An ethnopharmacological study of plants used for treatment of diabetes in the Southern and Tribal regions of Khyber Pakhtunkhwa province, Pakistan

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Research

Abstract

Background: In the southern and tribal districts of Khyber Pakhtunkhwa reside mainly Pashtun ethnic cultures that preferably use local plants to combat various health issues. We conducted surveys in this terrain to make an inventory of plants used traditionally for the treatment of diabetes.

Methods: A purposive sampling method was applied in the selection of participants, and semi-structured interviews were used for the collection of data. Voucher specimens of each plant species were preserved in the Herbarium Department of Botany University of Science and Technology Bannu, Pakistan.

Results: A total of 57 plant species, belonging to 31 plant families, were used to treat diabetes. Among plant parts, leaves were frequently used in the remedies. Similarly, decoction was the most common mode of preparation.

Conclusions: People living in this area commonly use medicinal plants in the traditional medicines to treat diabetes. However, they use such medicines without looking at their potential toxicological effects. Another matter is the immense use of some plants that has created a threat to the loss of their biodiversity in the area, and therefore requires to prioritizes plant resources for conservation and sustainable use.

Key words: Diabetes; ethnobotany; medicinal plants; traditional use; Pakistan.

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خلاصہ
پس منظر
خیبر پختونخوا کے جنو بی اور قبا یلی ا ضلاع میں پشتو ن ثقا فت کے لوگ ا با د ہیں۔ جو مقا می سطح پر صحت کے محتلف مسا ءنل کے لیے علا قے میں مو جو د پودوں کو استمعال کر تے ہیں۔ ہم نے اس حطے میں زیابطیس کے علاج میں آستمعال ہو نے وا لے پودوں کی سروے کیے ہیں۔
طریقہ کار
معلو مات دینے والے کو مقصد کی بنیاد پر منتحب کیا اور نیم خود سا حتہ سوالنامہ کے زریعے معلومات جمع کیے۔ پودوں کے نمونےباٹنی ڈیپارٹمینٹ یونیورسٹی اف سائنس اینڈ ٹیکنالوجی بنوں میں جمع اور محفو ظ کیے ۔
نتائج
اس خطے میں لوگ زیابیطس کے علاج میں 57 انواع کے پودے جو فیمیلیزسے تعلق رکھتے ہیں استعمال کرتے ہیں۔پودوں کے حصوں31 پتے اکثر استعمال کرتےتھے
جبکہ دواءوں کی تیاری میں جوشاندہ سب سےمعمول طریقہ تھا۔

اس خطے میں زیابیطس کے علاج کے لیے روایتی طور پرلوگ علاقے میں موجود پودے استعمال کرتے ہیں۔ تا ہم لوگ ان پودوں کے نقصاندہ اثرات کو جانچے بغیر استمعال کرتے ہیں۔ایک اہم مسلہ بعض پودوں کے زیادہ استعمال ہے۔ جس کی وجہ سے خیاتیاتی تنوع کے معدومی کا خطرہ ہے اس لیے پائیدار استعمال کیلئے علاقے میں خیاتیاتی تنوع کو بر قرار رکھنے کی ضرورت ہے۔
اہم نکات :زیابیطیس، ایھتنو باٹنی، دواوں کے پودے، روایتی استعمال، پاکستان

لنډیز
پس منظر
د خېبر پښتونخواه په سوېلی او قبائلی سېمه کښې په آساسی توګه پشتون کلتور لارونکی خلق استوګن دی چې په غوره توګه د ځاېې بوټو څخه کار اخلی چې هغه د ببله ببلو د صحت د ستونزو پر خلاف د مبارزې په مناسبت وکارول شی۔مونږ په دې سېمه کښې سروې تر سره کړې چې د هغو بوټو ېو لست جوړ کو کم چې په دودېز ډول د شکر ناروغې د درملنې لپاره کارول کېږی
طرېقه
د ګډون کونکو په انتخاب کښې د مقصد په آساس نمونو طرېقه وکارول شوه،او نېم جوړښت شوې مرکې د معلوماتو راټولولو لپاره کارول شوې دە۔د هر بوټی ېوه نمونه د سائنس او ټکنالوژی د بنو پاکسان پوهنتون د -نباتاتو ځانګې په هرترېوم کښې ساتل کېده
پاېلە
د 57 بوټو ټول ډولونه چې د 31 کورنېو څخه دی د شکر ناروغئ درملنې لپاره کارول شوې
د بوټو پانړې به اکثر په درملنو کښې کارول کېدې
.هم د ډول په اوبو کښې خټکول ېوه عمومی طرېقه وه
په د علاقه کښې مېشته ځاې خلق موجود بوټی د شکر ناروغئ د درملنو د پاره په دودېز ډول کاروی
سره له دې چې دوې دې ته پام نه کوی چې دغه بوټې چېرته زېا نمنونکی خو نه وی-او یوه بله مهمه ستونزه د بوټو په زېاته توګه کارول دی چې هغه د ژوندی تنوع د ختمېدو لپاره خطر دې- له دی -لقبله د بوټو دوامداره کارول لپاره د ژوندی تنوع ساتل پکار دی
کلېدی کلمې:د شکر ناروغې؛ اېتھنو باټنی،درملتونکې بوټې، دودېز کارول،پاکستان

Background

Diabetes is still an incurable health issue that continually increases around the world. A report from the International diabetic federation (IDF) indicates a continuous increase in diabetes prevalence in the last two decades (Ogurtsova *et al*., 2017). The global diabetes estimate (2010-2030) also points that there will be 69% increase in number of adults with diabetes in developing countries and 20% increase in developed countries (Diamond 2011).

People use a variety of antidiabetic medicines that are available in the pharmaceutical market. However, these medicines are expensive, and their side effects are problematic (Adegoke & Oloyede, 2013; Lo & Wasser, 2011). A part of modern medicinal research is based on ethnobotanical studies and traditional knowledge and many drugs have been derived from plants. A variety of species are currently undergoing investigation to ascertain their therapeutic efficacy (Torres *et al*. 2012). Investigations of traditional medicinal plants as alternative therapy are importnat to fight the havoc caused by diabetes. More than 1200 plants are used in the traditional treatment of diabetes (Marles & Farnsworth 1995; Grover *et al*. 2002). It is interesting that plant-based medicines for diabetes might still be the most reliable around the world. According to one estimate, 80% diabetics prefer herbal treatment due to the lesser side effects (Ezuruike & Prieto 2016). Diabetes management with plant-based medicines is more prevalent in traditional societies of the developing countries, because such medicines are more accessible than the conventional medicines in these societies.

Pakistan is located in the developing world, and diabetes is more prevalent as compared to other Asian countries (Shera *et al*. 2010). The number of diabetics is estimated to be almost nine million, with almost 11.7% in the North West Frontier Province (NWFP), now known as Khyber Pakhtunkhwa.

In the southern and tribal districts of Khyber Pakhtunkhwa reside mainly Pashtun ethnic cultures. The terrain is home to the most marginalized, vulnerable, and economically deprived segments of the population. Until recently, access to most of the region was restricted due to conflict. The area has faced harsh economic conditions on account of instability in Afghanistan and operations against terrorists in the area, with huge migration of people.

Several ethnobotanical studies from the region show that people utilize local plants in the treatment of diabetes. However, most of these studies (e.g. Gilani et al. 2003; Khan et al. 2011; Khan et al. 2009; Farooq et al. 2012; Qaisar *et al.* 2013; Hussain *et al.* 2013; Murad *et al.* 2013) lack relevant ethnopharmacological information essential for drug discovery purposes. Careful investigation of the traditional medicines is important, as improper remedies, ambiguous products, inappropriate dosage, and side-effects create a potential risk (Robinson & Zhang 2011). Our study aims to assess informant knowledge about diabetes, enlist and highlight the status of diversity of antidiabetic plants,

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examine the formulation and use of remedies, and assess ethnobotanical and pharmacological literature on the reported antidiabetic plants. We considered it important to carry out research as the indigenous knowledge has come under threat due to migration of the people.

Materials and methods

Study area

Khyber Pakhtunkhwa province lies between 34°1' 33.3012" N and 71°33' 36.4860" E, with an area of 128961 km^2 (Fig. 1). The terrain that extends from Himalaya to Suleiman Mountains shares a 1100 km border with Afghanistan. It borders Punjab in the east and Baluchistan in the south. Climatic conditions vary in the mountains and plain areas. In the mountain regions, summer remains pleasant while in the plain areas, it is very hot. Freezing temperatures occur in the mountains in winter. The climate in the southern districts is semi-arid with hot summers and mild winters. Autumn and winter are usually dry seasons while summer and spring receive much of the precipitation. The average annual rainfall varies from 600 to 1450 mm (Wiki, NWFP 2007). The great variability in the regional edaphic conditions, altitude and climatic factors have created a large great range of living places of biodiversity. Hence, biodiversity in this territory reflects a transition zone between Afghan provinces and Punjab and Baluchistan province in Pakistan. This territory is very rich in biodiversity and associated traditional practices.

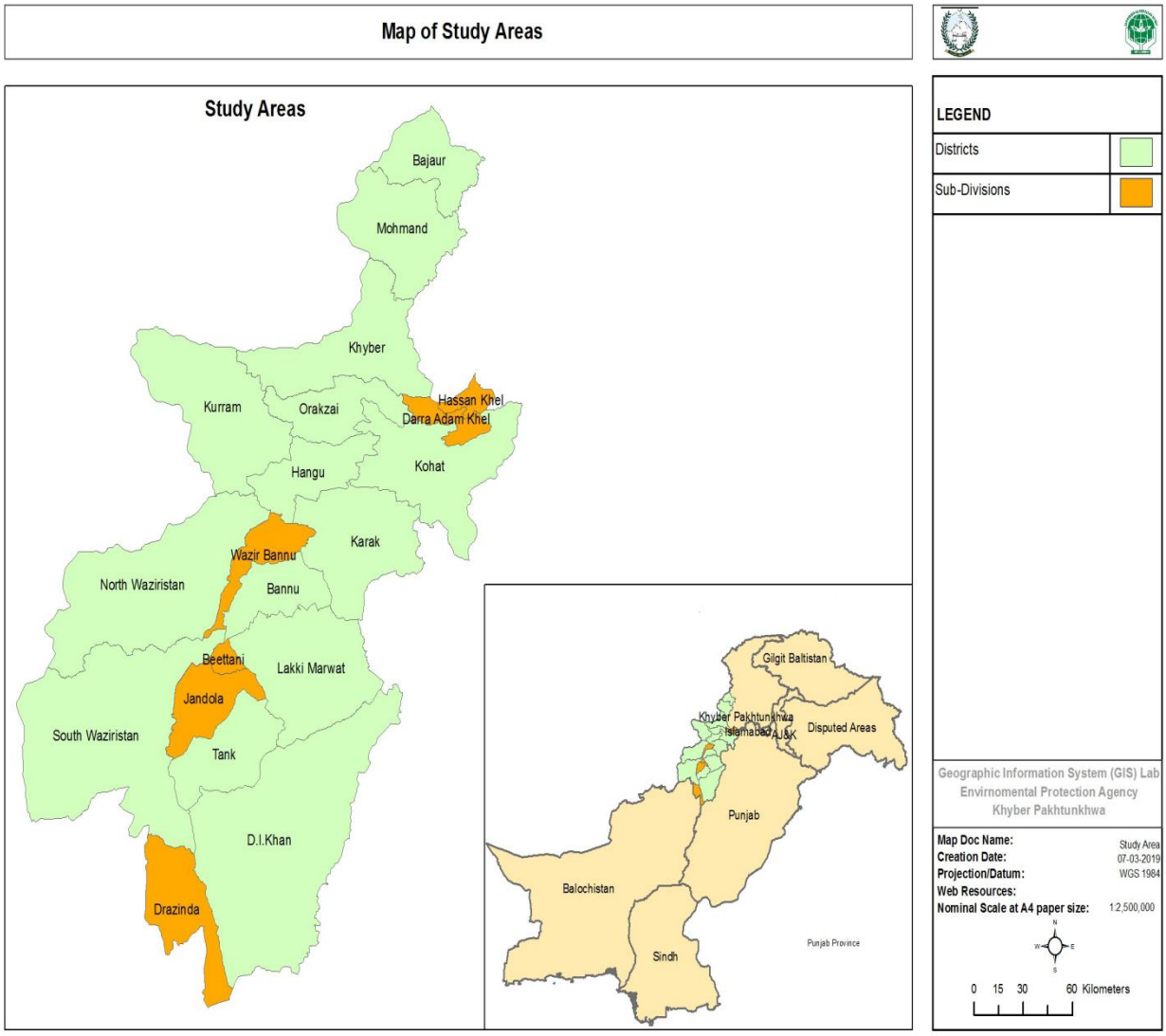

Figure 1. Map of the study area

Socioeconomic background of the study area

The study area comprises fourteen districts and six subdivision of Khyber Pakhtunkhwa province (Fig. 1). The main ethnic cultures are Afridi, Bangash, Banochi, Battani, Dawar, Gundapur, Khattak, Kundi, Mahsud, Marwat, Mohmand, Orakzai, Safi, Seraiki, Sherani, Shinwari, Tarkani, Turi and Wazir. The population are mainly Muslims and some minority religions such as Sikh, Christian, and Hindu. Most people speak the Pashto language while some

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speak other dialects such as Seraiki in Dera Ismail Khan and Tank. The local population in the tribal and frontier regions use Jirga (traditional assemblies) to resolve social problems.

Most of the people in the study area are poor, with very limited facilities. Decades of war and insurgency have wreaked havoc with social structure, economy and infrastructure of the area. Health and education facilities are still limited. Due to limited livelihood opportunities people economically depend on rearing domestic animals, farming, small-scale business, household jobs, recruitment in local security forces, and working on daily wages in the local markets and mining sector. Women along with covering all household duties, take part in farming, collection of fuel wood and carry water.

Data collection and questionnaire

The present ethnobotanical study was carried out from August 2016 to May 2018, following the Code of Ethics of the International Society of Ethnobiology (ISE, 2006). The first author visited the entire 14 districts and 5 sub-divisions, and 51 communities were selected randomly. A purposive sampling method was employed in selection of traditional healers and elders in which the interviewee assigned the next traditional healers and elders to be included in subsequent interviews. The author received prior informed consent and authorization from local authorities and discussed the research ideas with informants. After obtaining prior informed consent with each participant, antidiabetic plants data were gathered through face-to-face interviews held with participants using semi-structured questionnaires. Interviews were carried out in Pashto language in local dialect. A questionnaire for data collection was designed to address the following information from the informants: knowledge about diabetes, local name of plant, part used and mode of preparation of the herbal medicines. Demographic data of the participants including name, gender, age, age group, location and educational level were also noted (Table1, Annex Questionnaire).

Plant collection and preservation

The first author collected three fresh samples of each wild plant to create voucher specimens for herbarium deposit. The plant species were collected mostly in flowering stage with assistance of traditional healers and knowledgeable elders. Taxonomists were involved in identification while scientific names and family names of plant species follow (APG IV, 2016). The voucher specimens of the reported plants were prepared, labeled and deposited in the Herbarium of Botany Department University of Science and Technology Bannu.

Data analysis

Relative frequency of citation (RFC) was calculated as the number of citations (for a given species) divided by the number of all citations for all species (Ocvirk *et al*. 2013). Plant species that attained higher frequencies were validated by comparing with the available ethnobotanical and pharmacological studies in literature. The literature search was made mainly through Google Scholar, Science direct, PubMed, Scopus and open access journal sources.

Table 1. Detail of participants interviewed

Gender	Healer / Elder	Age group	Education Level	Education Level
Male				**253**
	Elder			**168**
		80-99		22
			Matriculation	12
			Illiterate	6
			Intermediate	4
		60-79		120
			Matriculation	60
			Graduation	20
			Illiterate	20
			Intermediate	19
			Middle	1
		40-59		26
			Illiterate	11
			Matriculation	8
			Intermediate	5
			Graduation	2
	Healer			**85**
		80-99		8
			Matriculation	5
			Illiterate	2
			Intermediate	1
		60-79		61
			Matriculation	36
			Intermediate	10
			Graduation	10
			Illiterate	5
		40-59		16
			Illiterate	9
			Matriculation	3
			Intermediate	3
			Graduation	1
Female				**19**
	Elder			**19**
		80-99		2
			Matriculation	2
		60-79		15
			Matriculation	8
			Illiterate	3
			Graduation	2
			Intermediate	2
		40-59		2
			Matriculation	2
Total				**272**

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Results

Informant's assessment on diabetes

Diabetes is commonly known as 'sugar' in all of the regions. The word is proposed because of excessive intake of sugar that leads to the metabolic disorder. The local people showed several views about diabetes. a majority of the healers (61: 72%) and elders (112: 60%) defined that consumption of more sugar as the main cause of diabetes; however, few healers (5: 6%) and elders (28:15%) mentioned genetic factors. The remaining healers 19 (22%) and elders 46 (25%) mentioned both genetic factors and consumption more sugar.

The disease was diagnosed through certain symptoms. They diagnosed the diseases e.g. by gathering of ants around urine, slow healing of wounds, high thirst, frequent urination, rough and hard skin, weight loss and weak legs. The inhabitants recommended reducing consumption of sugar as the main way to prevent the disorder. Similarly, some people declared that proper consumption of food items could halt the onset of this disorder. Most of the healers and knowledgeable elders considered exercise as the main way to prevent the severity of diabetes.

Plant species composition

The participants mentioned 57 plant species of 31 families used for management of diabetes in the study area (Table 2). Among the plant families, the highest number of plant species was reported for Asteraceae (8 species) followed by Lamiaceae (6), Amaryllidaceae (4), and Fabaceae (3). Eight plant families each contributed two species: Apocynaceae, Cucurbitaceae, Euphorbiaceae, Meliaceae, Myrtaceae, Pinaceae, Rhamnaceae and Solanaceae. The remaining 19 families contributed a single species each.

Plant parts used and formulation of remedies

The participants indicated leaves as the most frequently used plant part (20, 27%) in preparation of remedies followed by fruits (13, 27%), seeds (10, 14%) and aerial parts (10, 14%). Stem bark, branches and roots were less frequently used in preparation of recipes (Fig. 2). Decoction with (36) plant species (40%) was the common method of remedies preparation. However, seventeen plant parts (19%) are used directly mostly fruits. The other forms of formulations are vegetables, powder, juice and infusion (Fig. 3).

Relative frequency citation and use value

Relative frequency citation was calculated for each plant species (Table 2) and it was found that three species *Momordica charantia* L. (12.24), *Caralluma tuberculata* N.E. Br. (10.63) and *Citrullus colocynthis* (L.) Schrad. (7.84) attained the highest relative frequency of citation. In the other species, a high relative frequency was calculated for *Allium cepa* L. (4.83), *Allium sativum* L. (3.76), *Withania coagulans* (Stocks) Dunal (3.01), *Berberis lycium* Royle (2.90), *Melia azedarach* L. (2.79), *Trigonella foenum-graecum* L. (2.79), *Fagonia cretica* L. (2.69), *Allium ascalonicum* L. (2.36), *Azadirachta indica* A.Juss. (2.36), *Syzygium cumini* (L.) Skeels (2.36), *Ficus benghalensis* L. (2.26) and *Peganum harmala* L. (2.04). The relative importance of plants was evaluated throughthe Use Value index. *Momordica charantia* L. attained the highest use value (0.419), followed by *Caralluma tuberculata* N.E. Br. (0.364), *Citrullus colocynthis* (L.) Schrad. (0.268), *Allium cepa* L. (0.165), *Allium sativum* L. (0.129), *Withania coagulans* (Stocks) Dunal (0.103) etc. (Table 2). The lowest use value was calculated for *Euphorbia hirta* L. (0.007) and *Pinus gerardiana* Wall. ex D. Don (0.007).

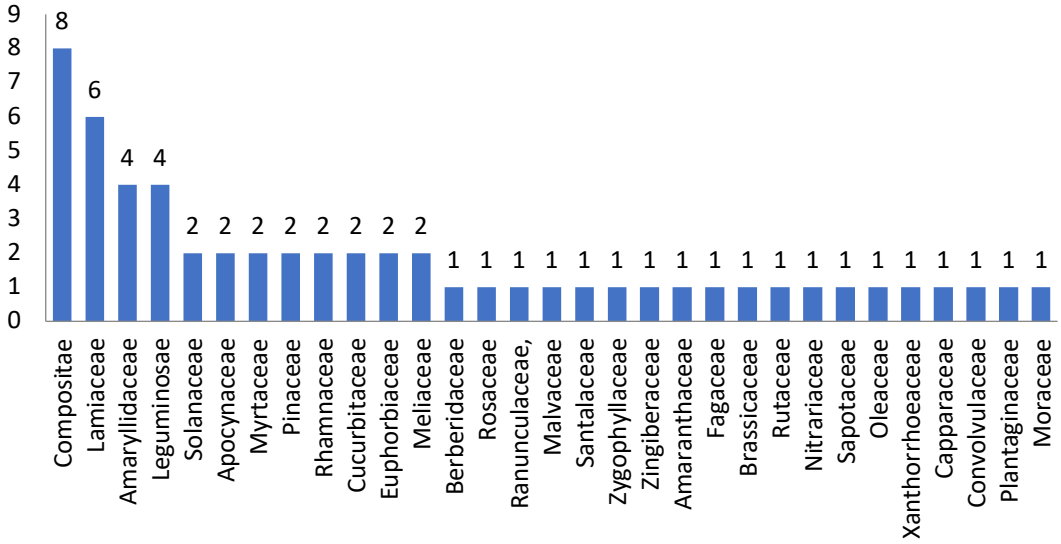

Figure 2. Family distributions of the reported plant species

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Table 2. Antidiabetic plants from Northwest Pakistan

Family and Scientific name	Local name	Part used	Life form	Cultivated / wild	Formulation and use	RFC	UV
AMARANTHACEAE							
Chenopodium murale L. (MU-HBD-USTB-19)	Shahkander boty/ Sormy	Whole plant	Herb	Wild	Cooked leaves or whole plant decoction is orally consumed by diabetes.	0.75	0.026
AMARYLLIDACEAE							
Allium ascalonicum L. (MU-HBD-USTB-06)	Sar pyoz	Bulb, leaves	Herb	Wild	Cooked bulbs or green leaves are directly used.	2.36	0.081
Allium carolinianum DC. (MU-HBD-USTB-07)	Jangli wezai	Bulb	Herb	Wild	Cooked bulbs or green leaves are directly used.	1.93	0.066
Allium cepa L. (MU-HBD-USTB-08)	Pyaz	Bulb, leaves	Herb	Cultivated	Leaves are directly used as raw. Bulb slices are eaten directly or cooked as vegetable.	4.83	0.165
Allium sativum L. (MU-HBD-USTB-09)	Woga	Bulbils	Herb	Cultivated	Leaves are directly used as raw. Bulb is also eaten directly or cooked as vegetable.	3.76	0.129
APOCYNACEAE							
Caralluma tuberculata N.E.Br. (MU-HBD-USTB-18)	Pamany or Pamanky	Stem	Herb	Wild	Stem is cut into pieces and cooked as vegetable. Sometimes directly eaten by diabetes as raw drug.	10.6	0.364
Rhazya stricta Decne (MU-HBD-USTB-42)	Ganderai	Leaves	Under shrub	Wild	50g of shade dried leaves are boiled in 300 ml water to get a decoction. The decoction is further diluted to 500 ml.	1.61	0.055
ASTERACEAE							
Artemisia absinthium L. (MU-HBD-USTB-12)	Mastyara	Leaves	Herb	Wild	Shade dried leaves (1 kg) are boiled in 5 L water to get a decoction, which is used in early morning or before meal one table spoon per day.	1.40	0.048
Artemisia scoparia Waldst. & Kitam. (MU-HBD-USTB-13)	Doorang	Whole plant	Herb	Wild	Dried plant material is boiled in water to get a decoction and diluted, which is used before meal once or two times per day in a table spoon amount.	0.64	0.022
Cichorium intybus L. (MU-HBD-USTB-20)	Shin guly	Leaves, root and stem	Herb	Cultivated	Leaves cooked as vegetable while decoction of stem and root (200g) prepared in 500 ml water is used for diabetes, hepatitis and malaria.	1.18	0.040
Lactuca sativa L. (MU-HBD-USTB-30)	Saalad	Leaves	Herb	Wild	Leaves are cooked as vegetable or eaten raw with bread.	0.86	0.029
Launaea procumbens (Roxb.) Ramayya & Rajagopal (MU-HBD-USTB-31)	Shwadi betai	Aerial parts	Herb	Wild	Powder of *Launaea procumbens* aerial parts (3 g) is put into hot water glass. The extract is filtered and a spoon of	0.86	0.029

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					infusion two times a day is taken by diabetes.		
Sonchus asper (L.) Hill (MU-HBD-USTB-47)	Tareza	Leaves, Root	Herb	Wild	Infusion of leaves or a decoction of dried roots is used.	0.43	0.015
Tanacetum artemisioides L. (MU-HBD-USTB-49)	Zawil	Aerial parts	Herb	Wild	Infusion of 10 g aerial parts in 50 ml is used prepared and then diluted to ten part of the original volume.	0.64	0.022
Taraxacum campylodes G.E. Haglund (MU-HBD-USTB-50)	Zer gul	Leaves	Herb	Wild	Leaves are cooked with other leafy vegetables.1/4 kg dried aerial parts are boiled in 2 liters water and decoction is filtered and used for diabetes. One cup twice a day.	1.07	0.037
CONVOLVULACEAE							
Cuscuta reflexa Roxb (MU-HBD-USTB-23)	Machi/ Chambel	Whole plant	Herb	Wild	Whole plant powder or decoction is used.	1.50	0.051
CUCURBITACEAE							
Citrullus colocynthis (L.) Schrad. (MU-HBD-USTB-21)	Maragonarye, Parpendu, or tuma	Fruit	Herb	Wild	Fruit powder 1g per day or fruit without pericarp is boiled in water and is mixed with syrup. Some peoples mix fruit decoction with syrup.	7.84	0.268
Momordica charantia L. (MU-HBD-USTB-35)	Karela	Fruit	Herb	Cultivated	Fruit slices are first mixed with salt and then cooked as vegetable. Some people prepare juice of fresh fruit.	12.2	0.419
EUPHORBIACEAE							
Euphorbia hirta L. (MU-HBD-USTB-26)	Chaptary	Leaves	Herb	Wild	Fresh leaves are crushed and juice is mixed with water and is orally taken for diabetes.	0.21	0.007
Euphorbia prostrata Aiton (MU-HBD-USTB-27)	Hara Chaptary	Aerial parts	Herb	Wild	A decoction of aerial parts 10 g prepared in 100 ml water is used.	0.86	0.029
FABACEAE							
Acacia modesta Wall. (MU-HBD-USTB-03)	Palosa	Leaves	Tree	Wild	A leaf (½ kg) is boiled in water and the decoction obtained taken two times a day through table spoon. Gum is directly used or treatment of diabetic.	1.40	0.048
Acacia nilotica (L.) Delile (MU-HBD-USTB-04)	Kiker	Leaves	Tree	Wild	Leaves are boiled in water to get a decoction.	0.86	0.029
Argyrolobium roseum (Cambess.) Jaub. & Spach (MU-HBD-USTB-11)	Makin betai	Whole plant	Herb	Wild	A juice of fresh plant is used.	0.75	0.026
Trigonella foenum-graecum L. (MU-HBD-USTB-52)	Shambreta / Methi	Aerial parts , seeds	Herb	Wild	A decoction (300 g/1 L water) of fresh plant is used two times a day before meal. The seeds powder mixed with flour and sugar is cooked and used for two months.	2.79	0.096

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FAGACEAE							
Quercus baloot Griff (MU-HBD-USTB-41)	Sayreye	Fruit	Tree	Wild	A decoction of 100 dried fruit in 500 ml water is used directly as a raw drug.	0.64	0.022
LAMIACEAE							
Ajuga integrifolia Buch. Ham. (MU-HBD-USTB-05)	Soi beetaie	Whole plant	Herb	Wild	Crushed plant juice is taken two times a day before meal.	0.43	0.015
Ballota pseudodictamnus (L.) Benth. (MU-HBD-USTB-15)	Kastoraie	Aerial parts	Herb	Wild	A decoction of the aerial part is used.	0.75	0.026
Marrubium vulgare L. (MU-HBD-USTB-32)	Dorshol/Bu taka	Aerial parts	Herb	Wild	Leaves decoction (100 g/ 1L water) one table spoon is taken early in morning.	0.64	0.022
Mentha longifolia (L.) L. (MU-HBD-USTB-34)	Zangli welany or podina	Aerial parts	Herb	Wild	Aerial parts cooked as vegetable or are boiled in water to get a decoction. Some informants mentioned powder.	0.54	0.018
Salvia reflexa Hornem. (MU-HBD-USTB-44)	Sugar boti	Aerial parts	Herb	Wild	A decoction of shade dried aerial parts (10 g / 250ml) is used.	0.75	0.026
Teucrium stocksianum Boiss. (MU-HBD-USTB-51)	Harboty/ Gul bahar	Aerial parts	Herb	Wild	Fresh or dried aerial parts are boiled in water to get a decoction and then diluted with water.	0.54	0.018
MALVACEAE							
Abelmoschus moschatus Medik. (MU-HBD-USTB-01)	Bhandi	Fruit	Herb	Cultivated	Fruit directly eaten as raw by diabetes or cooked as vegetable.	0.75	0.026
MELIACEAE							
Azadirachta indica A. Juss. (MU-HBD-USTB-14)	Neem	Leaves, seeds	Tree	Wild	1Kg fresh leaves and seeds in 5 L water is boiled to get a decoction, which is taken before meal two times a day. Crushed leaves juice is also used.	2.36	0.081
Melia azedarach L. (MU-HBD-USTB-33)	Bakayan	Leaves and seeds	Tree	Wild	1 Kg fresh leaves and seeds in 5 L water is boiled to get a decoction, which is taken before meal two times a day.	2.79	0.096
MORACEAE							
Ficus benghalensis L. (MU-HBD-USTB-29)	Bar	Bark and root	Tree	Cultivated	500 g bark or root decoction prepared in 1 L water is used for treatment of diabetes.	2.26	0.077
MYRTACEAE							
Eucalyptus globulus Labill. (MU-HBD-USTB-25)	Safida, L	Bark and leaves	Tree	Wild	Bark and leaves decoction is considered useful.	1.40	0.048
Syzygium cumini (L.) Skeels (MU-HBD-USTB-48)	Jamu	Fruit, leaves and seeds	Tree	Cultivated	5-10 dry or fresh fruit is directly used per day and 300 g dry or fresh leaves and seeds decoction is orally taken to control diabetic condition.	2.36	0.081

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NITRARIACEAE							
Peganum harmala L. (MU-HBD-USTB-39)	Spenalai or sponda	Seeds	Herb	Wild	10 g of seeds powder with a glass of water or seeds decoction (50/400 ml in water) is taken two times a day.	2.04	0.070
OLEACEAE							
Olea ferruginea Wall. ex Aitch. (MU-HBD-USTB-38)	Shwawan	Branches, leaves and seeds	Tree	Wild	Branches, leaves and seeds are boiled in water to get a decoction or hot water infusion of leaves is used. Fruit powder is also used.	1.93	0.066
PINACEAE							
Abies pindrow (Royle ex D. Don) Royle (MU-HBD-USTB-02)	Bejoor	Seeds	Tree	Wild	A decoction of seeds (½ Kg) prepared in water is taken orally two time per day one spoon before meal.	0.64	0.022
Pinus gerardiana Wall. ex D. Don (MU-HBD-USTB-40)	Nakhter	Seeds	Tree	Wild	Seeds are directly consumed as raw drug.	0.21	0.007
PLANTAGINACEAE							
Nanorrhinum ramosissimum (Wall.) Betsche (MU-HBD-USTB-36)	Sanoba	Whole plant	Herb	Wild	Dried plant in decoction or powder is considered useful in diabetes.	0.64	0.022
RANUNCULACEAE							
Nigella sativa L. (MU-HBD-USTB-37)	Kalwangi	Seeds	Herb	Wild	200mg seeds are used two times directly or grinded into powder.	1.83	0.063
RHAMNACEAE							
Ziziphus jajuba Mill. (MU-HBD-USTB-56)	Beer	Fruit	Tree	Wild	Fruit is directly consumed as drug.	0.86	0.029
Ziziphus nummularia (Burm.f.) Wight & Arn. (MU-HBD-USTB-57)	Elani/ karkanra	Whole plant	Shrub	Wild	A decoction of 50 g leaves in 300 ml water is used. Fresh or dried fruits are directly used.	0.43	0.015
ROSACEAE							
Rubus vestitus Weihe (MU-HBD-USTB-43)	Kauarch	Fruit	Shrub	Wild	100g fresh or 30g dry fruit per day is directly used.	0.64	0.022
RUTACEAE							
Citrus sinensis (L.) Osbeck (MU-HBD-USTB-22)	Malta	Fruit	Shrub	Cultivated	Dried pericarp slices are cooked in rice for treatment of diabetes.	0.86	0.029
SANTALACEAE							
Viscum album L. Wight & Arn (MU-HBD-USTB-53)	Verai	Whole plant	Shrub	Wild	250g of shade dried whole plant is boiled in 1L water and the decoction is taken orally two feeding spoons a day.	0.75	0.026
SAPOTACEAE							
Sideroxylon mascatense (A. DC.) T.D. Penn. (MU-HBD-USTB-45)	Gurgura	Seeds and fruit	Shrub	Wild	2g seeds powder or 20 dried fruit at night is considered useful.	0.43	0.015
SOLANACEAE							
Solanum surattense Burm. f. (MU-HBD-USTB-46)	Marghony	Fruit	Herb	Wild	2g fruit powder with sufficient water is taken before meal two times a day.	1.18	0.040

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Withania coagulans (Stocks) Dunal (MU-HBD-USTB-54)	Hamazeera, shapyanga or hafyanga	Fruit and leaves	Under shrub	Wild	Dried fruit powder 1-3g is taken before meal. Overnight infusion of 10g fruit in 50 ml water is used early in the morning. A diluted decoction of shade dried leaves is taken half of spoon two times a day.	3.01	0.103
XANTHORROEACEAE							
Aloe vera (L.) Burm. f. (MU-HBD-USTB-10)	Gurgunyal, Zargoya	Leaves	Under shrub	Wild	Leaves are pressed to get juice or dried leaves are boiled in water to get decoction. The juice mixed with water and decoction is taken thrice a day.	1.50	0.051
ZINGIBERACEAE							
Zingiber officinale Roscoe (MU-HBD-USTB-55)	Adrek	Rhizome	Herb	Cultivated	Powder eaten or put in water and drink.	0.64	0.022
ZYGOPHYLLACEAE							
Fagonia cretica L. (MU-HBD-USTB-28)	Spelaghzia, Azaghai	Aerial parts	Herb	Wild	Aerial parts are crushed, or cooked as decoction of the aerial part is used for the treatment of diabetes.	2.69	0.092

Abbreviations: RFC: Relative frequency of citation, UV: Use value

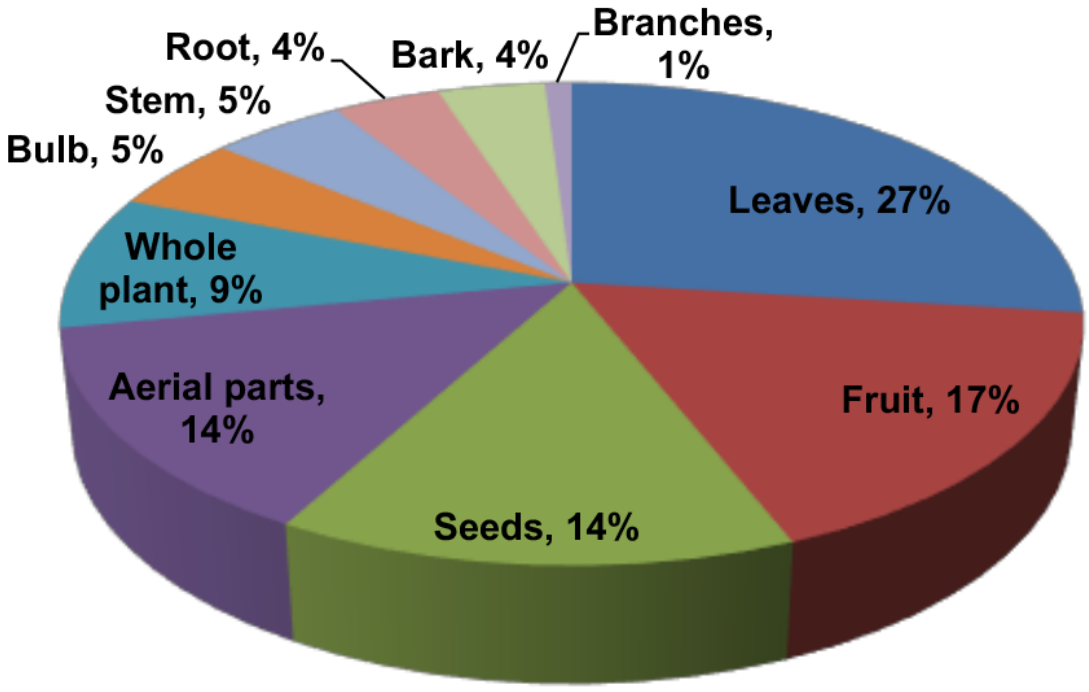

Figure 3. Plant parts used in management of diabetes

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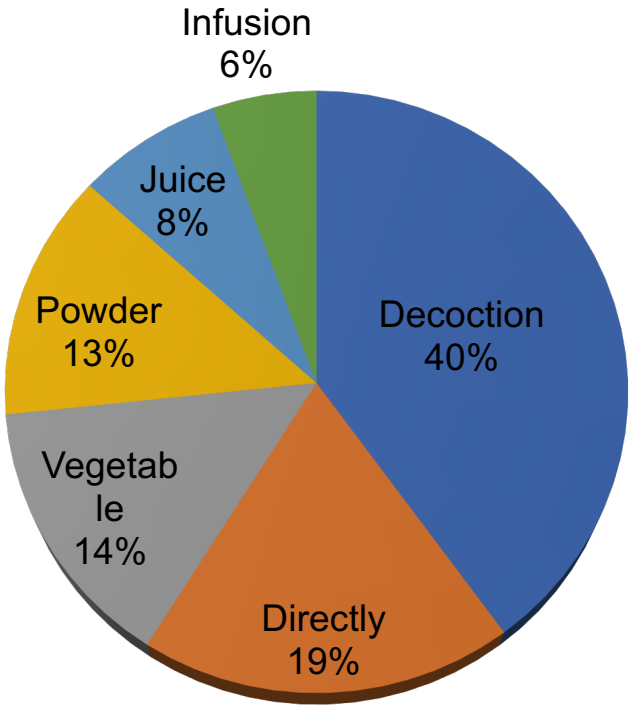

Figure 4. Methods of preparation of remedies

Discussion

The traditional healers (Hakeems) are the locals that mostly deal in treatment through medicinal plants. While shopkeepers selling herbals products or herbs are called 'Pansars'. The 'Pansars' are not necessarily involved in curing diseases. Many of the elders in the territory are recognized as the persons having greater knowledge after healers.

The traditional healers, knowledgeable elders and locals lay people commonly used the term 'sugar' for diabetes. A majority of the healers 61 (72%) and elders 112 (60%) linked diabetes to consumption of more sugar. Five traditional healers (6%) and 28 (15%) elders mentioned genetic factors as the cause of diabetes. The remaining healers 19 (22%) and elders 46 (25%) mentioned both genetic factors and consumption more sugar. Most of the healers and elders did not employ modern methods for diagnosis of diseases. They diagnosed diseases by certain symptoms as gathering of ants around urine, slow healing of wound, high thirst, frequent urination, rough and hard skin, weight loss and weak legs. The healers (84%) recommended the patients to reduce the consumption of sugar in order to prevent the severity of diabetes. The remaining (16 %) declared that proper consumption of food items can halt the onset of this disorder. Most of the healers and knowledgeable elders considered exercise as the main way to prevent the severity caused by diabetes.

The healers were found involved in diagnosis of diabetes patients; and they usually prescribed the available antidiabetic plants for the patients. The elder's belief in the traditional treatment through available plant resource also fortifies the local dependency on herbal remedies for treatment of diabetes. The communities of remote localities were more reliant and confident on traditional antidiabetic plants as compared to communities living around cities. The easy accessibility to synthetic medicines has now greatly affected the communities living around cities. A majority of the inhabitants in the remote communities are however unable to get access to modern health facilities due to poor economic conditions.

The ethnopharmacological information collected from elders in this study showed that much of the indigenous knowledge remains intact with the aged people. The elders disclosed that in time of need plant parts were mostly collected from the wild. The elders also pointed out that preparation of herbal recipes was a time-consuming process, and that the recipes needed preservation. Many residents purchase antidiabetic plants recipes from local market. The elders also stated that most of the residents did not keep antidiabetic plants on account of easy accessibility to traditional healers and modern synthetic medicines. Along these, two main factors responsible for elimination of traditional knowledge from the area were; lack of interest in the

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young generation to use available medicinal plants and that most of the traditional healers kept their knowledge secret (W. Hussain, Badshah, *et al*. 2018).

The dominance use of the two families Asteraceae and Lamiaceae is linked to their wide distribution and high diversity in the study area, and their activity has been linked to their compound composition (Güzel, Güzelşemme, and Miski 2015; Fortini *et al*. 2016). Our results agree with the findings of ethnobotanical studies conducted by (Demie, Negash, and Awas 2018) in South-eastern, Ethiopia, (Faruque *et al*. 2018) in the Bandarban District of Bangladesh and (Barkaoui *et al*. 2017) in Morocco. This study also specifies that most of the families contributed a single or two species which reflects the diversity of traditional antidiabetic plants in the area.

Among the plant parts leaves, fruit and seeds were also reported as the frequently used plant parts in the ethnobotanical study from the Algerian steppe (Miara *et al*. 2018). The frequent use of leaves in formulation of recipes has also been reported in the recent ethnobotanical studies (Demie, Negash, and Awas 2018; Faruque *et al*. 2018; Miara *et al*. 2018; Barkaoui *et al*. 2017; Krupa *et al*. 2018; Tag *et al*. 2012). This may linked to a higher amount of bio-active compounds in leaves (M. Ullah *et al*. 2013; Yemele *et al*. 2015; Ghorbani 2005)**.** The low use of roots in this study could be attributed to unavailability and more laborious job of harvesting, whilst the lesser use of stem bark and branches may relates to frequent use of herbs for treatment of diabetes (Semenya, Potgieter, and Erasmus 2012). In the perspective of conservation of plant species, the use of leaves in preparations of recipes has a more sustainable affect but collection of whole plant may lead to loss of biodiversity from the area. The over-exploitation of fruits and seeds may lead to loss of genetic diversity and distribution of species. All the remedies are administered orally, where water is used as solvent in preparation of remedies. Decoction was also a common method of remedies preparation as reported in the ethnobotanical studies (Adeniyi *et al*. 2018; W. Hussain, Ullah, *et al*. 2018; Miara *et al*. 2018; Barkaoui *et al*. 2017).

The indigenous use of the reported plants was compared with available literature in BioMed Central, Google Scholar, PubMed, PubMed, SCOPUS, and Web of Science. It was found that most of the current study plants have already been reported in the ethnobotanical studies conducted in other parts of the country and around the globe (Table 3). According to the findings of this study six plant taxa; *Allium carolinianum* DC., *Artemisia scoparia* Waldst. & Kitam., *Eruca vesicaria* (L.) Cav., *Salvia reflexa* Hornem. *Sideroxylon mascatense* (A.DC.) T.D. Penn. and *Viscum album* L. Wight & Arn were recorded for the first time as antidiabetic agent in comparison to the ethnobotanical literature. The results of this study indicate that on the basis of a single pathology a higher number of plants with accurate information were collected as compared to general ethnobotanical studies conducted in the area. The higher use of some of the wild plants e.g., *Withania coagulans* and *Caralluma tuberculata* in the area has created threats to loss of biodiversity from the area. Hence, conservation strategies are necessary to ensure sustainable use of these plants. Scientific validation of medicinal plants based on their traditional use is a very promising approach. Such approach needs careful observation and relevant data such as method of preparation, amount and toxicology of crude drug used. Many plants reported in this study were found having strong antidiabetic activities and several active constituents have been isolated from these plants.

Some details on antidiabetic plants used in the study area

Allium cepa L. (Onion)

A. cepa is an important antidiabetic plant cultivated throughout Pakistan as a culinary agent. The potential of *A. cepa* L. as antidiabetic has been investigated in both human and animal's model. The bulb aqueous extract (0.4g/100 g body weight) significantly decreased blood glucose level by (70%), urea (16%), creatinine (32%) and bilirubin (28%) in alloxan induced rats (El-Demerdash, Yousef, and El-Naga 2005). In another similar test in rabbit the aqueous extract at dose 100 and 300 mg/kg body weight significantly lowered blood glucose level and established the decreased levels of antioxidant enzymes (Ogunmodede *et al*. 2012). In a human model, the fresh bulb slices at a dose (100 g) were given to type 1 and 2 diabetic persons. The dose decreases blood glucose level by (50%) in type 1 diabetic person at 4 hours after administration in comparison to insulin-treated (70.8%) diabetic person. The reduction was 20% in type 2 diabetic person compared to 37.5% in insulin-treated person (Eldin, Ahmed, and Abd 2010). A diet supplemented with 3% freeze-dried onion powder was feed to Streptozotocin (STZ) induced rats for 8 weeks that significantly lowered blood glucose and showed strong anti-oxidant potential (Babu and Srinivasan 1997). The isolated sulphur amino acid S-methyl cysteine sulphoxide at a dose of (200 mg/kg body weight) for 45 days showed significant hypoglycaemic activity, controlled lipids in serum and tissues and restored the potential of liver hexokinase, glucose 6-phosphatase and 3-Hydroxy-3-Methyl-Glutaryl-CoA (HMG CoA) reductase (Kumari, Mathew, and Augusti 1995).

Allium sativum L. (Garlic)

A. sativum is cultivated throughout Pakistan as an important culinary agent. Its cloves are eaten as raw by diabetes patients to control blood sugar and cholesterol. Its potential as antidiabetic agent was investigated in animal's model. The aqueous extract of bulb at a dose of (0.4g/100 g) body weight significantly decreased blood glucose level by (68%), urea (14%), creatinine (26%) and bilirubin (25%) in alloxan induced rats (El-Demerdash, Yousef, and El-Naga 2005). In another experiment administration of aqueous extract for one week in alloxan induced diabetes rats significantly decreased blood glucose level (Eyo, Ozougwu, and Echi 2011). In 2006 (Eidi, Eidi, and Esmaeili 2006) evaluated the ethanolic

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extract in STZ induced rats. The extract at a dose of 250 and 500 mg/kg body weight administration for 14 days produced a dose-dependent decrease in serum glucose, lipid levels, liver function enzyme levels and increased serum insulin levels. The isolated constituent S-allyl cysteine sulphoxide from *A. sativum* has significantly decreased the concentration of serum lipids, blood glucose and activities of serum enzymes like alkaline phosphatase, acid phosphatase, lactate dehydrogenase and liver glucose-6-phosphatase in alloxan induced diabetes rats (Sheela and Augusti 1992).

***Aloe vera* (L.) Burm.f. (Indian Aloe)**

A well-known traditional medicinal plant *A. vera* is commonly used as wound healing agent in Pakistan. The aerial parts ethanolic extract (100 and 500 mg/kg body weight) was employed in normal and hyperglycaemic rats (Afaf, Osman, and Elmahdi 2008). The extract at dose 100 mg/kg exhibited similar effect to the standard drug glibenclamide in lowering plasma glucose level while highly significant reduction ($P< 0.01$) in plasma glucose level in the group received 500 mg/kg of the extract. Similarly, dried exudate of leaves at dose of 150 mg/kg body weight has reduced fasting blood glucose level and improved the levels of the antioxidant enzymes in STZ induced rats (Nwajo 2006). The gelatinous extract from leaves (350 mg/kg body weight) containing aloin (181.7 mg/g) and aloe-emodin (3.6 mg/g) has been investigated in experimentally insulin resistant mice administered for 4 weeks. The extract improved insulin tolerance and fasting blood glucose level (Pérez *et al*. 2007). In another long term experiment fresh leaf ethanolic extract (300, 500 mg/kg body weight) in alloxan and STZ induced diabetic rats have significantly reduced fasting blood glucose level at day 42 as (44%) and (73%), respectively (Shinde, Borkar, and Badwaik 2014).

***Azadirachta indica* A. Juss. (Neem)**

The most commonly used plant in Pakistan as refrigerant is *A. indica.* Its antidiabetic effect is evident as the leaves ethanolic extract in normal and STZ (25 mg/ml) induced diabetes rats enhance release of insulin from the pancreas (Chattopadhyay and Bandyopadhyay 2005) while leaves ethanolic extract (500 mg/kg) in STZ induced diabetes rats decreased blood glucose level and improved pancreatic lesions (Akinola, Caxton-Martins, and Dini 2010).

***Berberis lycium* Royle (Indian Barberry)**

An important ethnomedicinal plant *B. lycium* root ethanolic extract (50 mg/kg, 100 mg/kg) in alloxanized rats decreased blood glucose from 512 to 396 and 519 to 351, respectively (Gulfraz *et al*. 2007). In another test, the crude water extract at dose of (250, 500 mg/kg body weight) significantly reduced blood glucose level in both normal and diabetic rabbits (M. Ahmed and Alamgeer 2009).

***Caralluma tuberculata* N.E. Br. (Bitter cress)**

Among the wild vegetables, *C. tuberculata* was the most preferred plant for diabetes. The antidiabetic potential of its aerial parts methanol extract has been tested in STZ induced rats. The extract at dose of 500 mg/ kg body weight/day decreased fasting blood glucose level in hyperglycaemic condition up to 54% at 4th week with concomitant increase in plasma insulin by 206.8%. A significant decrease in total cholesterol, triglycerides and low density cholesterol levels by 41.5%, 36.7% and 49.1% have been justified, respectively. An increase of 147.97% in the cardio-protective lipid high density cholesterol with extract has been observed in comparison to diabetic rat value (Abdel-Sattar *et al*. 2011).

***Citrullus colocynthis* (L.) Schrad. (Desert gourd or bitter apple)**

Another important plant *C. colocynthis* fruit is considered useful remedy. Its fruit pulp extract in STZ induced rats has been found to decrease blood glucose level after 3 and 8 hours and standard drug after 1st & 6th hours, significantly. Insulin levels have also improved at same time intervals (Vinaykumar, Eswarkumar, & Roy). The saponin fraction from aqueous extract of rind was investigated in normoglycaemic and alloxan induced rabbit (Abdel-Hassan, Abdel-Barry, and Mohammeda 2000). The fraction with administration of 50 mg/kg body weight decreased plasma glucose in both types of rabbit. The administration of aqueous extract of leaves at a dose of 250 and 500 mg/kg body weight significantly reduced blood glucose level from 381 ± 34 to 105 ± 35 in alloxanized rats (Gurudeeban and Ramanathan 2010). (Sebbagh *et al*. 2009) fed STZ induced diabetes rats with 8% colocynth oil diet. They found significant decrease in plasma glucose levels and restored pancreatic β-cell mass to normal. In clinical study on 50 type II diabetic patients' 100 mg fruit capsules or placebos three times a day significantly decreased glycated haemoglobin (HbA1c) and fasting blood glucose level (Huseini *et al*. 2009).

***Fagonia cretica* L. (Virgin's Mantle)**

F. cretica is a common blood purifying agent in Pakistan and its aerial parts juice or decoction is used for treatment of diabetes. The water extract at dose of 500 mg/kg was effective in the management of diabetes, causing a 45% decrease in the plasma glucose level (Nazir *et al*. 2017).

***Melia azedarach* L. (Pride of India or chinaberry tree)**

The extract of *M. azedarach* injected intraperitoneally mice showed dose-dependent antidiabetic effects similar to glibenclamide (Seifu *et al*. 2017). It ethanolic extract in STZ induced diabetes rat significantly decrease blood glucose level (M. F. Khan *et al*. 2018).

***Momordica charantia* L. (Bitter gourd)**

M. charantia is a common vegetable and recognize as antidiabetic plant in Pakistan. The fresh fruit juice in oral administration test in type 1 diabetic rats at 10 ml/kg body weight lowered blood glucose level

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significantly after 30 and 90 minutes by about (30%) and (10%) (Matheka *et al*. 2012).

***Rhazya stricta* Decne (Harmel)**
The desert plant *R. stricta* fruit and leaves methanol extracts (80%) was evaluated in STZ induced mice. The fruit extract has lowered blood glucose level from (283.34±5.68) to (219±77.62) in male and from (344±31) to (146.00±40.36) in female while leaves extract from (289.67±64.36) to (178.34±17.03). Leaves extract has effectively lowered glycosylated hemoglobin to (6.3±0.7%) in male and also reduced total cholesterol content from (147.88±21.83 mg/dl) and (125.89±14.03 mg/dl) in male and female mice, respectively (A. Ahmed *et al*. 2015).

***Syzygium cumini* (L.) Skeels. (Black plum, Java plum)**
Syzygium cumini is an important antidiabetic plant with fruit, leaves and seeds used for treatment of diabetes. The leaves aqueous extract (25, 50, 75 and 100 mg/ml) inhibit α-amylase activity by (60.52%), (66.23%), (69.33%) and (71.71%) (Sathiavelu *et al*. 2013). In another experiment barks, leaves, root and seeds significantly ($P< 0.001$) reversed hyperglycaemic activity (Deb *et al*. 2013). Four active compounds (Lupeol, 12-oleanen-3-ol-3ß-acetate, stigmasterol and ß-sitosterol) have been isolated from leaves n-hexane fraction (Alam *et al*. 2012).

***Trigonella foenum-graecum* L. (Fenugreek)**
T. foenum-graecum seeds ethanolic extract (2g/kg, 1g/kg, 0.5g/kg and 0.1g/kg) in alloxan induced rats. The extract in diabetic rats significantly ($p<0.05$) reduced blood glucose by (33.92 %) comparable to that of standard drug, glimepiride (4mg/kg) (35.26%) (Mowl *et al*. 2009).

***Withania coagulans* Dunal (Vegetable rennet, Indian cheese maker)**
W. coagulans fruit aqueous extract in STZ induced diabetic rats at a dose of 1 g/kg significantly decrease blood glucose, serum lipid peroxidase, cholesterol, hepatic lipid peroxidase level (Hemalatha *et al*. 2004). The fruit aqueous extract in another experiment at a dose of 1000 mg/kg has shown maximum fall of 33.2% in fasting blood glucose after 4h and, by 52.9% on 30th day comparable to glipizide (49.2%) (Jaiswal, Rai, and Watal 2009). The fruits aqueous extract (1 g/kg body weight) after 7 days demonstrated significant decrease ($p < 0.01$) in the blood glucose by (52%), triglycerides, total cholesterol, low density lipid, very low density lipid and very significant increase ($p < 0.01$) in high density lipids (Hoda *et al*. 2010). The aqueous extract of flower and root (150, 200 mg/kg body weight) administration significantly reversed blood glucose and decreased the glycated haemoglobin level by 26 and 44%, respectively (Bharti *et al*. 2012).

Toxicology
Plant based medicines are often considered to be safe and effective agents (George 2011). However, the idea that traditional medicinal products which come from natural sources are completely safe is dangerously false (Calixto 2000). The documentation of medicinal plants and their toxic effects is very essential in the ethnobotanical studies. The locals in the area recognized this problem and were very cautious in selection of antidiabetic plants. Potentially toxic plants used as anti-diabetics in this study were *Artemisia scoparia* Waldst. & Kitam., *Citrullus colocynthis* (L.) Schrad. *Euphorbia hirta* L. *Marrubium vulgare* L. *Solanum surattense* Burm. f., *Tanacetum artemisioides* L. *Teucrium stocksianum* Boiss., and *Withania coagulans* (Stocks) Dunal. The participants stated that preparations of these plants were diluted before use.

Conclusions
This is the first ethnobotanical study on antidiabetic plants from communities residing in the southern and tribal districts of Khyber Pakhtunkhwa Pakistan. The results indicate that the communities residing in the area have a rich knowledge of antidiabetic plants. The study also highlights that most the plants are collected from wild. Further investigation on the reported plant based on their traditional use is essential. The higher use of some of the wild plants in the area has created threats to loss of biodiversity from the area. Hence, it also prioritizes plant resource for conservation and sustainable use.

Declarations
Conflict of interest: The authors declare that they have no conflict of interest.

List of Abbreviations:
HbA1c: Glycated haemoglobin
RFC: Relative Frequency of Citation
STZ: Streptozotocin
UV: Use value.

Ethics approval and consent to participate: All participants provided prior oral consent. The study followed the Code of Ethics of the International Society of Ethnobiology (ISE, 2006)

Consent for publication: Not applicable

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Author contribution: MU conducted the collection of field data and wrote the initial draft of the manuscript. SM and RAK supervised the project. MA and WH assisted in the field survey, sampling, and identification of taxon. RU, RB and MAS helped in the data analysis and revision of the manuscript.

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Annex

Questionnaire for collecting antidiabetic plant data

A. Informant details	
1. Name:	
2. Gender:	
3 Ages:	
4 Occupations:	
5. Location/Residence:	
B. Informant knowledge about antidiabetic plants	
1. Name the plants which are used for treatment of diabetes in the area?	
2. Which part of the plants is used in preparation of remedies?	
3. How the plant is formulated?	
4. How the plant is used?	
5. How you collect the plants and store their recipes?	
6. Mention any side effects of the plants.	
7. Any comment.	
C. Informants' consensus on diabetes	
1. How you recognize diabetes patient?	
2. How diabetes occurred?	

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