion (Abdel-Kader et al., 2019), and by inhibition of α-amylase (Komaki et al., 2003).

A. iva (Lamiaceae): Abundant in arid and semi-arid areas of Algeria (Bendif et al., 2017). It also grows in the study region (Béjaia), but not in abundance; it is found especially in dry and stony ground. This plant is used by 11.47% of diabetic using plants, either by decoction or infusion of aerial part in most cases.

The antidiabetic effect of *A. iva* has been demonstrated by many experimental studies (Boudjelal et al., 2015; Wang et al., 2017) without any observable signs of toxicity (El Hilaly et al., 2004; Fettach et al., 2019; Tafesse et al., 2017). The main compounds of this plant responsible for the reduction of blood glucose are flavonoids, in particular, apigenin and naringenin (Boudjelal et al., 2015), triterpenoids, especially phytoecdysteroids (Wang et al., 2017), and phenolic acids (Khatteli et al., 2020). The *in vivo* study conducted by Wang et al. (2017) showed that phytoecdysteroids extracted from *A. iva* reduce blood glucose by regenerating pancreatic islets and upregulating hexokinase-I mRNA expression. Other studies showed that phenolic compounds of *A. iva* are potent inhibitors of α-glucosidase and α-amylase *in vivo* and *in vitro* (Fettach et al., 2019; Hsieh et al., 2014); therefore, they can significantly reduce postprandial blood sugar in diabetic patients.

R. officinalis (Lamiaceae): Very widespread in the study area, especially between 0 to 600 m of altitude. It grows wild in arid and dry regions of hills and low mountains (Fadili et al., 2015). Rosemary is used in Algerian folk medicine to treat hepatic diseases, eczema, hypertension (Boudjelal et al., 2013), colon ailments, stomachache, and hair loss (Senouci et al., 2019). In the present investigation, *R. officinalis* is used by 8.19% of people with diabetes using plants, and the decoction of leaves is the most method adopted. Several studies realized *in vivo* and *in vitro* showed the heightened hypoglycemic effect of *R. officinalis* extracts (Belmouhoub et al., 2018; Khalil et al., 2012; Labban et al., 2014). The bioactive molecules of *R. officinalis,* especially phenolic compounds such flavonoids and phenolic acids (Bakırel et al., 2008; Ibarra et al., 2011), can reduce hyperglycemia by various mechanisms, they can inhibit the α-glucosidase and α-amylase *in vivo* and *in vitro* (Belmouhoub et al., 2017; Koga et al., 2006), increase secretion of insulin by pancreatic cells (Ayaz, 2012; Bakırel et al., 2008) and regulate glucose metabolism in the liver (Tu et al., 2013).

C. limon (Rutaceae): This plant is cultivated in the study area, but the production of fruit is relatively low, about 6 730 tonnes for the 2014/2015 season (ASWB, 2015). In the present investigation, the fruit of *C. limon* is used by 7.10% of diabetic using plants. Most patients consume fresh fruit as a juice, while others use it in infusion or decoction. Patients using this fruit have testified that it has an excellent anti-diabetic effect; some among them have testified that they were completely cured of diabetes (Type 2 diabetes).

Recent publications have reported that *C. limon* flavonoids, particularly hesperidin, hesperetin, naringin, and naringenin, significantly decrease hyperglycemia by several action mechanisms (Alam et al., 2014; Lv et al., 2018). Akiyama et al. (2009) conducted an experimental study that showed that hesperidin significantly reduces blood glucose in diabetic rats by stimulating insulin secretion and regulating glucose metabolism in the liver. Naringin, another flavonoid of *C. limon,* can decrease blood glucose level in experimental animal models by decreasing glucose-6-phosphatase activity in the liver and by increasing hepatic glucokinase activity responsible for glycogen synthesis (Punithavathi et al., 2008), while naringenin reduces hyperglycemia by increasing muscle cell glucose uptake via adenosine monophosphate-activated protein kinase (AMPK) (Zygmunt et al., 2010).

C. erythraea (Gentianaceae): This plant grows wild in the study area, especially in the hills and in the wet and sunny pasture. In the present investigation, people with diabetes adopting this plant (6.01%) use its aerial part, either by decoction, infusion, or maceration, and they have testified that it has an excellent anti-diabetic effect; some among them have testified that they were completely cured of diabetes (Type 2 diabetes).

It has been demonstrated that aerial part extract of *C. erythraea* decreases hyperglycemia significantly in experimental animals; the hypoglycemic effect of the extract is attributed to flavonoids, mainly to flavonoid glycosides (Stefkov et al., 2011). The studies realized on diabetic rats showed that phenolic compounds of *C. erythraea* improve the structural and functional properties of pancreatic beta-cells by antioxidant regulatory mechanisms (Đorđević et al., 2019; Stefkov et al., 2014). On the other hand, the *in vitro* study carried out by Bouyahya et al. (2019) showed that essential oils of *C. erythraea* exhibit an important inhibition against α-amylase and α-glycosidase activity.

T. polium (Lamiaceae): It grows wild in the study area, especially in semi-arid soil, but not truly widespread; it predominates in the Tell region of the country, the highlands, and the Saharan Atlas (Quezel et al., 1962). Patients using this plant (6.01%) use its aerial part extracts obtained by infusion or decoction. The hypoglycemic effect of *T. polium* aerial part is attributed to several compounds, among them flavonoids, such as aglycon luteolin (Stefkov et al., 2014).

The antidiabetic properties of *T. polium* have been shown by various *in vitro* and *in vivo* studies (Ardestani et al., 2008; Dastjerdi et al., 2015; Esmaeili and Yazdanparast, 2004). Some compounds of *T. polium,* such as apigenin, can reduce hyperglycemia by stimulating pancreatic insulin secretion (Mirghazanfari et al., 2010). Other compounds, such as aromatic saturated and unsaturated fatty acids, and phenolic compounds, increase GLUT4 (glucose transporter 4) translocation to the cell membrane and enhance glucose uptake by cells skeletal muscle (Kadan et al., 2018). Furthermore, rutin and apigenin, two flavonoids isolated from *T. polium* protect pancreatic beta-cell against destruction and damage caused by oxidative stress (Esmaeili et al., 2009). However, many toxicological studies carried out on animal models have shown the toxic effect of *T. polium* extracts on the liver and kidneys (Abu Sitta et al., 2009; Al-Ashban et al., 2006; Ghasemi et al., 2019; Krache et al., 2017).

T. serpyllum (Lamiaceae): It grows wild in the study area, especially in mountains and high pastures. It is used by 5.46% of people with diabetes using plants. In all recorded cases, people with diabetes use only the aerial part either by decoction or infusion. The antidiabetic effect of this plant is attributed to several compounds such as flavonoids, alkaloids, tannins, and terpenoids (Mushtaq et al., 2016). The *in vivo* study carried out by Alamgeer et al. (2014) showed that the aqueous extract of *T. serpyllum* significantly reduces hypoglycemia in glucose-fed mice. The mechanism of action and the toxic effect of *T. serpyllum* compounds are not truly elucidated, and there are very few studies in this way.

Although some plants constitute a part of the daily diet in Algeria, their relative frequency of citation in this investigation is very low (RFC < 0.05). These plants may be added daily to foods as condiments such as *Apium graveolens*, *Coriandrum sativum*, *Laurus nobilis*, *Ocimum basilicum*, *Petroselinum crispum*, and *Zingiber officinale* or consumed cooked as vegetables such as *Alium sativum*, *Cucurbita pepo*, *Cynara cardunculus*, *Phaseolus vulgaris* or consumed in herbal teas such as *Cinnamomum cassia* and *Mentha piperita*.

4. Conclusions

The present study clearly shows that phytotherapy is widely adopted by center Algerian society, and there is a huge diversity of medicinal plants used for the complementary treatment of diabetes. In addition, the majority of antidiabetic plants used are recognized by several scientific studies as antidiabetic and non-toxic plants. This confirms that the knowledge of societies about medicinal plants is a precious heritage, which must be preserved and transmitted to future generations.
Currently, it is accepted that the chronic complications of diabetes are caused mainly by oxidative stress generated by chronic hyperglycemia. In this context, certain hypoglycemic plants used by people with diabetes have a powerful antioxidant effect, which could considerably delay the onset of chronic complications when they are used as a complementary treatment.

During this study, some patients testified that they were completely cured of type 2 diabetes, and this is thanks to their daily use of medicinal plants, particularly patients using *C. limon* and *C. erythraea*.

Finally, this work constitutes a simple contribution of the Algerian heritage of medicinal plants in the treatment of diabetes; thorough pharmacological and phytochemical investigations are needed to reveal the real effect of these plants as well as their active components involved.

Acknowledgments

The authors thank Mr. Brahim Oukaour for his help in preparing the manuscript.

Conflict of interest

The authors confirm that there are no known conflicts of interest.

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Supplementary File

None.

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