An overview of documented medicinal plants used for the treatment of diabetes in Iran with ethnobotanical and evolutionary perspective (2002-2022)

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Research

Abstract

Background: Iran country with high plant species richness along with ethnic group diversity is significant for the application of medicinal plants in various types of disease treatments such as diabetes. Based on the WHO organization, the total prevalence of diabetes in Iran is 10.3%. In this review, we aimed to offer a comprehensive documentation of plants used for anti-diabetic purposes in Iran, incorporating phylogenetic aspects. Furthermore, we aim to spotlight the plants most commonly employed by local communities to introduce them as potential candidates for further pharmacological research.

Methods: In this study, ethnobotanical information from documents spanning the past twenty years, available on the "Ethnobotanical Database of Iran," has been collected, compiled, and analyzed. Phylogenetic analysis was carried out to identify lineages with the presentation of plant families used in the treatment of diabetes.

Results: There were 282 species of plants from 63 families reported for treating diabetes in Iran. Urtica dioica followed by *Citrullus colocynthis*, *Teucrium polium*, *Juglans regia*, and *Trigonella foenum-graecum* represent the most utilized species for diabetes treatments. Phylogenetic relationships between families and plant organs used in diabetes treatments was significantly correlated through plants evolutionary patterns.

Conclusions: This is the first comprehensive review studying medicinal plants used in the treatment of diabetes from ethnobotanical and phylogenetic perspectives in Iran. The findings of this research underscore the significance of further exploration into utilizing indigenous knowledge to address emerging advanced diseases.

Keywords: Blood sugar; Endemic species; Hyperglycemia; Medicinal plants; Traditional knowledge

Background

Diabetes has become an increasing pandemic disease, representing a serious threat to global health. The IDF predicts that there will be 739 million people with diabetes by 2045, which is a significant rise in prevalence of 46%. Diabetes related to

many complications including heart diseases, kidney problems, nerve damage, increased risk of amputations and blindness – affects significantly their quality of life and causes rising health care costs. Taking insulin, metformin, acarbose, pioglitazone and other medicines are often considered as part of treating diabetes in modern medicine (Obrosova 2009; Thomas *et al*. 2015; Strain & Paldánius 2018; Kropp *et al*. 2023). Consequently, the exploration of cost-effective and minimally invasive treatment options assumes paramount importance, particularly in underserved regions (Cousins 2017). The increasing popularity of natural and less invasive products for prevention and therapy is evident, driven by their relatively low cost and minimal side effects (Tabatabaei-Malazy *et al*. 2016; Lim *et al*. 2005).

Historically, medicinal plants as a less invasive product have played a crucial role in addressing diabetes. Various cultures, such as Traditional Persian Medicine (TPM), have played a significant role in the development of treatment approaches during the medieval era, and have recognized the therapeutic potential of numerous medicinal plants in controlling blood sugar levels (Marles & Farnsworth 1995). Most drugs derived from plants have been obtained through the study of traditional treatments and indigenous knowledge of ancient peoples. Local healers often die due to old age and their traditional knowledge is lost before being documented, and ethnobotany is a tool to preserve this knowledge (Ghannadi *et al*. 2011; Schmidt & Cheng 2017; Pandey & Tripathi 2017). It is interesting to know that linking ethnobotanical convergence, phytochemistry, and molecular phylogenies could be used to identify potential new applications of plants (Garnataje *et al*. 2017). Phylogenetic frameworks can provide key information about both morphological and chemical characters in plant families. (Soltis & Soltis 2003). Studying medicinal plants in the context of phylogeny can give insight into the prediction of plant species with the same chemical activities. Species with the same common ancestor share similar features, genes, and relevant chemical properties, therefore phylogenetic reconstruction of medicinal plants is so helpful in showing hot node clustering potentially useful in the future medicinal and ethnobotanical studies (Garnataje *et al*. 2017). Recently, many studies have been done with evolutionary aspects in different fields of plant science, and studying the evolutionary pattern in ethnobotanical investigation was highly overlooked (Gras *et al*. 2021; Zaman *et al*. 2021; Youssef *et al*. 2023).

There are limited ethnobotanical and ethnopharmacological studies on diabetes and its management in various parts of Iran (Bahmani *et al*. 2014; Salehi Nowbandegni *et al*. 2015; Baharvand-Ahmadi *et al*. 2015). There is still a gap for a comprehensive study summarizing a collection of anti-diabetic plants. This survey represents the comprehensive exploration of the plant species introduced in ethnobotanical and ethnopharmacological studies employed in the treatment of diabetes in different parts of Iran, with an evolutionary perspective. In this study, molecular data and a phylogenetic tree were used to evaluate whether certain plant families in different regions of Iran are more focused on specific plant parts (rhizome, root, aerial parts, etc.). The main purposes of the present study were as follows: (1) to collect, analyze, and evaluate the ethnomedicinal information on plant species used for diabetes; (2) to identify commonly used plants among indigenous peoples; (3) to highlight the plant species with anti-diabetic potential for further phytochemical and pharmacological exploration; (4) to elucidate the phylogenetic relationship between Iranian plant families used for diabetes, which will help us identify those lineages with more application in diabetic treatment.

Materials and Methods

Study area

Iran also known as Persia is a country in West Asia. Iran is a vast country with latitudes and longitudes extending from 44° to 64° east and from 34° to 64° north. This country with more than 8000 plant species, is known as one of the centers of floral diversity in the southwestern of Asia in which 2300 species of them are medicinal plants (Ghahremaninejad 2016). Many of these plants have been utilized by various ethnic communities as traditional treatments (Sheibani *et al*. 2018; Noroozi *et al*. 2019). The prevalence of diabetes in Iran has increased from 8.3 percent in 2005 to 10.3 percent in 2015; thus, controlling diabetes is very essential in the country (Saeedi *et al*. 2019).

Data collection

This study employed a retrospective analysis of data obtained from the Ethnobotanical database of Iran sourced from a comprehensive online plant database of Iran "https://netplant.ir/ebotany". These data have been collected from published papers (2002-2022). All documents are related to ethnobotanical studies which have been conducted in various parts of Iran. Currently, more than 200 documents, 9100 records, and 2300 plant species are reported in this database for anti-diabetic treatments. Among these 60.6% of them are research articles, 23.2% and 16.3% respectively belong to review articles. The documents assessed different online and offline resources, including almost all published articles and theses in English and Persian related to the plants reported in the ethnobotanical studies of Iran that have been considered for the treatment of diabetes from 2002 to 2022 in Iran. Many ethnobotanical studies in Iran have been conducted as master's and Ph. D's theses, which were written in Persian and have not yet been published as articles. We also collected such information in this study. The ethnobotanical database was searched using keywords related to the study objectives including "blood glucose", "blood sugar", "cardiovascular disorders", "diabetes", and "glycemia". A comprehensive ethnobotanical table was created, featuring: the scientific name of the species, their corresponding families, the plant part(s) used, mode(s) of preparation, localities where the study, relative frequency of species, and references was conducted (Table 3). The accuracy of the scientific names of the species was checked through POWO (https://powo.science.kew.org/).

Data analysis

The accumulated data was compiled, and the simple quantitative analyses of descriptive statistics for categories (species, families, and medicinal uses) were done using the features in Microsoft Excel 2016.

For phylogenetic analyses, a total of 186 nuclear data (ITS) belonging to 192 species were obtained from GenBank (https://www.ncbi.nlm.nih.gov/genbank/). Alignments were performed with the MAFFT plugin in Geneious (Biomatters, Auckland, New Zealand) with manual adjustment. Maximum likelihood analysis was performed using the CIPRES Science Gateway with RAxML HPC v.8 on XSEDE using the GTRGAMMA model with -Fa (rapid bootstrapping analysis/search for the best ML tree) with 1000 iterations for bootstrapping. Default settings were used for other options. The results were summarized using the heatmap in phytools s v 0.7.78 R-package (Revell, 2012) to find the correlation of each plant used through phylogeny. The family level of phylogeny was recognized based on APGIV (2016).

The phylogenetic signal is known as closely related species sharing the same trait values due to their phylogenetic relationship (Keck *et al*. 2016). We used the phylosig function in phytools R-package (Revell, 2012) to realize whether the part of the plants used for each part is correlated with phylogenetic relationships. The phylogenetic signal is tested by the null hypothesis that trait value is independent of phylogeny. The null hypothesis is rejected when the p-value is lower than 0.05. We used Blomberg's K index (Blomberg *et al*. 2003) to evaluate the correlation of phylogeny and trait (each part of the plant used). Blomberg's K assumes a BM (Brownian motion) Model of trait evolution through phylogeny. K values significantly higher or lower than 1 suggest a stronger or weaker phylogenetic signal.

Results and Discussion

Regions of the study area

The study area, Iran, is located in the Southwest of Asia, covering 1.7 million km^2. After Turkey, Iran is recognized as one of the primary centers of plant diversity in southwestern Asia, boasting around 8000 species, with approximately 30% of them being endemic (Memariani *et al*. 2019). The two main mountain ranges in Iran are the Alborz and Zagros. The Alborz Mountain stretches along the northern border of Iran, south of the Caspian Sea, while the Zagros Mountain extends from the northwest to the southwestern part of the country. The central part of Iran, known as the Kavir Desert, is distinguished by its salt crust, leading to low vegetation in this area (Figure 1). The geographical distribution of medicinal plants for diabetes treatment in Iran reveals regional variations in their utilization. The size of the circles on the distribution map corresponds to the frequency of plant species used in each area, reflecting local availability and regional ethnomedicinal practices. These divergences underscore the intricate interplay between ecological factors, cultural diversity, and the utilization of medicinal plants.

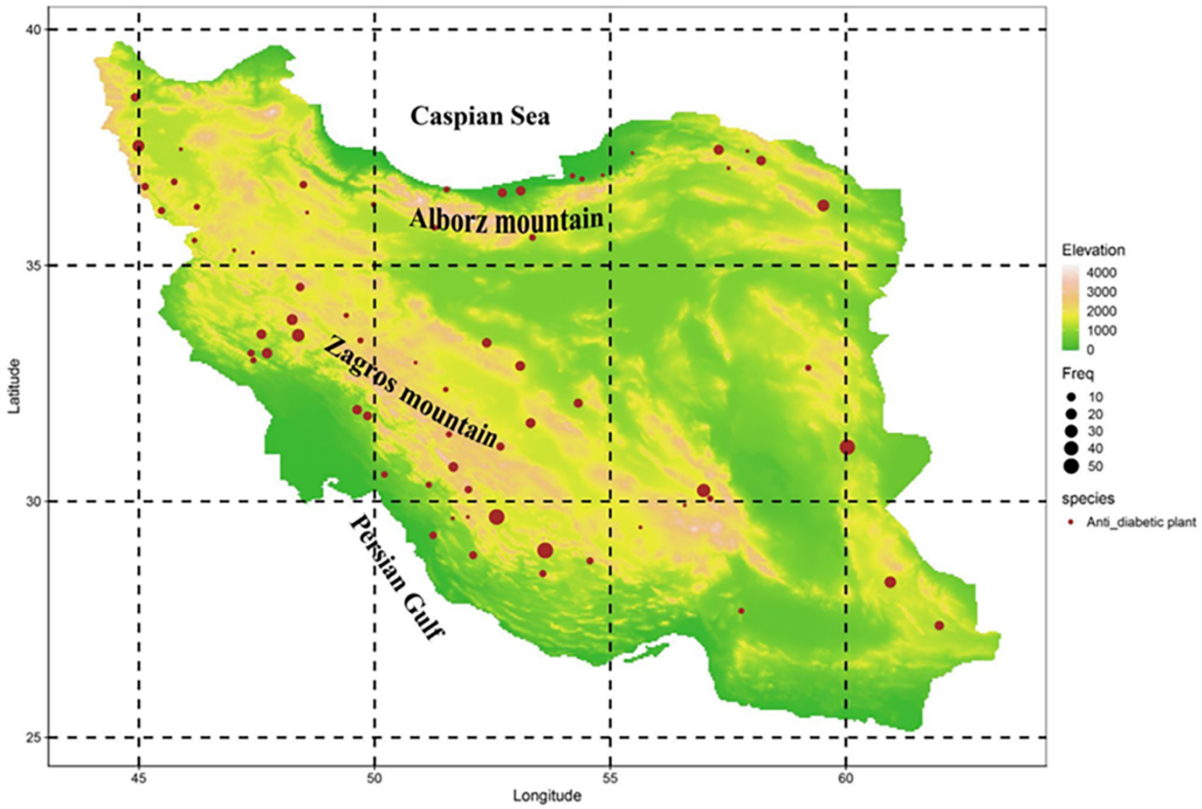

Figure 1. The distribution map of plants used for Diabetes treatment in Iran region (The size of the circle shows the relevant frequency of species.

Diversity of medicinal plants

In the survey, 282 medicinal plants belonging to 63 plant families and 182 genera for the treatment of diabetes were documented (Table 1). They have been utilized as blood sugar reducers, blood sugar regulators, and anti-diabetic agents for the treatment of diabetes mellitus, gestational diabetes, and diabetic foot ulcers among indigenous people. Asteraceae, with 45 species, was the predominant family in the treatment of diabetes, followed by Lamiaceae (32 species), Fabaceae (23 species), Rosaceae (23 species), and Apiaceae (21 species). This study aligns with previous ethnobotanical research, consistently highlighting the prevalence of these families, especially Asteraceae (Karou *et al*. 2011; Tetik *et al*. 2013; Kaval *et al*. 2014; Barkaoui *et al*. 2017; Mrabti *et al*. 2021). Asteraceae and Lamiaceae are rich in essential oils and phenolic compound properties. (Bakar *et al*. 2015; Sonmezdag *et al*. 2017). Previous studies noted the prominence of these families in diabetes treatment, emphasizing their potential for further investigation (Adinortey *et al*. 2016). However, the availability and species richness of these families in the study areas may be linked to their use by local people and in traditional medicine as Kunwar *et al*. (2020) showed, the availability of plant species could be associated with the use of plants *Urtica dioica* L. (3.84%), *Citrullus colocynthis* (L.) Schrad. (3.70%), *Teucrium polium* L. (3.29%), *Juglans regia* L. (2.61%), *Trigonella foenum-graecum* L. (2.19%), *Cichorium intybus* L. (1.92%), *Achillea wilhelmsii* K.Koch (1.92%), *Peganum harmala* L. (1.65%), and *Berberis integerrima* Bunge (1.51%), *Arctium lappa* L. (1.37%), *Capparis spinosa* L. (1.23%), were the most widely used species for diabetes in Iran (Table 2). The photos of some of them are indicated in Figure 2

Of course, Plants that have less relative frequency may not be set aside, as they could be used by local people in other parts of the world. Such ethnobotanical and phylogenetic studies provide nice information on the traditional use and phylogenetic relationships of medicinal plants for treating diabetes in Iran but should be complemented by clinical studies and reviews to check their scientific validity. In vitro and in vivo studies, as well as clinical investigations and reviews, have contributed to our current knowledge regarding the efficacy and safety of these medicinal plants. They furnished useful evidence for support of the traditional use of certain plants in the treatment of diabetes. For example, in the ethnobotanical studies conducted in Algeria (Boudjelal *et al*. 2013) and Turkey (Dalar, 2018), *Urtica dioica* was predominantly consumed by local communities for diabetes treatment. Clinical trials have investigated the hypoglycemic effects of *U. dioica* in diabetic patients, with results indicating its potential to lower blood sugar levels (Kianbakht *et al*. 2013). The fruit of *Citrullus colocynthis* and leaves of *Juglans regia* have been used traditionally in the treatment of diabetes in Mediterranean countries. (Al-Aboudi & Afifi 2011). *J. regia* exhibited antidiabetic activity due to its high polyphenol content, supporting its traditional use in diabetes treatment (Janda *et al*. 2021). Clinical studies have suggested that *Teucrium polium* may contribute to glycemic control and c. (Albadr *et al*. 2022) *Cichorium intybus* by having caffeic and chlorogenic acid is known as one of the major herbal remedies in treating diabetes, comprising. These compounds increase glucose tolerance and lower glucose concentrations (Dalar & Konczak 2014; Janda *et al*. 2021). These examples prove that clinical research plays a very vital role in validating the traditional use of plants for the treatment of diabetes.

Parts of the medicinal plants used

To provide better and clearer results in calculating the frequencies, we merged plant parts with lower frequencies into similar categories with higher frequencies. We placed the petal, inflorescence, flowering branches, and bud in the flower category, the fruit skin and endocarp in the fruit category, the rhizome in the stem category, and plant parts with an abundance of less than 1% were all placed in a new category named "Other," which includes bark, pollen, and tuber. Leaves were the most commonly utilized plant part in curing diabetes (24.7%), followed by fruits (16.98%), aerial parts (12.46%), flowers (12.15%), seed (10.3%), root (8.3%), stem (5.45%), whole plant (4.5%), bulb (1.65%), gum (1%), and latex (1%) (Figure 3). It should be noted that over-harvesting of fruits, flowers, and seeds of plant species in the long term may lead to a decrease in the plant population or its extinction, while it is safer and more sustainable to use leaves and aerial parts (Mahmood *et al*. 2012). Leaves are usually applied in herbal recipes due to their richness in bioactive secondary metabolites. Most of the photosynthesis process occurs in the leaves, and they are also the storage place for exudates or photosynthates (Ullah *et al*. 2013; Ahmad *et al*. 2014; Yemele *et al*. 2015; Umair *et al*. 2019). In previous studies, leaves were reported as the most abundantly utilized plant organ (Ghorbani 2005; Maleki & Akhani 2018; Hosseini *et al*. 2021; Mrabti *et al*. 2021).

Table 1. Plants species used for diabetic treatments based on Iranian ethnobotany information.

No.	Taxon	Plant part(s) used	Preparation	City/ region	Relative frequency (%)	References
Amaranthaceae						
1	*Agriophyllum lateriflorum* (Lam.) Moq.	Seed	Cooked	Nain	0.14	Tabatabaei *et al*. 2019
2	*Bassia eriophora* (Schrad.) Asch.	Aerial parts	Decoction, Infusion	Jahrom	0.14	Khajoei Nasab & Esmailpour 2019
3	*Dysphania botrys* (L.) Mosyakin & Clemants	Aerial parts	-	Mashhad	0.14	Amiri & Joharchi 2013
4	*Noaea mucronata* (Forssk.) Asch. & Schweinf.	Flower	Decoction	Ardestan	0.14	Haerinasab & Abbasi 2018
5	*Seidlitzia rosmarinus* Bunge ex Boiss.	Flower, Leaf	Soaking	Nain	0.14	Tabatabaei *et al*. 2019
6	*Spinacia oleracea* L.	Leaf, Whole plant	-	Faruj, Khoy	0.27	Eslami Farouji & Khodayari 2016; Younessi-Hamzekhanlu *et al*. 2020
7	*Suaeda altissima* (L.) Pall.	Aerial parts	Cooked, Raw	Nain	0.14	Tabatabaei *et al*. 2019
Amaryllidaceae						
8	*Allium atroviolaceum* Boiss.	Bulb	Raw (as fresh)	Kerman	0.27	Sharififar *et al*. 2013; Hosseini *et al*. 2021
9	*Allium cepa* L.	Bulb	-	Aleshtar, Dashtestan, Faruj	0.41	Dolatkhahi & Ghorbani Nohooji 2013; Eslami Farouji and Khodayari 2016; Mehrnia and Hosseini 2020

10	*Allium koelzii* (Wendelbo) Perss. & Wendelbo	Twig	Infusion, Raw	Lorestan	0.14	Delfan *et al*. 2014
11	*Allium minutiflorum* Regel	Leaf, Stem	-	Biranshahr, Zaqeh	0.14	Delfan 2016
12	*Allium oreophilum* C.A.Mey.	Aerial parts, Bulb	Raw	Taftan mountain	0.41	Maleki 2015; Maleki & Akhani 2018
13	*Allium paradoxum* (M.Bieb.) G.Don	Bulb, Leaf	-	Sari, Susan (Khuzestan)	0.27	Karimi 2017; Baroonian 2018
14	*Allium sativum* L.	Bulb, Leaf	Powder (mixed with food)	Aleshtar, Darkhatun (Lorestan), Khoy, Shiraz	0.69	Afkari 2017; Shekari 2017; Mehrnia & Hosseini 2020; Younessi-Hamzekhanlu *et al*.2020
15	*Allium schoenoprasum* L.	Leaf, Root	Raw	Tabas (South Khorasan)	0.14	Fathi 2014
16	*Allium stipitatum* Regel	Bulb, Leaf, Root	Powder	Ardestan, Biranshahr, Darkhatun (Lorestan), Zaqeh	0.14	Delfan 2016; Shekari 2017; Haerinasab & Abbasi 2018
17	*Allium tripedale* Trautv.	Twig	Infusion, Raw	Lorestan	0.14	Delfan *et al*. 2014
Anacardiaceae						
18	*Pistacia atlantica* Desf.	Juice	-	Lorestan	0.14	Delfan *et al*. 2014
19	*Pistacia atlantica* subsp. *mutica* (Fisch. & C.A.Mey.) Rech.fil.	Fruit, Latex, Leaf, Root	Decoction	Taftan mountain	0.41	Maleki 2015; Maleki & Akhani 2018
20	*Pistacia vera* L.	Fruit	-	Sari	0.14	Karimi 2017
21	*Rhus coriaria* L.	Fruit, Seed	Compound in food, Cooked,	Darab, Hamedan, Khoy, Mashhad, Tuyserkan	0.69	Amiri & Joharchi, 2013; Amiri *et al*. 2014; Moein *et al*. 2015; Mosaddegh *et al*. 2016; Younessi-Hamzekhanlu *et al*.2020

			Infusion, Raw, Soaking			
Apiaceae						
22	*Anethum graveolens* L.	Fruit, Latex, Leaf, Seed, Stem	Decoction, Infusion, Powder, Raw	Fasa, Jiroft, Kerman, Sardasht, Shiraz, Tabas (South Khorasan)	0.96	Fathi 2014; Azizi & Keshavarzi 2015; Salehi Nowbandegni *et al*. 2015; Bibak & Moghbeli 2017; Hosseini *et al*. 2021
23	*Anthriscus sylvestris* (L.) Hoffm.	Leaf, Root	-	Susan (Khuzestan)	0.14	Baroonian 2018
24	*Apium graveolens* L.	Leaf, Stem	-	Khoy	0.14	Younessi-Hamzekhanlu *et al*. 2020
25	*Bunium persicum* (Boiss.) B.Fedtsch.	Seed	Powder	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
26	*Coriandrum sativum* L.	Aerial parts, Fruit, Leaf, Seed, Stem	Decoction, Distillation, Powder, Raw (as dried vegetable),	Fasa, Hamedan, Kerman, Kermanshah, Khoy, Kouhdasht, Mobarakeh, Shiraz, Tuyserkan	1.37	Mardani-Nejad & Vazirpour, 2012; Tahvilian *et al*. 2014; Salehi Nowbandegni *et al*. 2015; Mosaddegh *et al*. 2016; Azar 2017; Sadat-Hosseinia *et al*. 2017; Younessi-Hamzekhanlu *et al*.2020; Hosseini *et al*. 2021
27	*Cuminum cyminum* L.	Fruit, Seed	Decoction, Powder	Fasa, Shiraz	0.27	Salehi Nowbandegni *et al*. 2015
28	*Daucus carota* L.	Root	-	Pol-e Dokhtar	0.14	Falahat-pour 2018
29	*Dorema aucheri* Boiss.	Not Determined	-	All of Iran	0.14	Mostafavi *et al* 2013
30	*Ducrosia anethifolia* (DC.) Boiss.	Aerial parts, Flower, Leaf, Seed	Decoction, Infusion, Powder	Taftan mountain	0.41	Maleki 2015; Maleki & Akhani 2018
31	*Eryngium bungei* Boiss.	Root	-	Sari	0.14	Karimi 2017

32	*Eryngium* L.	Leaf		Ziarat region (Golestan)	0.14	Abbasi 2018
33	*Eryngium amethystinum* L.	Aerial parts	Distillation	Khoy	0.14	Younessi-Hamzekhanlu *et al*. 2020
34	*Eryngium billardierei* F.Delaroche	Roots, Whole plant	-	Chaharmahal and Bakhtiari	0.14	Qahfarokhi *et al*. 2021
35	*Gongylosciadium falcarioides* (Bornm. & H.Wolff) H.Wolff	Aerial parts	-	Aleshtar	0.14	Mehrnia & Hosseini 2020
36	*Ferula assa-foetida* L.	Latex, Leaf	Raw and Cooked (Leaves)	Nain	0.14	Tabatabaei *et al*. 2019
37	*Haussknechtia elymaitica* Boiss.	Aerial parts	-	Kohgiluyeh and Boyer-Ahmad	0.27	Mosaddegh *et al*. 2012
38	*Kelussia odoratissima* Mozaff.	Whole plant	-	Andika, Baghmalek, Izeh, Kouhdasht, Lali, Masjedsoleyman, Susan (Khuzestan)	0.41	Khodayari *et al*. 2014; Azar 2017; Baroonian 2018
39	*Levisticum officinale* W.D.J.Koch	Fruit, Leaf, Root, Seed	Infusion, Raw (as fresh and dried vegetable with yogurt)	Hezar Mountain (Kerman)	0.14	Rajaei & Mohamadi 2012
40	*Petroselinum crispum* (Mill.) Fuss	Fruit	Infusion	Mobarakeh	0.14	Mardani-Nejad & Vazirpour 2012
41	*Pimpinella eriocarpa* Banks & Sol.	Leaf, Root	-	Pol-e Dokhtar	0.14	Falahat-pour 2018
42	*Smyrnium cordifolium* Boiss.	Inflorescence, Leaf	Cooked (in food and yogurt), Raw (as fresh vegetable)	Abadeh	0.27	Kiasi & Forouzeh 2019

Apocynaceae						
43	*Calotropis procera* (Aiton) Dryand.	Latex	Latex	Kerman	0.14	Hosseini *et al*. 2021
44	*Caudanthera edulis* (Edgew.) Meve & Liede	Fruit, Stem	Decoction, Powder	Baluchestan, Saravan	0.27	Sadeghi *et al*. 2014; Didehvar *et al*. 2021
45	*Rhazya stricta* Decne.	Bark, Leaf, Stem	Decoction	Saravan	0.14	Sadeghi *et al*. 2014
Araceae						
46	*Arum orientale* subsp. *orientale*	Leaf, Stem	Cooked	Fars (Sepidan)	0.14	Rahemi Ardakani & Pour-sakhi 2020
47	*Biarum carduchorum* (Schott) Engl.	Leaf, Root, Stem	-	Biranshahr, Lorestan, Susan (Khuzestan), Zaqeh	0.41	Delfan 2016; Baroonian 2018; Delfan *et al*. 2020
48	*Biarum straussii* Engl.	Leaf, Root	-	Pol-e Dokhtar	0.14	Falahat-pour 2018
Arecaceae						
49	*Phoenix dactylifera* L.	Fruit, Pollen, Seed	Distillate, Powder, Raw	Dashtestan, Fasa, Mashhad	0.41	Dolatkhahi & Ghorbani Nohooji 2013; Ramezanian & Minaeifar 2016; Motahhari *et al*. 2022
Asparagaceae						
50	*Asparagus officinalis* L.	Stem	Decoction, Soaking	Khash, Mehrestan, Saravan, Suran	0.14	Khashi Jamalzehi 2019
51	*Muscari neglectum* Guss. ex Ten.	Root	-	Biranshahr, Darkhatun (Lorestan), Zaqeh	0.27	Delfan 2016; Shekari 2017
Asphodelaceae						

52	*Aloe vera* (L.) Burm.f.	Latex, Leaf	Decoction, Extract, Poultice (for diabetic wound), Powder	Fasa, Kerman, Mashhad, Saravan, Shiraz	0.69	Sadeghi *et al*. 2014; Salehi Nowbandegni *et al*. 2015; Hosseini *et al*. 2021; Motahhari *et al*. 2022
Aspleniaceae						
53	*Asplenium laciniatum* subsp. *laciniatum*	Whole plant	-	Faruj	0.14	Eslami Farouji & Khodayari 2016
Asteraceae						
54	*Achillea arabica* Kotschy	Flower, Leaf, Root, Whole plant	Extraction, Decoction, Infusion	Hamedan, Tuyserkan	0.14	Mosaddegh *et al*. 2016
55	*Achillea eriophora* DC.	Aerial parts, Latex, Leaf, Root, Stem	Decoction, Powder, Soaking	Birjand, Shiraz, Taftan mountain	0.55	Maleki 2015; Afkari 2017; Maleki & Akhani 2018; Mohammadi *et al*. 2021
56	*Achillea filipendulina* Lam.	-	-	Kohgiluyeh and Boyer-Ahmad	0.14	Sayadian Si-Sakht 2013
57	*Achillea millefolium* L.	Aerial parts, Flower, Inflorescence, Leaf, Stem	Decoction, Distillate, Infusion, Soaking	Abadeh, Farsh-abad (Fars), Saravan, Urmia	0.96	Bahmani *et al*. 2014; Sadeghi *et al*. 2014; Zali & Tahmasb 2016; Kiasi & Forouzeh 2019; Salehi *et al*.2020
58	*Achillea teretifolia* Willd.	Flower, Leaf, Stem	Decoction, Infusion	Farsh-abad (Fars)	0.14	Zali & Tahmasb 2016
59	*Achillea wilhelmsii* K.Koch	Aerial parts, Flower, Flowering branch, Leaf, Root	Decoction, Powder and infusion of dried flowers, Soaking	Aleshtar, Fasa, Jahrom, Kohgiluyeh and Boyer-Ahmad, Mashhad, Semirom, Shiraz, Taftan mountain, Yasouj	1.92	Asgary *et al*. 2000; Mosaddegh *et al*. 2012; Forouzeh *et al*. 2014; Maleki 2015; Salehi Nowbandegni *et al*. 2015; Afkari 2017; Maleki & Akhani 2018; Khajoei Nasab & Esmailpour 2019; Mehrnia & Hosseini 2020; Salehi *et al*. 2020; Asadi Samani *et al*. 2021; Motahhari *et al*. 2022

60	*Anthemis adonidifolia* Boiss.	Flower	Decoction, Raw (Dried)	Ardestan	0.14	Haerinasab & Abbasi 2018
61	*Arctium lappa* L.	Leaf, Root, Seed	Decoction, Infusion, Soaking	Abhar, Andika, Baghmalek, Biranshahr, Dehdez, Fasa, Hezar Mountain (Kerman), Izeh, Kerman, Khuzestan, Kouhdasht, Lali, Masjedsoleyman, Pol-e Dokhtar, Shiraz, Urmia, Zaqeh	1.37	Rajaeia & Mohamadi 2012; Bahmani *et al*. 2014; Khodayari *et al*. 2014; Salehi Nowbandegni *et al*. 2015; Delfan 2016; Azar 2017; Falahat-pour 2018; Asadi Samani *et al*. 2019; Vafadar & Toqranegar 2019
62	*Arctium minus* (Hill) Bernh.	Fruit, Leaf, Root	Distillation	Bojnourd, Hamedan, Tuyserkan	0.27	Mosaddegh *et al*. 2016; Asaadi 2021
63	*Artemisia aucheri* Boiss.	Flower	Decoction	Ardestan	0.14	Haerinasab & Abbasi 2018
64	*Artemisia deserti* Krasch.	Aerial parts, Flower, Leaf	Decoction, Infusion, Liniment, Powder, Smoking, Soaking, Tablet	Taftan mountain	0.27	Maleki 2015; Maleki & Akhani 2018
65	*Artemisia maritima* L.	-	-	Shiraz	0.14	Afkari 2017
66	*Artemisia quettensis* Podlech	Aerial parts, Flower, Leaf	Decoction, Infusion, Liniment, Powder,	Taftan mountain	0.27	Maleki 2015; Maleki & Akhani 2018

			Smoking, Soaking, Tablet			
67	*Artemisia sieberi* Besser	Aerial parts, Flower, Leaf, Stem	Decoction, Soaking	Basht, Fasa, Gachsaran, Kohgiluyeh and Boyer-Ahmad, Saravan, Shiraz	0.55	Sadeghi *et al*. 2014; Salehi Nowbandegni *et al*. 2015; Ramezanian & Minaeifar 2016; Amiri-Ardekani *et al*. 2021
68	*Artemisia vulgaris* L.	Flower, Leaf	Decoction, Infusion	Saravan	0.14	Sadeghi *et al*. 2014
69	*Calendula arvensis* M.Bieb.	Flower	-	Susan (Khuzestan)	0.14	Baroonian 2018
70	*Carthamus oxyacanthus* M.Bieb.	Aerial parts, Petal, Seed	Aromatic water	Biranshahr, Darkhatun (Lorestan), Jahrom, Pol-e Dokhtar, Zaqeh	0.55	Delfan 2016; Shekari 2017; Falahat-pour 2018; Khajoei Nasab & Esmailpour 2019
71	*Centaurea bruguierana* (DC.) Hand.-Mazz.	Fruit	Infusion	Arjan-Parishan region (Fars)	0.14	Dolatkhahi *et al*. 2014
72	*Cichorium intybus* L.	Aerial parts, Flower, Leaf, Root, Stem, Whole plant	Cooked (mixed with yogurt), Decoction, Distillation, Extract, Hydrodistilation, Infusion, Powder, Raw (as vegetable, alone or mixed with yogurt)	Abadeh, Abhar, Behbahan, Darab, Faruj, Fasa, Hezar Mountain (Kerman), Kerman, Khoy, Kohgiluyeh and Boyer-Ahmad, Neka, Shiraz, Yasouj, Zanjan	1.92	Mosaddegh *et al*. 2012; Rajaeia & Mohamadi 2012; Forouzeh *et al*. 2014; Gholipour *et al*. 2014; Moein *et al*. 2015; Moghanloo 2015; Salehi Nowbandegni *et al*. 2015; Eslami Farouji & Khodayari 2016; Afkari 2017; Razmjouyi *et al*. 2017; Kiasi & Forouzeh 2019; Vafadar & Toqranegar 2019; Asadi Samani *et al*. 2020; Younessi-Hamzekhanlu *et al*. 2020

73	*Cichorium pumilum* Jacq.	Whole plant	Decoction, Distillation	Zanjan	0.14	Moghanloo 2015
74	*Cirsium arvense* (L.) Scop.	Leaf, Stem, Whole plant	-	Chaharmahal and bakhtiari, Ziarat region (Golestan)	0.27	Abbasi, 2018; Qahfarokhi *et al*. 2021
75	*Cirsium palustre* (L.) Scop.	Fruit	-	Pol-e Dokhtar	0.14	Falahat-pour 2018
76	*Cirsium spectabile* DC.	Fruit	-	Biranshahr, Lorestan, Zaqeh	0.27	Delfan 2016; Delfan *et al*. 2020
77	*Cousinia belangeri* DC.	Fruit, Latex	-	Biranshahr, Lorestan, Zaqeh	0.27	Delfan 2016; Delfan *et al*. 2020
78	*Cousinia cylindracea* Boiss.	Fruit, Latex	-	Biranshahr, Darkhatun (Lorestan), Lorestan, Pol-e Dokhtar, Zaqeh	0.55	Delfan 2016; Shekari 2017; Falahat-pour 2018; Delfan *et al*. 2020
79	*Crepis foetida* L.	Seed	Powder	Susan (Khuzestan)	0.14	Baroonian 2018
80	*Gundelia tournefortii* L.	Leaf, Stem	-	Lorestan	0.14	Delfan *et al*. 2014
81	*Helianthus annuus* L.	Flower, Leaf, Root, Seed	-	Faruj	0.14	Eslami Farouji & Khodayari 2016
82	*Helianthus tuberosus* L.	Leaf, Tuber	-	Faruj, Kordestan	0.27	Eslami Farouji & Khodayari 2016; Asadi-Samani *et al*. 2022
83	*Lactuca orientalis* (Boiss.) Boiss.	Leaf	-	Farsh-abad (Fars)	0.14	Zali & Tahmasb 2016
84	*Lactuca sativa* L.	Leaf, Seed, Stem	-	Faruj	0.14	Eslami Farouji & Khodayari 2016
85	*Lactuca serriola* L.	-	-	Marivan	0.14	Asghari *et al*. 2018

86	*Launaea acanthodes* (Boiss.) Kuntze	Aerial parts, Gum, Latex	Raw gum	Nain, Yazd	0.27	Nabizadeh Harati 2018; Tabatabaei *et al*. 2019
87	L*aunaea* Cass.	Leaf	-	Yazd	0.14	Nabizadeh Harati 2018
88	*Matricaria chamomilla* L.	Flower, Leaf, Stem	Decoction, Infusion	Farsh-abad (Fars)	0.14	Zali & Tahmasb 2016
89	*Rhaponticum repens* (L.) Hidalgo	Aerial parts, Stem	Decoction	Bojnourd, Mahabad, Taftan mountain	0.41	Maleki 2015; Jafarirad *et al*. 2019; Asaadi 2021
90	*Onopordum carmanicum* (Bornm.) Bornm.	Flower, Leaf	Decoction, Infusion	Taftan mountain	0.27	Maleki 2015; Maleki & Akhani 2018
91	*Prangos ferulacea* (L.) Lindl.	Aerial parts	-	Fasa, Khoy	0.27	Ramezanian & Minaeifar 2016; Younessi-Hamzekhanlu *et al*.2020
92	*Pulicaria arabica* (L.) Cass.	Flowering branches	Ddecoction	Nain	0.14	Tabatabaei *et al*. 2019
93	*Pulicaria gnaphalodes* (Vent.) Boiss.	Aerial parts, Flower	Decoction, Infusion, Liniment, Powder, Soaking	Taftan mountain	0.27	Maleki 2015; Maleki & Akhani 2018
94	*Silybum marianum* (L.) Gaertn.	Flowering branches, Leaf, Root, Seed, Stem	Decoction, Distillate, Infusion, Raw (as fresh)	Kerman, Neka	0.41	Jafarzadeh Zoghalchali 2020; Hosseini *et al*. 2021
95	*Tanacetum polycephalum* Sch.Bip.	Flower, Leaf	-	Chaharmahal and bakhtiari	0.14	Asadi Samani *et al*. 2018
96	*Taraxacum sonchoides* (D.Don) Sch.Bip.	Latex, Leaf, Root	-	Chaharmahal and bakhtiari	0.14	Qahfarokhi *et al*. 2021

97	*Tragopogon caricifolius* Boiss.	Flower, Leaf, Stem	Decoction, Dried	Ardestan	0.14	Haerinasab & Abbasi 2018
98	*Tragopogon pratensis* L.	Leaf, Root	-	Ajabshir	0.14	Maleki Khezrlou *et al*. 2017
Berberidaceae						
99	*Berberis integerrima* Bunge	Bark, Flower, Fruit, Leaf, Root, Stem	Cooked, Infusion, Decoction, Juice, Raw, Soaking	East Mazandaran, Fasa, Hezar Mountain (Kerman), Jiroft, Kerman, Kohgiluyeh and Boyer-Ahmad, Lorestan, Qazvin (Alamut region), Shiraz, Taftan mountain, Urmia	1.51	Ahvazi *et al*. 2012; Mosaddegh *et al*. 2012; Rajaeia & Mohamadi 2012; Bahmani *et al*. 2014; Maleki 2015; Bibak & Moghbeli 2017; Maleki & Akhani 2018; Salehi Nowbandegni *et al*. 2015; Hosseini *et al*. 2021
100	*Berberis vulgaris* L.	Fruit, Leaf, Root, Stem	Compound in food, Decoction, Extract, Juice	Khoy, Nowshahr, Semnan	0.69	Farhadi *et al*. 2008; Jalali *et al*. 2009; Ibadullayeva *et al*. 2010; Younessi-Hamzekhanlu *et al*.2020
Bignoniaceae						
101	*Tecomella undulata* (Sm.) Seem.	Bark, Leaf, Stem	Decoction	Kerman	0.14	Hosseini *et al*. 2021
Boraginaceae						
102	*Echium amoenum* Fisch. & C.A.Mey.	Flower, Leaf	-	-	0.14	Sharifi & Bakhshaei 2017
Brassicaceae						
103	*Alyssum desertorum* Stapf	Seed	-	Urmia	0.14	Bahmani *et al*. 2014

104	*Brassica napus* L.	Leaf, Root, Seed	-	Andika, Baghmalek, Izeh, Lali, Masjedsoleyman, Sardasht, Yazd	0.41	Khodayari *et al*. 2014; Azizi & Keshavarzi, 2015; Nabizadeh-Harati 2018
105	*Crambe cordifolia* Steven	Root	-	Bojnourd	0.14	Asaadi 2021
106	*Lepidium draba* L.	Leaf	Raw, Cooked	Nain	0.14	Tabatabaei *et al*. 2019
107	*Nasturtium officinale* W.T.Aiton	Aerial parts, Flowering branch, Leaf, Root, Seed, Stem, Whole plant	Decoction, Extract, Infusion, Raw	Abhar, Aleshtar, Biranshahr, Darkhatun (Lorestan), Mashhad, Urmia, Zanjan, Zaqeh	0.96	Amiri & Joharchi 2013; Bahmani *et al*. 2014; Moghanloo 2015; Delfan 2016; Shekari 2017; Vafadar & Toqranegar 2019; Mehrnia & Hosseini 2020
Burseraceae						
108	*Boswellia serrata* Roxb.	Gum	Raw	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
Capparaceae						
109	*Capparis spinosa* L.	Flower, Fruit, Bark, Leaf, Root, Seed, Stem, Whole plant	Decoction, Extract, Powder, Raw	Jahrom, Kermanshah, Khash, Lorestan, Saravan, Suran, Mehrestan, Turkmen Sahra, Zanjan, Arjan-Parishan region (Fars), Golestan	1.23	Ghorbani 2004; Ghorbani, 2005; Delfan *et al*. 2014; Tahvilian *et al*. 2014; Moghanloo 2015; Khashi Jamalzehi 2019; Dolatkhahi *et al*. 2014; Khajoei Nasab & Esmailpour 2019
Caprifoliaceae						
110	*Cephalaria dichaetophora* Boiss.	Seed	Decoction	Kermanshah	0.14	Tahvilian *et al*. 2014

111	*Valeriana officinalis* L.	Fruit, Root	Decoction, Distillate (Unripe fruit), Extract, Infusion, Raw (Ripe fruit)	Dareshahr (Ilam), Lorestan	0.27	Delfan *et al*. 2014; Yousofvand *et al*. 2022
112	*Valeriana sisymbriifolia* Vahl	Flowering branches, Rhizome	Decoction, Infusion	Rooieen (Esfarayen, North Khorasan)	0.14	Aboutorabi 2002
Caryophyllaceae						
113	*Silene montbretiana* var. *montbretiana*	Flowering branches	-	Chaharmahal and bakhtiari	0.14	Qahfarokhi *et al*. 2021
Cornaceae						
114	*Cornus sanguinea* subsp. *australis* (C.A.Mey.) Jáv.	Bark, Fruit	-	Ziarat region (Golestan)	0.14	Abbasi 2018
Cucurbitaceae						
115	*Bryonia multiflora* Boiss. & Heldr.	Gum, Whole plant	-	Aleshtar	0.14	Mehrnia & Hosseini 2020

116	*Citrullus colocynthis* (L.) Schrad.	Aerial parts, Fruit, Leaf, Root, Seed	Decoction, Poultice, Powder, Raw, Smoking, Soaking, Tablet	Abdanan, Andika, Arjan-Parishan region (Fars), Baghmalek, Balochistan, Biranshahr, Borazjan, Dareshahr (Ilam), Darkhatun (Lorestan), Dashtestan, Dehdez, Dehloran, Farsh-abad (Fars), Fasa, Izeh, Kerman, Khash, Kohgiluyeh and Boyer-Ahmad, Kouhdasht, Lali, Lorestan, Masjedsoleyman, Mehrestan, Nain, Saravan, Shiraz, Sirjan, Suran, Tabas (South Khorasan), Taftan mountain, Yasouj, Yazd, Zaqeh	3.7	Sharififar *et al*. 2010; Mosaddegh *et al*. 2012; Dolatkhahi & Ghorbani Nohooji 2013; Ghasemi Pirbalouti *et al*. 2013; Delfan 2014; Dolatkhahi *et al*. 2014; Dolatkhahi & Nabipour 2014; Fathi 2014; Forouzeh *et al*. 2014; Khodayari *et al*. 2014; Sadeghi *et al*. 2014; Maleki 2015; Salehi Nowbandegni *et al*. 2015; Hatami & Zahedifar 2016; Ramezanian & Minaeifar 2016; Delfan 2016; Zali & Tahmasb 2016; Afkari 2017; Azar 2017; Shekari 2017; Maleki & Akhani 2018; Khashi Jamalzehi 2019; Tabatabaei *et al*. 2019; Delfan *et al*. 2020; Didehvar *et al*. 2021; Hosseini *et al*. 2021; Yousofvand *et al*. 2022
117	*Cucumis melo* L.	Seed	Decoction	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
118	*Cucurbita pepo* L.	Fruit	-	Mobarakeh	0.14	Mardani-Nejad & Vazirpour 2012
Cyperaceae						
119	*Carex stenophylla* Wahlenb.	Aerial parts	-	Chaharmahal and bakhtiari	0.14	Qahfarokhi *et al*. 2021

Ebenaceae						
120	*Diospyros lotus* L.	Fruit	Distillation	Babol	0.14	Esmaeilpour 2015
Equisetaceae						
121	*Equisetum arvense* L.	Aerial parts, Branches, Stem, Whole plant	Decoction, Extract, Infusion	Abhar, Arasbaran, Babol, Neka, Urmia, Zanjan	0.41	Zolfaghari *et al*. 2012; Bahmani *et al*. 2014; Gholipour *et al*. 2014; Niknafas Malekshah 2014; Moghanloo 2015; Vafadar & Toqranegar 2019
122	*Equisetum ramosissimum* Desf.	Stem, Whole plant	Infusion	Mamulan (Lorestan)	0.14	Suri 2018
123	*Equisetum telmateia* Ehrh.	Aerial parts	Decoction, Infusion	Neka	0.14	Gholipour *et al*. 2014
Ericaceae						
124	*Vaccinium arctostaphylos* L.	Flower, Fruit, Seed	Decoction, Powder	Fasa, Mashhad, Shiraz	0.14	Amiri & Joharchi 2013; Salehi Nowbandegni *et al*. 2015
Euphorbiaceae						
125	*Ricinus communis* L.	Leaf, Root, Seed	-	Faruj	0.14	Eslami Farouji & Khodayari 2016
Fabaceae						
126	*Astragalus fasciculifolius* Boiss.	Flower, Gum, Root	Decoction, Raw	Kohgiluyeh and Boyer-Ahmad, Shiraz	0.55	Mosaddegh *et al*. 2012; Afkari 2017; Amiri-Ardekani *et al*. 2021
127	*Astragalus fischeri* Buhse	Aerial parts, Fruit, Root, Seed, Stem	Decoction, Poultice, Powder, Raw, Smoking	Taftan mountain	0.27	Maleki 2015; Maleki & Akhani 2018
128	*Cassia fistula* L.	Fruit	-	Shiraz	0.14	Afkari 2017

129	*Coronilla varia* L.	Leaf	-	Urmia	0.14	Bahmani *et al*. 2014
130	*Coronilla securidaca* L.	Fruit, Leaf, Seed	Decoction, Powder	Fasa, Northeast of Khuzestan, Mashhad, Shiraz	0.27	Amiri & Joharchi 2013; Khodayari *et al*. 2014; Salehi Nowbandegni *et al*. 2015
131	*Galega officinalis* L.	Flower	Decoction	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
132	*Glycyrrhiza glabra* L.	Leaf, Rhizome	Decoction, Infusion, Powder, Raw	Jahrom, Shiraz	0.41	Afkari 2017; Khajoei Nasab & Esmailpour 2019
133	*Lathyrus oleraceus* Lam.	Fruit, Seed	Cooked, Extract, Raw	Abhar, Dehgolan, Faruj	0.41	Eslami Farouji & Khodayari 2016; Abaszade 2018; Vafadar & Toqranegar 2019
134	*Medicago sativa* L.	Leaf, Whole plant	Decoction, Distillate, Infusion, Raw	Abadeh, Abhar	0.27	Kiasi & Forouzeh 2019; Vafadar & Toqranegar 2019
135	*Melilotus* sp.	Flowering branches, Leaf, Stem	-	Chaharmahal and bakhtiari	0.14	Qahfarokhi *et al*. 2021
136	*Melilotus officinalis* (L.) Lam.	Aerial parts, Flower, Flowering branch, Leaf, Stem, Whole plant	Decoction, Extract, Infusion, Juice, Raw	Abhar, Loresran, Hamedan, Tuyserkan	0.41	Delfan *et al*. 2014; Mosaddegh *et al*. 2016; Vafadar & Toqranegar 2019
137	*Prosopis farcta* (Banks & Sol.) J.F.Macbr.	Fruit	-	Abdanan, Dehloran	0.27	Ghasemi Pirbalouti *et al*. 2013
138	*Sophora alopecuroides* L.	Aerial parts, Inflorescence, Leaf	Decoction, Powder	Taftan mountain, Urmia	0.41	Bahmani *et al*. 2014; Maleki 2015; Maleki & Akhani 2018

139	*Trifolium pratense* L.	Flowering branches	-	Urmia	0.14	Bahmani *et al*. 2014
140	*Trifolium purpureum* Loisel.	Flowering branches	-	Urmia	0.14	Bahmani *et al*. 2014
141	*Trigonella* sp .	Leaf, Seed	-	Chaharmahal and Bakhtiari	0.14	Qahfarokhi *et al*. 2021
142	*Trigonella filipes* Boiss.	Leaf, Seed	-	Biranshahr, Pol-e Dokhtar, Zaqeh	0.27	Delfan 2016; Falahat-pour 2018
143	*Trigonella foenum-graecum* L.	Aerial parts, Flower, Leaf, Seed, Stem, Whole plant	Decoction, Distillate, Extract, Infusion, Powder, Raw	Andika, Baghmalek, Basht, Fasa, Gachsaran, Izeh, Kerman, Khash, Kohgiluyeh and Boyer-Ahmad, Lali, Mashhad, Masjedsoleyman, Mehrestan, Saravan, Semirom, Shiraz, Suran, Tabas (South Khorasan), Turkmen Sahra, Yazd	2.19	Ghorbani 2005; Mosaddegh *et al*. 2012; Amiri & Joharchi 2013; Fathi 2014; Khodayari *et al*. 2014; Salehi Nowbandegni *et al*. 2015; Hatami & Zahedifar 2016; Afkari 2017; Safari 2016; Nabizadeh Harati 2018; Khashi Jamalzehi 2019; Amiri-Ardekani *et al*. 2021; Hosseini *et al*. 2021; Motahhari *et al*. 2022
144	*Trigonella glabra* subsp. *uncata* (Boiss. & Noë) Lassen	Leaf, Seed	-	Kouhdasht	0.14	Azar 2017
145	*Trigonella persica* (Boiss.) E.Small	Leaf, Seed, Stem	-	Biranshahr, Zaqeh	0.14	Delfan 2016
146	*Trigonella spruneriana* Boiss.	Flower, Leaf, Seed, Stem	Decoction, Distillate, Dried	Ardestan	0.14	Haerinasab & Abbasi 2018

147	*Vicia faba* L.	Flower, Flowering branch, Seed	Cooked	Fasa	0.14	Hatami & Zahedifar 2016
148	*Vicia sativa* L.	Fruit	Decoction	Kermanshah	0.14	Tahvilian *et al*. 2014
Fagaceae						
149	*Quercus brantii* Lindl.	Fruit	-	Lorestan	0.14	Delfan *et al*. 2014
150	*Quercus infectoria* G.Olivier	Fruit, Gum, Leaf	-	Aleshtar	0.14	Mehrnia & Hosseini 2020
151	*Quercus persica* Jaub. & Spach	Fruit, Seed	-	Abdanan, Dehloran	0.14	Ghasemi Pirbalouti *et al*. 2013
Gentianaceae						
152	*Gentiana olivieri* Griseb.	-	-	Kurdistan (Saqqez)	0.14	Derakhshan *et al*. 2017
153	*Gyrandra tenuifolia* (M.Martens & Galeotti) G.Mans.	Flower, Leaf	Infusion	Hormozgan	0.14	Safa *et al*. 2013
Grossulariaceae						
154	*Ribes khorasanicum* Saghafi & Assadi	Fruit	-	Mashhad	0.14	Amiri & Joharchi, 2013
Juglandaceae						
155	*Juglans regia* L.	Aerial parts, Bark, Fruit, Flower, Leaf, Root, Seed, Stem	Decoction, Distillate, Infusion, Powder, Raw (fruit), Tablet	Aleshtar, Ardabil (Kowsar country), Babol, Behshahr, East Mazandaran, Faruj, Fasa, Galugah, Hamedan, Hezar	2.61	Zargari 1997; Ahvazi *et al*. 2012; Rajaeia & Mohamadi 2012; Mardani-Nejad & Vazirpour 2012; Bahmani *et al*. 2014; Gholipour *et al*. 2014; Khajoei Nasab & Khosravi 2014; Niknafas Malekshah 2014; Maleki 2015; Salehi Nowbandegni *et al*. 2015; Eslami Farouji & Khodayari 2016; Hatami &

				Mountain (Kerman), Isfahan, Mashhad, Neka, Qazvin (Alamut region), Shiraz, Sirjan, Taftan mountain, Tuyserkan, Urmia		Zahedifar 2016; Mosaddegh *et al*. 2016; Afkari 2017; Maleki & Akhani 2018; Keshavarzi & Mosaferi 2019; Mehrnia & Hosseini 2020; Dadjou *et al*. 2021; Motahhari *et al*. 2022
Lamiaceae						
156	*Dracocephalum polychaetum* Bornm.	Flowering branches, Leaf	Decoction, Infusion	Kerman	0.14	Hosseini *et al*. 2021
157	*Hyssopus officinalis* L.	Flower, Leaf	Decoction	Abadeh	0.14	Kiasi & Forouzeh 2019
158	*Lamium album* L.	Aerial parts, Flower, Flowering branches, Leaf	Decoction	Nowshahr, Sardasht, Sari, Urmia	0.82	Zolfaghari *et al*. 2012; Bahmani *et al*. 2014; Azizi & Keshavarzi 2015; Karimi 2017
159	*Lamium amplexicaule* L.	Aerial parts	Infusion, Poultice	Aligudarz (Lorestan)	0.14	Asghari *et al*. 2017
160	*Marrubium vulgare* L.	Flower, Leaf	Decoction	Kerman	0.14	Hosseini *et al*. 2021
161	*Melissa officinalis* L.	Aerial parts	Decoction	Kermanshah	0.14	Tahvilian *et al*. 2014
162	*Mentha spicata* L.	Flowering branches, Leaf	-	Mobarakeh	0.14	Mardani-Nejad & Vazirpour 2012
163	*Nepeta bracteata* Benth.	Flowering branches	-	Urmia	0.14	Bahmani *et al*. 2014

164	*Nepeta meyeri* Benth.	Flowering branches	-	Urmia	0.14	Bahmani *et al*. 2014
165	*Phlomis anisodonta* Boiss.	Aerial parts	Infusion	Aleshtar, Kurdiatan (Saqqez)	0.27	Derakhshan *et al*. 2017; Mehrnia & Hosseini 2020
166	*Phlomis aucheri* Boiss.	Flowering branches, Leaf	Decoction	Abadeh	0.14	Kiasi & Forouzeh 2019
167	*Phlomis cancellata* Bunge	Aerial parts	-	Bojnourd	0.14	Asaadi 2021
168	*Phlomis herba-venti* L.	Aerial parts	Infusion	Sari	0.14	Khanverdi 2017
169	*Phlomis olivieri* Benth.	Aerial parts, Flower, Flowering branches, Leaf	Decoction, Infusion	Aleshtar, Fars (Sepidan), Shazand (Markazi), Yazd	0.55	Nabizadeh Harati 2018; Abtahi 2019; Mehrnia & Hosseini 2020; Rahemi Ardakani & Poursakhi 2020
170	*Phlomis polioxantha* Rech.f.	Aerial parts	Infusion	Fars (Sepidan)	0.14	Rahemi Ardakani & Poursakhi 2020
171	*Prunella vulgaris* L.	Whole plant	Infusion	Aleshtar, Sari	0.27	Khanverdi 2017; Mehrnia & Hosseini 2020
172	*Rydingia persica* (Burm.f.) Scheen & V.A.Albert	Aerial parts, Flower, Fruit, Leaf, Stem, Whole plant	Decoction, Powder, Soaking	Arjan-Parishan region (Fars), Balochistan, Fasa, Kerman, Khash, Mehrestan, Saravan, Shiraz, Suran, Taftan mountain, Yazd	1.1	Dolatkhahi *et al*. 2014; Sadeghi *et al*. 2014; Maleki, 2015; Salehi Nowbandegni *et al*. 2015; Afkari 2017; Maleki & Akhani, 2018; Nabizadeh Harati 2018; Khashi Jamalzehi 2019; Didehvar *et al*. 2021; Hosseini *et al*. 2021
173	*Salvia eremophila* Boiss.	Flower, Fruit, Leaf, Stem	Decoction	Ardestan, Yazd	0.27	Haerinasab & Abbasi, 2018; Nabizadeh Harati 2018
174	*Salvia indica* L.	Fruit, Leaf	-	Kouhdasht	0.14	Azar 2017

175	*Salvia leriifolia* Benth.	Aerial parts	-	Mashhad	0.14	Amiri & Joharchi, 2013
176	*Salvia macrosiphon* Boiss.	Flowering branches, Fruit, Leaf, Seed, Whole plant	Decoction, Infusion, Raw	Abhar, Fasa, Kerman, Susan (Khuzestan)	0.55	Hatami & Zahedifar 2016; Baroonian 2018; Vafadar & Toqranegar 2019; Hosseini *et al*. 2021
177	*Salvia mirzayanii* Rech.f. & Esfand.	Flower, Leaf, Stem	Decoction	Fasa, Shiraz, Taftan mountain	0.27	Maleki 2015; Salehi Nowbandegni *et al*. 2015
178	*Salvia nemorosa* L.	Aerial parts, Flowering branches	Decoction	Fars (Sepidan), Urmia	0.27	Bahmani *et al*. 2014; Rahemi Ardakani & Poursakhi 2020
179	*Salvia officinalis* L.	Flowering branches, Fruit, Leaf	Infusion	Andika, Baghmalek, Izeh, Lali, Masjedsoleyman, Pol-e Dokhtar, Semirom, Shiraz	0.69	Khodayari *et al*. 2014; Afkari 2017; Safari 2016; Falahat-pour 2018
180	*Salvia reuteriana* Boiss.	Flower, Flowering branches, Leaf	Decoction, Essential oils of leaves, Powder	Biranshahr, Lorestan, Kurdistan (Saqqez), Saravan, Zaqeh	0.82	Sadeghi *et al*. 2014; Delfan 2016; Derakhshan *et al*. 2017; Asadollahi *et al*. 2019; Delfan *et al*. 2020
181	*Salvia sclarea* L.	Leaf	Infusion	Babol	0.27	Niknafas Malekshah 2014; Esmaeilpour 2015
182	*Salvia syriaca* L.	Flowering branches, Leaf	Essential oils of Leaves	Biranshahr, Darkhatun (Lorestan), Zaqeh	0.41	Delfan 2016; Shekari 2017
183	*Teucrium orientale* L.	Aerial parts, Leaf	Decoction	Urmia, Yazd	0.27	Bahmani *et al*. 2014; Nabizadeh-Harati 2018

184	*Teucrium polium* L.	Aerial parts, Branches, Flower, Flowering branches, Leaf, Stem	Decoction, Infusion, Juice, Powder, Raw	Aligoudarz (Lorestan), Andika, Arjan-Parishan region (Fars), Baghmalek, Basht, Bojnourd, Fasa, Gachsaran, Izeh, Kashan, Kazeroun, Kerman, Khash, Kohgiluyeh and Boyer-Ahmad, Kouhdasht, Lali, Mashhad, Masjedsoleyman, Mehrestan, Mobarakeh, Nain, Qeydar, Saravan, Sari, Shiraz, Sojas-rud (Zanjan), Suran, Susan (Khuzestan), Tabas (South Khorasan), Urmia	3.29	Amiri and Joharchi 2013; Sayadian-Sisakhat 2013; Sharififar *et al*. 2013; Bahmani *et al*. 2014; Dolatkhahi *et al*. 2014; Fathi, 2014; Khodayari *et al*. 2014; Sadeghi *et al*. 2014; Salehi Nowbandegni *et al*. 2015; Ramezanian & Minaeifar 2016; Afkari 2017; Asghari *et al*. 2017; Azar 2017; Khanverdi 2017; Saadatpour *et al*. 2017; Baroonian 2018; Khashi Jamalzehi 2019; Tabatabaei *et al*. 2019; Amiri-Ardekani *et al*. 2021; Asaadi 2021; Hosseini *et al*. 2021; Motahhari *et al*. 2022
185	*Thymus daenensis* Celak.	Aerial parts	Extract, Infusion, Smoking	Kohgiluyeh and Boyer-Ahmad	0.14	Mosaddegh *et al*. 2012
186	*Zataria multiflora* Boiss.	Leaf	Decoction, Powder	Fasa, Hormozgan, Shiraz	0.27	Safa *et al*. 2013; Salehi Nowbandegni *et al*. 2015
187	*Ziziphora clinopodioides* Lam.	Aerial parts	-	Zanjan	0.14	Moghanloo 2015
Lauraceae						

188	*Cinnamomum verum* J.Presl	Bark, Stem	Decoction, Powder	Fasa, Shiraz, Urmia	0.27	Bahmani *et al*. 2014; Salehi Nowbandegni *et al*. 2015
Liliaceae						
189	*Fritillaria imperialis* L.	Bulb	-	Kohgiluyeh and Boyer-Ahmad	0.14	Forouzeh *et al*. 2014
Lythraceae						
190	*Punica granatum* L.	Fruit, Leaf	Decoction, Raw	Chaharmahal and Bakhtiari, Neka	0.27	Gholipour *et al*. 2014; Qahfarokhi *et al*. 2021
Malvaceae						
191	*Abelmoschus esculentus* (L.) Moench	Fruit	Raw	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
192	*Althaea officinalis* L.	Flower, Leaf, Root	-	Sardasht	0.14	Azizi & Keshavarzi 2015
193	*Hibiscus rosa-sinensis* L.	Flower, Whole plant	Raw	Behbahan	0.14	Razmjoue *et al*. 2017
194	*Hibiscus sabdariffa* L.	Flower	Decoction	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
195	*Malva neglecta* Wallr.	Leaf	Infusion	Behshahr, Galugah, Neka	0.27	Gholipour *et al*. 2014; Ahvazi *et al*. 2012
Moraceae						
196	*Morus alba* L.	Bark, Branches, Fruit, Leaf, Root, Stem	Extract, Raw (Dried)	Aleshtar, Andika, Ardestan, Baghmalek, Borazjan, Dashtestan, Fasa, Izeh, Lali, Maasjedsoleyman, Semnan, Shiraz, Yazd	1.37	Jalali *et al*. 2009; Dolatkhahi & Ghorbani Nohooji 2013; Khodayari *et al*. 2014; Ramezanian & Minaeifar 2016; Afkari 2017; Haerinasab & Abbasi 2018; Nabizadeh-Harati 2018; Mehrnia & Hosseini 2020; Hosseini *et al*. 2021

197	*Morus nigra* L.	Bark, Fruit, Leaf, Root, Stem	Decoction, Infusion, Powder, Raw	Chaharmahal and Bakhtiari, Faruj, Semnan, Taftan mountain	0.69	Jalali *et al*. 2009; Maleki, 2015; Eslami Farouji & Khodayari 2016; Maleki & Akhani 2018; Qahfarokhi *et al*. 2021
Myrtaceae						
198	*Eucalyptus globulus* Labill.	Leaf	Decoction	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
199	*Myrtus communis* L.	Leaf	Infusion	Chaharmahal and Bakhtiari, Darab	0.27	Moein *et al*. 2015; Qahfarokhi *et al*. 2021
Nitrariaceae						
200	*Peganum harmala* L.	Flower, Fruit, Leaf, Root, Seed, Stem	Decoction, Infusion, Powder, Raw (Dried), Smoking	Aleshtar, Ardestan, Bojnourd, Kerman, Kouhdasht, Mashhad, Nain, Saravan, Tabas (South Khorasan), Taftan mountain	1.65	Amiri & Joharchi, 2013; Sharififar *et al*. 2013; Fathi, 2014; Sadeghi *et al*. 2014; Maleki 2015; Azar 2017; Haerinasab & Abbasi 2018; Tabatabaei *et al*. 2019; Mehrnia & Hosseini 2020; Asaadi 2021; Hosseini *et al*. 2021
Oleaceae						
201	*Olea aucheri* A.Chev. ex Ehrend.	Leaf, Root	Decoction, Liniment	Kerman	0.14	Sadat-Hosseini *et al*. 2017
202	*Olea europaea* L.	Fruit, Leaf	Decoction, Infusion, Powder	Chaharmahal and Bakhtiari, Fasa, Khash, Mehrestan, Saravan, Semnan, Shiraz, Suran	0.82	Jalali *et al*. 2009; Salehi Nowbandegni *et al*. 2015; Khashi Jamalzehi, 2019; Qahfarokhi *et al*. 2021
203	*Olea europaea* subsp. *cuspidata* (Wall. & G.Don) Cif.	Leaf	Infusion	Saravan	0.14	Sadeghi *et al*. 2014

Orchidaceae						
204	*Orchis coriophora* L.	Bulb, Leaf, Seed	-	Biranshahr, Zaqeh	0.14	Delfan 2016
205	*Orchis palustris* Jacq.	Bulb, Leaf, Seed	-	Biranshahr, Zaqeh	0.14	Delfan 2016
Papaveraceae						
206	*Glaucium corniculatum* (L.) Rudolph	Aerial parts, Flower	Decoction	Aleshtar, Chaharmahal and Bakhtiari, Shazand (Markazi)	0.41	Abtahi 2019; Mehrnia & Hosseini, 2020; Qahfarokhi *et al*. 2021
207	*Glaucium elegans* Fisch. & C.A.Mey.	Aerial parts	-	Bojnourd	0.14	Asaadi 2021
208	*Glaucium oxylobum* Boiss. & Buhse	Leaf	Decoction, Powder	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
209	*Papaver rhoeas* L.	Fruit, Seed	-	Urmia	0.14	Bahmani *et al*. 2014
210	*Papaver somniferum* L.	Latex	Liniment	Saravan	0.14	Sadeghi *et al*. 2014
Phyllanthaceae						
211	*Phyllanthus emblica* L.	Fruit	Decoction	Mashhad	0.14	Amiri *et al*. 2014
Plantaginaceae						
212	*Plantago major* L.	Fruit, Leaf, Root	-	Nowshahr	0.14	Mozaffari Nejad *et al*. 2013
213	*Plantago ovata* Forssk.	Seed	Decoction	Khash, Saravan, Shiraz, Suran, Mehrestan	0.27	Afkari 2017; Khashi Jamalzehi 2019
Poaceae						

214	*Avena barbata* Pott ex Link	Seed	-	Bojnourd	0.14	Asaadi 2021
215	*Avena fatua* L.	Seed, Stem	Decoction, Raw (as dried)	Mamulan (Lorestan)	0.14	Suri 2018
216	*Avena sativa* L.	Seed	Decoction	Dareshahr (Ilam)	0.14	Yousofvand *et al*. 2022
217	*Cynodon dactylon* (L.) Pers.	Whole plant	-	Ardabil (Kowsar country, Chaharmahal and Bakhtiari	0.27	Dadjou *et al*. 2021; Qahfarokhi *et al*. 2021
218	*Hordeum bulbosum* L.	Seed, Stem	-	Aleshtar	0.14	Mehrnia & Hosseini 2020
219	*Hordeum vulgare* L.	Fruit, Seed, Stem	Decoction, Powder, Raw	Aleshtar, Kerman, Kouhdasht, Mobarakeh, Sardasht, Tabas (South Khorasan)	0.96	Mardani-Nejad & Vazirpour, 2012; Fathi, 2014; Azizi & Keshavarzi 2015; Azar 2017; Sadat-Hosseinia *et al*. 2017; Mehrnia & Hosseini 2020; Hosseini *et al*. 2021
220	*Psathyrostachys fragilis* (Boiss.) Nevski	Flower, Leaf	-	Chaharmahal and Bakhtiari	0.14	Qahfarokhi *et al*. 2021
221	*Secale strictum* (C.Presl) C.Presl	Fruit	-	Farsh-abad (Fars)	0.14	Zali & Tahmasb 2016
222	*Setaria glauca* (L.) P.Beauv.	Seed	Cooked, Powder	Neka	0.14	Gholipour *et al*. 2014
223	*Zea mays* L.	Fruit	Decoction	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
Polygonaceae						
224	*Polygonum aviculare* L.	Aerial parts, Branches, Root	Infusion	Bojnourd, Faruj, Mashhad, Sari, Urmia	0.69	Amiri & Joharchi 2013; Bahmani *et al*. 2014; Eslami Farouji & Khodayari 2016; Khanverdi 2017; Asaadi 2021

225	*Polygonum* L.	Flower, Leaf, Stem	Decoction	Ardestan	0.14	Haerinasab & Abbasi 2018
226	*Pteropyrum aucheri* Jaub. & Spach	Aerial parts, Flower, Fruit, Root, Stem	Decoction, Extract, Powder, Smoking, Soaking	Taftan mountain	0.27	Maleki 2015; Maleki & Akhani 2018
227	*Rheum ribes* L.	Aerial parts, Root	Decoction, Infusion	Kerman, Mahabad, Shiraz	0.41	Afkari 2017; Jafarirad *et al*. 2019; Hosseini *et al*. 2021
228	*Rheum turkestanicum* Janisch	Root	Extract	Mashhad	0.27	Amiri & Joharchi, 2013; Amiri *et al*. 2014
229	*Rumex crispus* L.	Root, Whole plant	Cooked, Decoction	Faruj, Fars (Sepidan)	0.27	Eslami Farouji & Khodayari 2016; Rahemi Ardakani & Poursakhi 2020
230	*Rumex vesicarius* L.	Leaf, Petiole	Raw (as fresh vegetable)	Kerman	0.14	Hosseini *et al*. 2021
Portulacaceae						
231	*Portulaca oleracea* L.	Aerial parts, Leaf, Seed	Infusion, Raw, Cooked	Aleshtar, Biranshahr, Dashtestan, Fasa, Kouhdasht, Mahabad, Nain, Pol-e Dokhtar, Zaqeh	1.23	Dolatkhahi & Ghorbani Nohooji 2013; Delfan 2016; Ramezanian & Minaeifar 2016; Azar 2017; Falahat-pour 2018; Jafarirad *et al*. 2019; Tabatabaei *et al*. 2019; Mehrnia & Hosseini 2020
Ranunculaceae						
232	*Nigella sativa* L.	Fruit, Seed	Infusion, Raw	Aleshtar, Saravan	0.69	Iranmanesh *et al*. 2010; Sadeghi *et al*. 2014; Mehrnia & Hosseini 2020
233	*Nigella segetalis* M.Bieb.	Seed	-	Biranshahr, Zaqeh	0.14	Delfan 2016
234	*Ranunculus arvensis* L.	Flower, Flowering branches	-	Andika, Baghmalek, Bojnourd, Izeh, Kouhdasht, Lali,	0.82	Khodayari *et al*. 2014; Afkari 2017; Azar 2017; Baroonian 2018; Nabizadeh Harati 2018; Asaadi 2021

				Masjedsoleyman, Shiraz, Susan (Khuzestan), Yazd		
Rhamnaceae						
235	*Paliurus spina-christi* Mill.	Fruit, Leaf, Root	Infusion	Babol, Shirvan	0.27	Habibi *et al*. 2014; Esmaeilpour 2015
236	*Ziziphus jujuba* Mill.	Flower, Fruit	Decoction	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
237	*Ziziphus spina-christi* (L.) Desf.	Fruit, Leaf	-	Fasa	0.14	Ramezanian & Minaeifar 2016
Rosaceae						
238	*Agrimonia eupatoria* L.	Flowering branches	Infusion	Sari	0.14	Khanverdi 2017
239	*Prunus* × *keredjensis* (Browicz) A.E.Murray	Branches, Fruit, Stem	Heating with fire	Nain	0.14	Tabatabaei *et al*. 2019
240	*Prunus amygdalus* Batsch	Seed	Raw	Hamedan, Tuyserkan	0.14	Mosaddegh *et al*. 2016
241	*Prunus lycioides* (Spach) C.K.Schneid.	Branches, Fruit, Gum, Leaf, Seed	Decoction (Branches), Raw (Fruit)	Abadeh, Aleshtar, Chaharmahal and Bakhtiari, Hamedan, Isfahan, Kouhdasht, Nain, Tuyserkan	0.69	Mosaddegh *et al*. 2016; Azar 2017; Tabatabaei *et al*. 2018; Kiasi & Forouzeh 2019; Tabatabaei *et al*. 2019; Mehrnia & Hosseini 2020; Qahfarokhi *et al*. 2021
242	*Cerasus mahaleb* (L.) Mill.	Fruit	-	Andika, Baghmalek, Izeh, Lali, Masjedsoleyman, Shiraz	0.27	Khodayari *et al*. 2014; Afkari 2017
243	*Crataegus aronia* (L.) Bosc ex DC.	Bark, Fruit, Leaf	-	Fasa, Urmia	0.27	Bahmani *et al*. 2014; Ramezanian & Minaeifar 2016

244	*Crataegus oxyacantha* Thuill.	Bark, Flower, Fruit, Root	-	Urmia	0.14	Bahmani *et al*. 2014
245	*Malus domestica* Borkh.	Fruit, Leaf	Vinegar, Raw (Fresh)	Chaharmahal and Bakhtiari, Fasa, Sari, Shiraz	0.41	Salehi Nowbandegni *et al*. 2015; Khanverdi 2017; Qahfarokhi *et al*. 2021
246	*Mespilus germanica* L.	Fruit, Leaf	Decoction, Raw	Neka, Sari	0.27	Gholipour *et al*. 2014; Karimi 2017
247	*Prunus cerasus* L.	Fruit	-	Sari	0.14	Karimi 2017
248	*Prunus divaricata* A.Sav.	Fruit	Raw	Neka	0.14	Gholipour *et al*. 2014
249	*Prunus scoparia* (Spach) C.K.Schneid.	Branches, Fruit, Gum, Leaf, Stem	Decoction, Raw	Ardestan, Baloushistan, Bojnourd, Nain, Pol-e Dokhtar, Susan (Khuzestan), Yazd	0.69	Baroonian 2018; Falahat-pour 2018; Haerinasab & Abbasi 2018; Nabizadeh Harati 2018; Tabatabaei *et al*. 2019; Asaadi 2021; Didehvar *et al*. 2021
250	*Prunus spinosa* L.	Bark, Flower, Fruit, Leaf	Infusion, Raw (Fresh)	Sari	0.14	Khanverdi 2017
251	*Rosa* × *damascena* Herrm.	Flower	Essential oils	Kouhdasht	0.14	Azar 2017
252	*Rosa canina* L.	Flower, Fruit, Leaf	Decoction, Extract, Infusion	Abhar, Mahabad	0.27	Jafarirad *et al*. 2019; Vafadar & Toqranegar 2019
253	*Rosa foetida* Herrm.	Petal	-	Urmia	0.14	Bahmani *et al*. 2014
254	*Rosa persica* Michaut ex Juss.	Fruit, Root	-	Bojnourd	0.14	Asaadi 2021
255	*Rubus caesius* L.	Flower, Fruit, Root	-	Bojnourd	0.27	Asaadi 2021
256	*Rubus creticus* Tourn. ex L.	Fruit	Raw	Mamulan (Lorestan)	0.14	Suri 2018

257	*Rubus fruticosus* L.	Flower, Fruit	-	Ziarat region (Golestan)	0.14	Abbasi 2018
258	*Rubus hyrcanus* Juz.	Fruit, Leaf, Seed, Root	Decoction, Raw, Juice, Infusion (Leaf)	Babol, Neka	0.41	Gholipour *et al*. 2014; Niknafas Malekshah 2014; Esmaeilpour 2015
259	*Rubus persicus* Boiss.	Fruit, Root	Decoction, Juice, Raw	Neka	0.14	Gholipour *et al*. 2014
260	*Sanguisorba minor* Scop.	Fruit, Leaf	-	Urmia	0.14	Bahmani *et al*. 2014
Rubiaceae						
261	*Plocama aucheri* (Guill.) M.Backlund & Thulin	Aerial parts	Decoction, Infusion	Kerman	0.14	Hosseini *et al*. 2021
Rutaceae						
262	*Citrus* × *aurantiifolia* (Christm.) Swingle	Fruit	Decoction	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
263	*Zanthoxylum asiaticum* (L.) Appelhans, Groppo & J.Wen	Fruit	Decoction	Mashhad	0.14	Amiri *et al*. 2014
Salicaceae						
264	*Salix aegyptiac*a L.	Flowering branches	Decoction	Aleshtar	0.14	Mehrnia & Hosseini 2020
265	*Salix excelsa* S.G.Gmel.	Bark, Flowering branches, Leaf	Decoction, Extract, Infusion	Abhar, Shiraz	0.27	Afkari 2017; Vafadar & Toqranegar 2019
Sapindaceae						

266	*Acer monspessulanum* L.	Fruit, Latex	-	Chaharmahal and Bakhtiari	0.14	Qahfarokhi *et al*. 2021
Solanaceae						
267	*Capsicum annuum* L.	Fruit	Powder	Khash, Mehrestan, Saravan, Suran	0.14	Khashi Jamalzehi 2019
268	*Hyoscyamus niger* L.	Seed	Decoction	Fras (Sepidan)	0.14	Rahemi Ardakani & Poursakhi 2020
269	*Solanum nigrum* L.	Aerial parts, Fruit, Leaf	-	Bojnourd, Fasa, Kazeroun, Northeast of Khuzestan, Shiraz	0.69	Dolatkhahi *et al*. 2012; Khodayari *et al*. 2014; Ramezanian & Minaeifar 2016; Afkari 2017; Asaadi 2021
270	*Withania coagulans* (Stocks) Dunal	Leaf, Root, Seed	Decoction, Powder (as tablet)	Baluchistan, Saravan	0.27	Sadeghi *et al*. 2014
271	*Withania somnifera* (L.) Dunal	Fruit, Leaf	Powder	Baluchistan, Saravan	0.14	Didehvar *et al*. 2022
Tamaricaceae						
272	*Tamarix ramosissima* Ledeb.	Leaf	Decoction, Distillate, Dried	Ardestan	0.14	Haerinasab & Abbasi 2018
Theaceae						
273	*Camellia sinensis* (L.) Kuntze	Leaf	Decoction	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
Urticaceae						
274	*Parietaria debilis* G.Forst.	Whole plant	Infusion	Mamulan (Lorestan)	0.14	Suri 2018
275	*Parietaria judaica* L.	Flowering branches, Whole plant	Infusion	Darkhatun (Lorestan), Kouhdasht, Mamulan (Lordestan)	0.41	Azar 2017; Shekari 2017; Suri 2018

276	*Urtica dioica* L.	Aerial parts, Branches, Flower, Leaf, Root, Seed, Stem, Whole plant	Cooked, Decoction, Distillation, Extract, Infusion, Poultice, Powder, Raw (as dried and fresh vegetable)	Aleshtar, Ali Abad, Andika, Ardestan, Babol, Baghmalek, Bardsir, Behbahan, Bojnourd, Dareshahr (Ilam), Hamedan, Izeh, Kalaleh (Golestan), Kechik (Golestan), Kerman, Kermanshah, Kohgiluyeh and Boyer-Ahmad, Lali, Lorestan, Mamulan (Lorestan), Mashhad, Masjedsoleyman, Neka, Pol-e Dokhtar, Shiraz, Siah-Marzkooh (Golestan), Turkmen Sahra, Tuyserkan, Urmia, Ziarat region (Golestan)	3.84	Ghorbani 2005; Mirdeilami 2011; Mosaddegh *et al*. 2012; Bahmani *et al*. 2014; Delfan *et al*. 2014; Gholipour *et al*. 2014; Khodayari *et al*. 2014; Niknafas Malekshah 2014; Tahvilian *et al*. 2014; Esmaeilpour 2015; Mosaddegh *et al*. 2016; Afkari 2017; Razmjoue *et al*. 2017; Abbasi 2018; Soleymani 2018; Suri 2018; Jafarzadeh Zoghalchali 2020; Hosseini *et al*. 2021; Asaadi 2021; Sarhadynejad *et al*. 2021; Motahhari *et al*. 2022; Yousofvand *et al*. 2022
277	*Urtica dioica* subsp. *dioica*	Aerial parts, Leaf, Root, Stem	Cooked, Decoction	Hezar Mountain (Kerman, Marivan (Zarivar)	0.27	Rajaeia & Mohamadi 2012; Tabad & Jalilian 2015
278	*Urtica pilulifera* L.	Flower, Leaf, Stem, Whole plant	Decoction	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015

Viscaceae

279	*Viscum album* L.	Leaf, Fruit	-	Nowshahr	0.14	Jalali *et al*. 2009; Shahaboddin *et al*. 2011
Zingiberaceae						
280	*Zingiber officinale* Roscoe	Rhizome	Powder	Fasa, Shiraz	0.14	Salehi Nowbandegni *et al*. 2015
Zygophyllaceae						
281	*Tribulus terrestris* L.	Flower, Fruit, Leaf, Whole plant	Decoction, Extract, Infusion	Behbahan, Farsh-abad (Fars), Fasa, Shiraz	0.41	Salehi Nowbandegni *et al*. 2015; Zali & Tahmasb 2016; Razmjoue *et al*. 2017
282	*Zygophyllum atriplicoides* subsp. *eurypterum* (Boiss. & Buhse) Popov	Aerial parts, Fruit, Latex, Leaf, Root, Stem	Decoction	Taftan mountain	0.14	Maleki 2015

Table 2. The most used medicinal plants of Iran with their phytochemicals and their antidiabetic properties.

Species	Phytochemicals	Antidiabetic properties	References
1. Urtica diocia	Carvacrol, carvone, naphthalene, (E)-anethole, hexahydrofarnesyl acetone, (E)-β-Ionone, and phytol	α-glucosidase and α-amylase inhibitory activity, improving diabetes-related enzymes, insulin resistance, insulin sensitivity, glucose uptake, improving glycoprotein components and controling glucose metabolism	El Haouari & Rosado 2019; Taheri *et al*. 2022; Bhattacharya *et al*. 2024
2. Citrullus colocynthis	Saponine, phenolic antioxidants, flavonoids, steroid, and glycosidic components	Reducing the mean serum level of HbA1c and FBS	Barghamdi *et al*. 2016 ; Perveen *et al*. 2020, Abdel-Hassan & Abdel-Barry 2000; Kumar *et al*. 2008
3. Teucrium polium	Flavonoids (such as apigenin, quercetin, and rutin)	Reducing TNF-α levels in serum, increasing insulin levels in serum and pancreas	Venditti *et al*. 2017; Noumi *et al*. 2020; Albadr *et al*. 2022
4. Juglans regia	Flavonoids (such as quercetin), alkaloids, juglone, polyphenol	Blood glucose lowering effect, reducing the absorption of glucose from the intestine, increasing insulin secretion, increasing the number of beta cells	Schwindl *et al*. 2017
5. Trigonella foenum-graecum	4-hydroxyisoleucine, galactomannan, polyphenols	Enhancing peripheral glucose utilization and tolerance, delaying the uptake of glucose in the small intestine, improving glucose control as well as decreasing insulin resistance	Visuvanathan *et al*. 2022
6. Cichorium intybus	Hydroxycinnamic acid, chicoric acid, cinnamic acid, caftaric acid, tannin, and polyphenol	Increasing glucose uptake, increasing glucose transport and insulin secretion, reducing blood glucose level	Singh & Chahal 2018, Riaz *et al*. 2024; Alam *et al*. 2022
7. Achillea wilhelmsii	Flavonoids (quercetin)	Decreasing blood glucose level	Hosseini *et al*. 2013, Akbar *et al*. 2023 ; Sadeghi *et al*. 2009
8. Peganum harmala	Flavonoids, alkaloids (such as harmine)	Decreasing in blood glucose level, enhancing insulin secretion from residual pancreatic beta cells	Li 2024; Komeili *et al* 2016
9. Berberis integrrima	Alkaloids (berberine)	Reducing fast blood sugar, increasing insulin sensitivity and increase insulin secretion	Bayani *et al*. 2016 ; Behrad *et al*. 2023
10. Arctium lappa	Fructose (Inulin), polysaccharides	Lowering the levels of glucose, increasing the levels of insulin in blood, improving glucose homeostasis, and reducing insulin-resistance.	Mir *et al*. 2022; Li *et al*. 2019
11. Capparis spinosa	Phenolic compounds, flavonoids, carotenoids, tocopherols, and terpenes	reduction of fast blood glucose levels, reducing carbohydrate absorption from the small intestine, inhibiting gluconeogenesis in the liver, enhancing glucose uptake by tissues, and beta cell protection/regeneration.	Sun *et al*. 2023, Annaz *et al*. 2022; Vahid *et al*. 2017

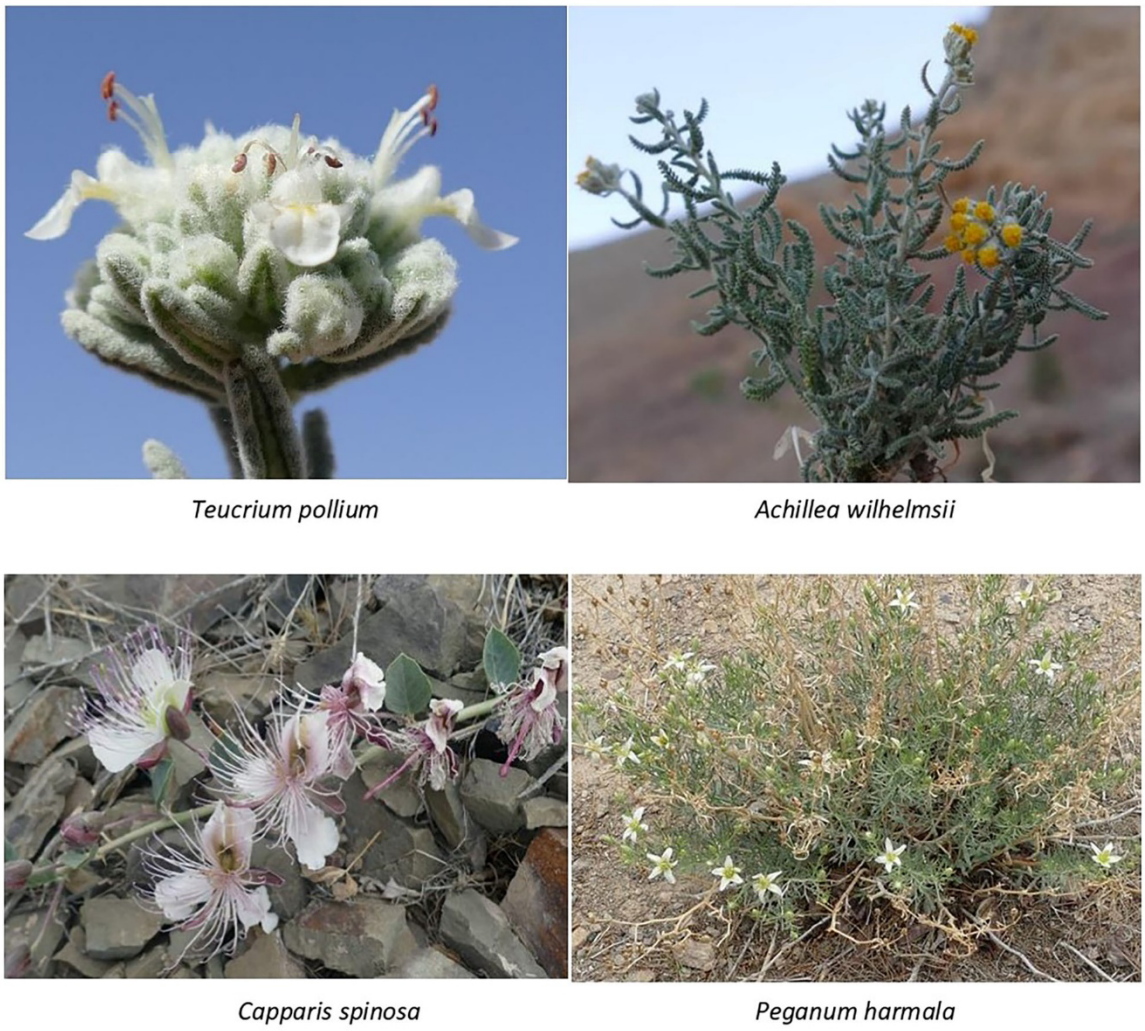

Figure 2. Photos of the four main Iranian plant species using for antidiabetic treatment.

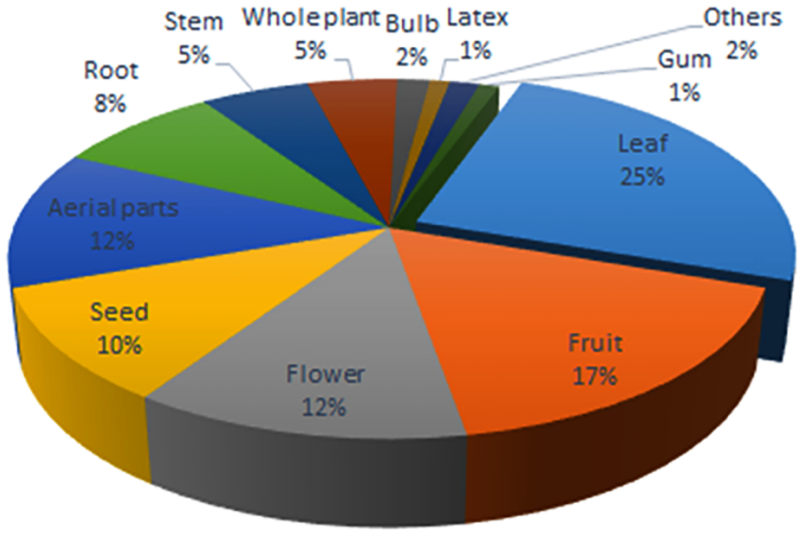

Figure 3. Plant parts used for the treatment of diabetes.

Modes of preparation

Medicinal plants were utilized in various forms, including cooked, decoction, liniment, juice, soaking, infusion, powder, poultice, raw, distillate, vinegar, extract, tablet, gum, latex, and smoking. The most frequently employed method of preparation was decoction (37.11%), followed by infusion (16%), powder (12.4%), poultice (9.33%), and raw (9.13%), while the remaining preparations were used for less than 5% of indications (Figure 4). Preparation methods such as cooking, vinegar, liniment, soaking, latex, gum, and juice, each with a frequency below 1%, were classified under a separate category named "Other." Decoctions are widely regarded as one of the main forms of preparation methods in ethnobotanical studies due to their simplicity in preparation, often by mixing with water or tea (Ssegawa & Kasenene 2007; El Amri *et al*. 2015). Additionally, this mode of preparation can be absorbed quickly and has demonstrated optimal effectiveness among all traditional preparation types (Yang & Ross 2010). Similar research has reported that decoction is the most common preparation mode in herbal recipes (Farooq *et al*. 2019; Mehrnia *et al*. 2021; Hosseini *et al*. 2022).

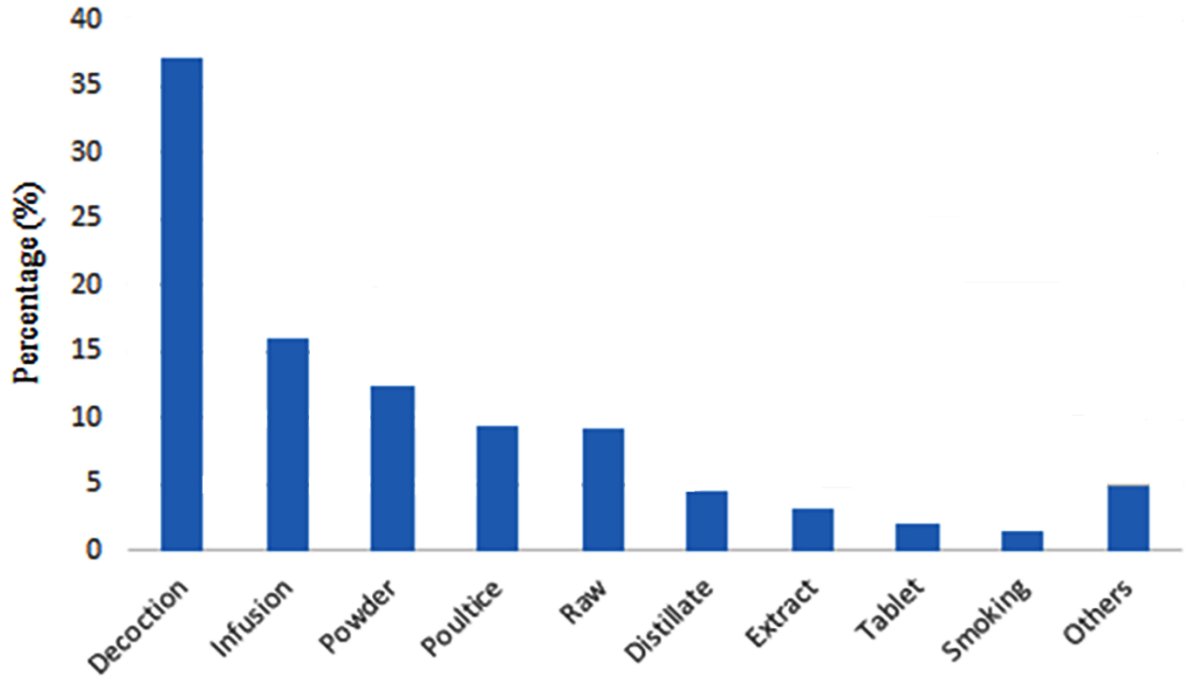

Figure 4. Methods of preparation of herbal recipes for the treatment of diabetes.

Phylogenetic analyses

One of the main parts of this study is to understand the possible relationship between Iranian plants used in diabetic treatments, in which 192 species belonging to 42 families were subjected to phylogeny analysis. Those species without available or high-quality data in the GenBank were removed (90 species). The analyses of the number of reports for diabetic use within each family revealed significant disparities at the phylogenetic scale. The phylogenetic relationships between families and parts of plants used in diabetes treatments demonstrated diverse phylogenetic signals within Iranian angiosperms (Figure 5). Phylogenetic signal of each part of plants used for diabetes treatment is indicated in Table 3. The Asterids and Rosids clades exhibited the largest number of uses. Basal eudicots, such as Papaveraceae and Ranunculaceae, were also used in diabetes treatments. In Asterids, Lamiaceae and Asteraceae are the two families with the most reported use of leaves and flowers. This result is not far from expected by the large number of Lamiaceae and Asteraceae species with various essential compounds and secondary metabolites (Gras *et al*. 2021). This study contributes to the burgeoning field of research that explores the evolutionary dimensions of ethnobotanical inquiries; an area previously neglected.

Closely related organisms sharing a common ancestor may produce similar chemical compounds of medicinal value. Therefore, providing evolutionary patterns among medicinal plants is crucial for identifying potential plants with similar properties. Phylogenetic trees can serve as valuable tools for discovering new medicinal plants. Fabaceae, comprising more than 20 species, is one of the principal families rich in hyperglycemia treatments. According to APG IV (2016), Fabaceae is placed in the order Fabales within the Rosids group of eudicots. The Fabales order encompasses four families, including Fabaceae and Polygalaceae, which are distributed in Iran. We propose that Polygalaceae, as a sister clade to the Fabaceae family, may possess similar properties in reducing blood sugar. However, there are no reported instances of using Polygala species in the Iran region for diabetic treatments. We recommend the investigation of Polygala (milkworts) as a potential plant in future studies focusing on hyperglycemia treatment. Lamiaceae (Lamiales order), Apiaceae (Apiales), and Asteraceae (Asterales) are classified in the Asterids group according to APG IV. The presence of Iridoids is a significant common chemical feature that unites the 14 orders in this group (Simpson 2019). Iridoids have demonstrated various pharmacological effects,

including anti-inflammatory, anti-tumor, neuroprotective, and hyperglycemia activities (Hussain *et al*. 2019; Wang *et al*. 2020). Therefore, we suggest that, given the presence of Iridoids in the Asterids group, there may be numerous undiscovered plant species with antidiabetic activities within this group. Based on the phylogenetic signal result, fruit, aerial parts, root, and stem showed significant phylogenetic correlation with the tree. We suggest that the anti-diabetic properties of these parts of the plant are significant through an evolutionary pattern of angiosperm families with a reduction of blood sugar properties. Phylogenetic reconstruction among medicinal plants is so significant in conservation management as well. Climate change and anthropogenic drivers are widely considered the most important threats to biodiversity (Muluneh 2021). The phylogenetic tree allows us to define the status of the threatened species with the relevant species. Understanding the evolutionary pattern among species and how these species are related together is helpful for conservation policymakers to identify endangered species and try to prevent them from extinction. According to the International Union for Conservation of Nature (IUCN), approximately 15000 medicinal plant species may be threatened with extinction due to habitat loss and overharvesting (Roberson 2008). *Salvia majdae* and *Phlomis herba_venti*, two recorded species used for diabetic treatments are defined as Critically endangered (CR) and endangered (EN) based on IUCN criteria (Heidari *et al*. 2021; Soltanipour *et al*. 2020). Therefore, it is crucial to stop exploiting these species for medicinal applications. The phylogenetic tree can provide us with great genetic information about these two species with their related species. Based on the phylogenetic tree, it is suggested to use other species used for diabetic treatments like *Salvia nemorosa*, which is distributed in most parts of the country and is not classified as an endangered species. This species may produce similar chemical compounds to *S. majdae*. Therefore, it is highly recommended instead of harvesting endangered species from Nature, using those species with similar shared genetic properties.

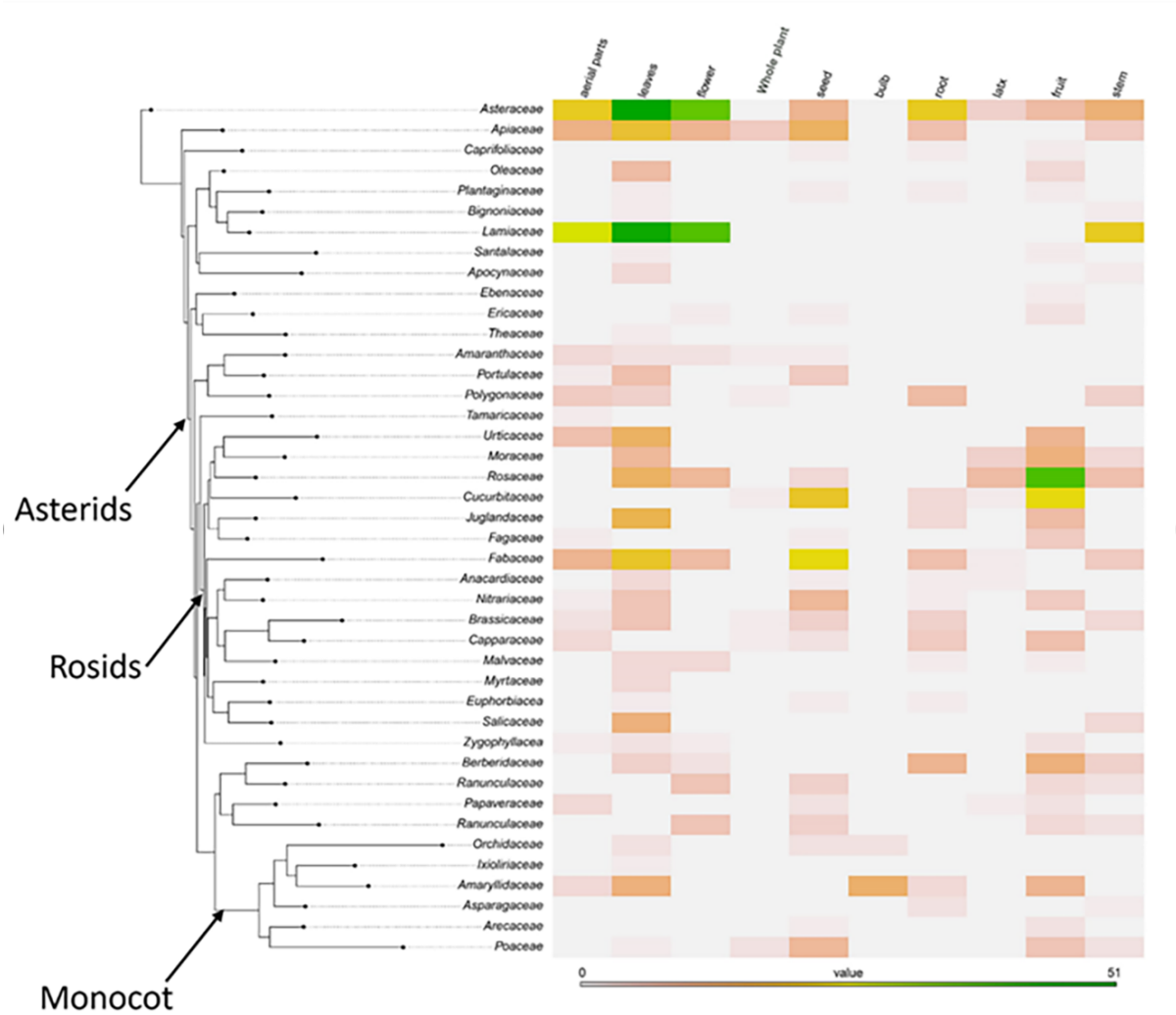

Figure 5. Phylogenetic relationships among Iranian flowering plant families used for diabetic treatments. The heatmap shows the proportion of the parts of the plant used based on the records in each family. The legend shows the proportion of the parts of the plant used by people by the colors.

Table 3. Phylogenetic signal of each part of plants used for diabetes treatment through plant family's phylogeny.

Part of plants	K-index	P-value
*Fruit	0.58	0.04
*Leaves	3.1	0.04
*Aerial parts	3.1	0.04
*Root	8.86	0.001
*Stem	1.84	0.04
Flower	4.04	0.4
Total	0.4	0.8
Seed	1.36	0.07
Bulb	0.69	0.2
Latex	2.01	0.05

* Parts of plant with anti-diabetic treatment shows significant correlation with significant phylogenetic correlation.

Plant-based drugs for diabetes in Iran

In recent years in Iran, some medicinal plants have been offered as herbal medicines following production and clinical studies in pharmaceutical research labs for the treatment of various diseases. Some of these herbal medicines used in the treatment of diabetes include Galga tablets (from *Galega officinalis*), Glycogel tablets (derived from *Salvia officinalis*), Sugarheal capsules (a mixture of several medicinal plant species), Urtiherb capsules (derived from *Urtica dioica*), which were produced in 2020 by the Iranian Institute of Medicinal Plants, and Viabet capsules (a mixture of several medicinal plants). All mentioned herbal medicines have been discovered through a combination of traditional knowledge and modern medicine. They result from the use of effective medicinal plants with anti-diabetic properties to treat all complications of diabetes and their therapeutic effects have been proven by clinical studies. It is interesting to note that most of the plant species used in these herbal medicines have already been reported in previous ethnobotanical studies for the treatment of diabetes. The importance of preserving the traditional knowledge of local people is highlighted as a window to discovering new drugs. However, many natural products and some herbal remedies used today are derived from plant species that were utilized long ago by indigenous cultures (Pandey & Tripathi 2017).

Conclusions

This study presents a comprehensive perspective on documented medicinal plants used for diabetes treatment in Iran, emphasizing ethnobotanical and evolutionary viewpoints. Out of 282 species, 11 plant species (constituting 3.9% of the total) were consistently reported in most ethnobotanical studies in Iran like *Urtica dioica*, *Citrullus colocynthis*, *Teucrium polium*, *Juglans regia*, *Trigonella foenum-graecum*, etc., suggesting potential anti-diabetic properties for drug discovery. The findings highlight the significance of preserving and delving further into indigenous knowledge to address contemporary health challenges. Results obtained from phylogenetic analyses open further investigations into plant-based remedies against diabetes and more accessible and economically viable therapeutic solutions. The ethnobotany and phylogenetics research set the base for the study of the cultural and phylogenetic contextualization of medicinal plants. In contrast, clinical studies and reviews make the bridge from traditional knowledge to evidence-based medicine. They bring valuable insight into the potential of these plants as low-cost and minimally invasive treatments for diabetes in Iran, particularly in medically underserved areas. As Diabetes is classified to hot and cold types in TPM, this approach is not yet considered by modern medicine. While considering the approach may help prevent and treat diabetes.

Declarations

List of abbreviations: IDF-International Diabetes Federation; TPM-Traditional Persian Medicine; APG-Angiosperm Phylogeny Group; MAFFT-Multiple Alignment using Fast Fourier Transform; TOM-Traditional Persian Medicine; ITS-internal transcribed spacer**;** IUCN-International Union for Conservation of Nature**;** IranDoc-Iranian Research Institute for Information Science and Technology.

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Availability of data and materials: All the collected data regarding the ethnomedicinal information are given in the manuscript itself. The original articles and theses are available with the authors.

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