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# INDIGENOUS PLANTS OF PAKISTAN FOR THE TREATMENT OF DIABETES: A REVIEW

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## ABSTRACT

Diabetes is the most growing disease and becoming the third 'killer' of mankind, after cancer and cardiovascular diseases due to its high prevalence, morbidity, and mortality. According to the Diabetes Prevalence Survey of Pakistan (2017), approximately 21.9 million adult population of Pakistan is suffering from diabetes mellitus. Pakistan's National Diabetes Survey stated that 26 percent of Pakistanis are victims of diabetes. According to a fresh survey (2017) conducted by Hayatabad Medical Complex, Peshawar "One in every six persons is diabetic in Pakistan". The severity of this disease is increasing day by day in the world as well as in Pakistan. As Pakistan is a developing country, it is impossible to provide modern medical facilities for the treatment of diabetes to every person. But indigenous medicinal plants are the potential candidates to cure this disease. A variety of chemical compounds (i.e., polyphenols, flavonoids, alkaloids, terpenoids, phenolic content, tannins, saponin and glycoside) present in the various parts of the indigenous plants e.g. leaves, roots, stem, wood, fruit, seeds, flowers etc which alone or with the combination of other compounds gives superior effects in the management of this disease. This review will provide information about the antidiabetic potential of indigenous plants of Pakistan along with the local names, their region of availability in Pakistan, and their antidiabetic bioactive compounds which are reported in research studies.

***Keywords*:** Diabetes mellitus, Hyperglycemia, Indigenous plants of Pakistan, Medicinal Plants, Herbal Medicines

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## 1. INTRODUCTION

Diabetes mellitus is very common disease of developed and developing countries which increasing day by day. It is due to abnormal metabolism of carbohydrates and elevated the blood glucose level in the patient. Main source of energy in our body is glucose. In our body, food is converted into glucose after digestion and move toward cells through blood stream. Our cells utilize glucose for energy. A hormone excreted by pancreas known as insulin, is essential for glucose uptake into cells (Riaz 2009). By any problem, if insulin is not excreted by pancreas, then body cells are unable to uptake glucose which leads to high glucose level in the blood. This creates hyperglycemic condition in the blood (Piero et al. 2015).

### 1.1. Classification of Diabetes mellitus

Diabetes is divided into three types, Types 1 Diabetes, Types 2 Diabetes and Gestational Diabetes. Type 1 diabetes is produced when pancreas fail to generate insulin. Body cells can't uptake glucose to produce energy in the absence of insulin which creates hyperglycemic condition in the blood (Gao et al. 2017) And insulin is provided to the type 1 diabetes patient through injection every day to control blood glucose level. That's why it also known as insulin dependent diabetes mellitus. But, Type 2 diabetes is due to resistance of body cell to use insulin. Glucose in the blood increased because cells are unable to use insulin properly to uptake glucose (Gao et al. 2017). That's why it's also called Non-insulin dependent diabetes mellitus. While, Gestational Diabetes is the form of diabetes in which during pregnancy blood glucose increases and reduce or become normal after the baby birth. It is due to hormonal changes in the mother body during pregnancy (Riaz 2009). Mostly traditional medicines are used to cure gestational diabetes.

Medicinal plants are the part of traditional medicinal system for the human health care (Karunamoorthi et al. 2013). Curing of different diseases by using the herbal remedies is very common in Pakistan. Herbal based medicine has fewer side effects in the human body as compare to synthetic products. Pakistan has hug diversity of medicinal plant due to it topography and variety of climatic zone (Shinwari 2010). In the world, more than 1200 medicinal plants are used to cure diabetes. There are many medicinal plants in Pakistan that have significant

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potential to control and cure the diabetes disorders. Plants contain different phytochemical and bioactive compound like polyphenols, flavonoids, alkaloids Terpenoids, Phenolic content, Tannins Saponin, glycoside and different protein-based compound, which play their role in insulin production and glucose uptake (Tran et al. 2020).

Indigenous plants of Pakistan, which have potential to treat the diabetes mostly belongs to the families like Acanthaceae, Amaranthaceae, Amarylldaceae, Anacardiaceae, Annonaceae, Apiaceae, Apocynaceae, Arecaceae, Aristolochiaceae, Asphodelaceae, Asteraceae, Bombacaceae, Brassicaceae, Burseraceae, Combretaceae, Commelinaceae, Cucurbitaceae, Euphorbiaceae, Fabaceae, Gentianaceae, Ginkgoaceae, Lamiaceae, Lythraceae, Malvacea, Meliaceae, Menispermaceae, Moraceae, Musaceae, Myrtaceae, Nelumbonaceae, Nyctaginaceae, Oleaceae, Phyllanthaceae, Plantaginaceae, Poaceae, Ranunculaceae, Rhamnaceae, Rosaceae, Rutaceae, Sapotaceae, Solanaceae, Theaceae, Urticaceae, Verbenaceae and Zingiberaceae.

### 1.2. Traditional antidiabetic plants

There are numerous indigenous plants of Pakistan that are being used as antidiabetic remedies throughout the world. Details of plants including their plant's botanical name, vernacular name, English name, family they belong to, part being used, plant location in Pakistan and active ingredient used for the remedy of diabetes (Table 1), diabetes type 1 (Table 2), diabetes type 2 (Table 3) and diabetes type 1 and type 2 (Table 4) have been presented.

There are some identified plants that used by peoples in northern areas traditionally and also use in Unani medicine by hakims in Pakistan. Those plants are *Allium cepa*, *Artemisia herba-alba*, *Cassia absus*, *Cassia fistula*, *Cichorium intybus*, *Eclipta alba*, *Eucalyptus globulus*, *Ficus benghalensis*, *Glycyrrhiza glabra*, *Gymnema sylvestre*, *Justicia adhatoda*, *Momordica charantia*, *Murraya koenigii*, *Phyllanthus amarus*, *Silybum marianum*, *Syzygium cumini*, *Terminalia chebula*, *Trigonella foenum-graecum*, *Ocimum sanctum* and *Zingiber officinale* (Ahmad et al. 2009).

**Table 1:** Indigenous plants of Pakistan being used for diabetes mellitus

| Sr. No. | Botanical Name | Vernacular Name | English Name | Family | Part Used | Location | Active Ingredient | References |
|---|---|---|---|---|---|---|---|---|
| 1. | *Dichrostachys cinerea* L. | Viravriksha | Bell mimosa, Chinese lantern tree | Fabaceae | Whole plant | Punjab (Cholistan Desert) | Flavonoid (Mesquitol) | Suresh et al. (2012) |
| 2. | *Lepidium sativum* L. | Hailon | Garden cress | Brassicaceae | Seed | Wild in KPK, Central Punjab, Baluchistan | Imidazole Alkaloids (Lepidine and Semilepidine) | Shukla et al. (2012a) |
| 3. | *Madhuca longifolia* | Mahua, Gilaunda, Gul-chikan, Gulu | Honey tree, Butter tree | Sapotaceae | Leaf, Bark | Punjab, Sindh | Phenolic compounds | Prashanth et al. (2010) |
| 4. | *Olea ferruginea* | Jangli Zaetoon, Kahu | Indian olive | Oleaceae | Fruit | KPK, Punjab, FATA, Baluchistan | - | Ahmad et al. (2004) |
| 5. | *Pongamia pinnata* | Sukh chain | Pongam tree, Indian beech tree | Fabaceae | Leaf, Flower, Stem bark | Punjab, Sindh, Baluchistan | Flavonoids, Furoflavones, Triterpenoids, Phytosterols, Tannins | Sikarwar and Patil (2010) |
| 6. | *Senna sophera* | Kasundi | Pepper-leaved senna | Fabaceae | Leaf | Punjab (Sargodha) | Hexahydroxy diphenic acid and Kaempferol. | Kharat et al. (2019) |
| 7. | *Terminalia bellirica* | Baherra | Beach almond | Combretaceae | Fruit (pulp) | Northern Punjab (Rawalpindi) | Octyl gallate | Latha and Daisy et al. (2013) |
| 8. | *Withania somnifera* (L) *Dunal* | Ashwagandha | Poison gooseberry, Winter cherry | Solanaceae | Leaf, Root | KPK, Punjab | Withaferin A | Gorelick et al. (2015) |
| 9. | *Ziziphus sativa Gaertn* | Annab | Red date tree | Rhamnaceae | Leaf | KPK (Swat) | - | Anand et al. (1989) |

### 1.3. *Allium cepa*

It is biennial plant but usually grow as annual, belong to the family Amaryllidaceae. It is bulbous vegetable and cultivated throughout the world. In Pakistan it is cultivated in Punjab, Sindh, Baluchistan province and some areas of KPK. But Sindh province is the contributor in its production. It is commonly known as Onion; in Urdu it's called "Piaz" in Pakistan. It contains certain chemical substances which irritate the eyes. Generally, it is used for cooking purpose and pungent when chopped. It contains flavonoid and polyphenols (Slimestad et al. 2007). Its bulb has anti-pathogenic activity (Shams-Ghahfarokhi et al. 2006), anticancer activity (Shrivastava and Ganesh 2010), hypolipidemic activity (Vidyavati et al. 2010), cardioprotective activity (Cavagnaro et al. 2007), hepatoprotective activity (Ige et al. 2009), anti-depressant activity (Sakakibara et al. 2008) and anti-diabetic activity (El-Demerdash et al. 2005). A Sulphur containing amino acid, S-methyl cysteine sulphoxide compound has antidiabetic and antihyperlipidemic effect, extracted from *Allium cepa* (Kumari et al. 1995). But in recent studies Kim et al. (2011) reported that quercetin is the most bioactive compound in *Allium cepa* that have blood glucose lowering potential via α-glucosidase inhibition in type 2 diabetes with other bioactive compounds. El-Soud and Khalil (2010) reported that antidiabetic property of *Allium cepa* may be due to antioxidant characteristics of its essential oil parts, avoiding hyperglycemia and dropping lipid shape composed with convert liver and kidney pathology formed by diabetes to normal pattern. El-Demerdash et al. (2005) reported that onion and garlic juices induce antioxidant and antihyperglycemic effects and consequently may alleviate liver and renal damage caused by alloxan-induced diabetes. Taj Eldin et al. (2010) reported that *Allium cepa* produced hypoglycemic effects, and can be used as a dietary supplement for the management of type 1 and type 2 diabetes mellitus (Table 4).

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**Table 2:** Indigenous plants of Pakistan being used for Type I diabetes mellitus

| Sr. No. | Botanical Name | Vernacular Name | English Name | Family | Part Used | Location | Active Ingredient | References |
|---|---|---|---|---|---|---|---|---|
| **1.** | *Alstonia scholaris* L. | Alstonia | Devil's tree | Apocynaceae | Stem bark | Punjab | Alkaloids, Terpenoids, Flavonoids, Saponins, Tannins, | Boggula et al. (2017) |
| 2. | *Beta vulgaris* L. | Chukandar | Beet | Amaranthaceae | Leaf, Root | KPK, Punjab and Sindh | Flavonoids, Phenolic compound (*C*-glycosidic flavones) | El-Ghffar et al. (2019) |
| 3. | *Cynodon dactylon* L. | Khabal or Barmuda grass | Barmuda grass, Dog's tooth grass | Poaceae | Root stalk | KPK, Punjab, Sindh, Baluchistan | Alkaloids, Flavonoids, Saponins, Tri Terpenoids, Phenolic, compounds | Kumar et al. (2011b) |
| 4. | *Elephantopus scaber* | Prickly-leaved Elephant's foot | Elephant foot | Asteraceae | Leaf, Root | Different parts of Pakistan | Steroids | Daisy et al. (2009) |
| 5. | *Gmelina arborea* | Kumbar | Goomar teak, Malay beechwood | Lamiaceae | Stem bark | Punjab | Flavonoids, Polyphenol compounds | Attanayake et al. (2016) |
| 6. | *Hibiscus rosa-sinensis* L. | Gurhal, Gudhal | Chinese Hibiscus, Shoe black plant | Malvacea | Leaf, Flower | Throughout the Pakistan | Flavonoid, Polyphenols | Pethe et al. (2017) |
| 7. | *Olea europaea* | Zatoon | Olive, European olive | Oleaceae | Leaf, Fruit | Punjab., Baluchistan, KPK, FATA | Oleuropein | Qadir et al. (2016) |
| 8. | *Origanum vulgare* L. | Sathar, Ban ajwain | Oregano | Lamiaceae | Leaf | KPK, Kashmir, Sindh | Rosmarinic acid | Vujicic et al. (2015) |
| 9. | *Trigonella foenum-graecum* | Methi | Fenugreek | Fabaceae | Seed | Punjab, KPK Baluchistan | GII compound | Moorthy et al. (2010) |

### 1.4. *Artemisia herba-alba*

*Artemisia herba-alba* is a perennial herb, contains strongly aromatic grayish green foliage, and belongs to family Asteraceae (Table 3). It is distributed in Iran, Turkey, Middle East, North Africa, India and Pakistan. It is widely grown in Quetta district of Baluchistan, Pakistan (Hayat et al. 2009). It is also known as white wormwood. But in Pakistan, it is called Mushki afsantheen. It has various classes of chemicals like flavonoids, phenolic compounds, sesquiterpene lactones, monoterpenoids (1,8-cineole, chrysanthenone, chrysanthenol, borneol and camphor) Entire plant is utilized in various traditional medicine due to its properties including antioxidant, antivenom, antibacterial, antispasmodic, anthelmintic, pesticidal activity, antibiotic resistance, antidiabetic, hypolipidemic, antifungal, antimicrobial and autoinflammatory (Mohamed et al. 2010). According to Awad et al. (2012), *Artemisia herba-alba* has traditionally been used for the curing jaundice, diabetes and gastric disturbance such as abdominal cramps, diarrhea, for healing wounds in Egyptians folk medicines. Awad et al. (2012) have reported the anti-diabetic activity of Artemisia herba-alba extract which is mainly due to presence of four compounds in it. These four compounds are β-sitosterol, cycloartenol, 24-methylenecycloartanol and apigenin which cure the diabetes by stimulating insulin production, by β-cells protective effects, inhibiting glucose absorption and insulinomimetic effect (increasing insulin secretion) respectively. Jemaa et al. (2015) reported that ethanolic extract of *Artemisia herba-alba* has not any effect on diabetic type 1 streptozotocin rat antidiabetic, hypolipidemic and antioxidant enzyme activities in type 2 diabetic rat. While, Bushara et al. (2017) reported that ethanolic extract of *Artemisia herba-alba* showed clear improvement in behavioral sign in diabetic rats. Plants may reserve catabolism of body glucose in the deficiency of insulin by increasing insulin production, by increasing glucose removal from blood, by stimulating glycolysis in peripheral tissue or reducing absorption of glucose from gastrointestinal tract. Aqueous extract of *Artemisia herba-alba* plant showed hypoglycemic effect after 2 hours of administration in alloxan induced diabetic rat, may be due to glucose utilization in peripheral tissues (Tastekin et al. 2006). Abdallah et al. (2015) reported that STZ-induced diabetic Wistar rats showed reduction in blood glucose level and hyperlipidemia along with improvement in hepatic and renal impairment when ethanolic extract of *Artemisia herba-alba* was orally administered for the 14 days.

### 1.5. *Cassia absus*

It is a small annual or small perennial plant of Caesalpiniaceae family. *Cassia absus* is the flowering plant with sparingly branches and found in India, Bhutan, Java, Bangladesh, East Timor, Pakistan, Indonesia, Nepal, Sri Lanka and Myanmar. In Pakistan, it is widely grown in Punjab and also found in Khyber Pakhtunkhwa (Table 3). It has different common names in literature like Pig's Senna, karum and Jasmeejaz but traditionally *Cassia absus* seeds are known as Chaksu in Pakistan. It contains different secondary metabolites like cardiac glycosides, saponins, flavonoids and steroids (Paul et al. 2016). Its seeds are reported as hypotensive, laxative, and anti-spasmodic. *Cassia absus* also prevents hemorrhage and useful for kidney, skins and liver diseases (Ahmad et al. 2017). Aqueous extract of *Cassia absus* seeds has hypoglycemic activity by decreasing blood glucose level, increasing insulin level and return the liver functions and serum lipid level to normal in diabetic rats (Rashid et al. 2017).

### 1.6. *Cassia fistula*

*Cassia fistula* is a Southeast Asian plant belongs to fabaceae family. It is commonly called golden shower tree. It is found in Asian countries like India, China, Philippines, Malaysia, Thailand, Hong Kong, Bangladesh and Pakistan. In Pakistan it is found in Punjab and KPK with the local name of Gurr di nail and Amaltaas. Traditionally,

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**Table 3:** Indigenous plants of Pakistan being used for Type 2 diabetes mellitus

| Sr. No. | Botanical Name | Vernacular Name | English Name | Family | Part Used | Location | Active Ingredient | References |
|---|---|---|---|---|---|---|---|---|
| 1. | *Acacia arabica* | Babul, keekar | Indian gum Arabic tree, black babul | Fabaceae | Seed, Bark | Punjab, Sindh, KPK and Baluchistan | Polyphenols, Tannins, flavonoids (Quercetin) | Hegazy et al. (2013) |
| 2. | *Achyranthes aspera* L | Pathlkanda | chaff-flower, prickly chaff flower | Amaranthaceae | Leaf | Punjab (Wild in D.G khan) | Ursolic acid, Oleonolic acid | Lakshmi et al. (2018) |
| 3. | *Aegle marmelos* | Belpather, Bel | Stone apple | Rutaceae | Leaf, Fruit | Sindh, Punjab, Lower Baluchistan | Aegelin, Eugenol, Limonene, Umbelliferon | Thokchom and Singh (2018) |
| 4. | *Allium sativum* L. | Lehsan, Thom | Garlic | Amaryllidaceae | Cloves | Punjab, KPK, Sindh, Baluchistan | S-allyl cysteine sulphoxide | Sheela and Augusti (1992) |
| 5. | *Aloe vera* | Kunwarghandel | Aloe vera | Asphodelaceae | Leaf, | Punjab, KPK, Sindh, Baluchistan | Aloin, Aloe-emodin | Younus and Anwar (2018) |
| 6. | *Annona squamosa* L. | Sharifa, Sitaphal | Sugar apple, custard apple | Annonaceae | Leaf | Sindh (Karachi) | Flavonoids | Shirwaikar et al. (2004) |
| 7. | *Areca catechu* L. | Supari, Phiki chaliya | Areca nut palm, Betel palm | Arecaceae | Nuts, Leaf, Stem | Sindh | Arecoline | Akhter et al. (2014) |
| 8. | *Aristolochia indica* L. | Hukka-bel | Indian birthwort | Aristolochiaceae | Leaf, Root | Punjab (Layyah) | β-sitosterol | Karan et al. (2012) |
| 9. | *Artemisia dracunculus* | Targoon, Sheni tarkha | Tarragon | Asteraceae | Leaf | Chitral, Kashmir and Gilgit (Nathar valley) | Flavonoids, Polyphenolic compounds | Mansoor et al. (2015) |
| 10. | *Artemisia herba-alba* | Mushki Afsantheen | White wormwood | Asteraceae | Whole plant | Baluchistan (Quetta) | β-sitosterol, Cycloartenol, 24-methylenecycloartanol, Apigenin | Awad et al. (2012) |
| 11. | *Azadirachta indica* | Neem | Indian lilac | Meliaceae | Leaf, Seed | Punjab, Sindh and Lower Baluchistan | Azadirachtolide (Tetranortriterpenoid) | Kumar et al. (2011a) |
| 12. | *Boerhavia diffusa* | Tukhm-e-ispat | Hogweed, Pigweed | Nyctaginaceae | Leaf, Root | KPK, Punjab (Rawalpindi, Attock Multan, Lahore) Sindh (Karachi), Baluchistan (Lasbella) | Alkaloid and Sterol compounds | Satheesh and Pari (2004) |
| 13. | *Brassica juncea* L. | Sarson or Saag | Mustard greens, Indian mustard | Brassicaceae | Leaf, Seed | Punjab | - | Thirumalai et al. (2011) |
| 14. | *Camellia sinensis* L. | Chai ka Powda | Tea plant | Theaceae | Leaf | KPK (Mansehra), Azad kashmir | Caffeine, Polyphenols compounds | Fu et al. (2017) |
| 15. | *Capsicum annuum* L. | Lal Mirch | Bell pepper | Solanaceae | Fruit | Sindh, Punjab, KPK and Baluchistan | Capsaicin, Dihydrocapsaicin, Eugenol, Tridecanoic acid, Phytol | Mohammed et al. (2017) |
| 16. | *Cassia absus* | Chaksu | Pig's senna | Caesalpiniaceae | Seed | Punjab, KPK | Glycosides, Saponins, Flavonoids, Steroids | Paul et al. (2016) |
| 17. | *Cassia fistula* L. | Gurr di nail, Amaltas | Golden shower | Fabaceae | Flower, Stem Bark | Punjab, KPK | Alkaloids, Flavonoid | Akhila and Aleykutty (2015) |
| 18. | *Catharanthus roseus* | Sada bahar | Madagascar periwinkle, Rosy periwinkle | Apocynaceae | Leaf | Punjab, KPK | Alkaloids (Vindolidine, Vindolinine) | Tiong et al. (2013) |
| 19. | *Chamaemelum nobile* | Babuna | Garden chamomile | Asteraceae | Arial part | Central Punjab, KPK | Flavonoid glucoside (Chamaemeloside) | Al-Snafi (2016b) |
| 20. | *Cichorium intybus* | Kasni | Chicory | Asteraceae | Whole plant | KPK (Hazara, Swat) Punjab, Gilgit, Azad Jammu and Kashmir | Chicoric acid | Tousch et al. (2008) |
| 21. | *Cinnamomum verum* | Darchini | Cinnamon | Lauraceae | Leaf | Sindh | Polyphenols | Cao et al. (2007) |
| 22. | *Citrullus colocynthis* | Tumba | Bitter cucumber, desert gourd | Cucurbitaceae | Rind (Fruit) | Desert areas of Pakistan | Saponin | Abdel-Hassan et al. (2000) |
| 23. | *Coccinia grandis* L. | Kanduri, Kundur | Ivy gourd, kovai fruit | Cucurbitaceae | Leaf, Fruit | Punjab | Pectin, Flavonoids, Triterpines, Alkaloid | Pekamwar et al. (2013) |
| 24. | *Commelina communis* L. | Commelina | Asiatic dayflower | Commelinaceae | Leaf, Dry flower | KPK (Abbottabad, Haripur) | Alkaloids (Pyrrolidine, Piperidine) | Kim et al. (1999b) |
| 25. | *Cuminum cyminum* L. | White Zeera | Indian cumin | Apiaceae | Seed | KPK, Central Punjab, Baluchistan | Cuminaldehyde, Cuminol | Patil et al. (2013) |
| 26. | *Cuminum nigrum* L. | Zira | Black cumin | Apiaceae | Seed | Pakistan | Flavonoids | Ahmad et al. (2000) |
| 27. | *Curcuma longa* L. | Haldi | Turmeric | Zingiberaceae | Rhizome | Punjab, KPK, Gilgit, Baltistan | Curcumin | Chuengsamarn et al. (2012) |
| 28. | *Cyamopsis tetragonoloba* L. | Guar | Cluster bean | Fabaceae | Seed (Beans) | Punjab | Tannins, Flavonoids, Coumarins | Mukhtar et al. (2006) |
| 29. | *Derris scandens* | Hog Creeper | Jewel vine | Poaceae | Leaf | Pakistan | Terpenoids, Saponins, Tannins, Flavonoids | Bhuiyan et al. (2019) |
| 30. | *Eclipta alba* | Bhangra | False daisy, Trailing Eclipta Plant | Asteraceae | Whole plant | Punjab, Azad Jammu and Kashmir | Glycosides, Flavonoids, Triterpenoids, Tannins | Nivedita and Vijay (2015) |
| 31. | *Eucalyptus globulus* | Nilgir, Safaida | Blue gum tree | Myrtaceae | Leaf | Sindh, KPK, Punjab, Baluchistan | Eucalyptol (Cineol) | Kumar and Laxmidhar (2011) |
| 32. | *Euphorbia neriifolia* L. | Thohr | Hedge euphorbia, Oleander spurge | Euphorbiaceae | Leaf | Central Punjab (Wild) | Fiber content | Mansuri and Patel (2012) |
| 33. | *Ficus benghalensis* | Bohr, Bargad | Indian banyan | Moraceae | Fruit, Bark, Arial roots | Punjab, Sindh, KPK | Alpha-amyrin acetate | Singh et al. (2009b) |
| 34. | *Fraxinus excelsior* L. | Sum | Common ash, English ash | Oleaceae | Seed | KPK | Secoiridoid Glucosides (Excelsides A and B) | Ibarra et al. (2009) |
| 35. | *Galega officinalis* L. | Goatsrue, Galega | Galega, Professorweed | Fabaceae | Leaf, Flowering top | KPK | Alkaloid galegine | Shokri et al. (2019) |
| 36. | *Garuga pinnata* | Kharpat, Mandvi | Garuga | Burseraceae | Bark | Punjab (Lahore) | Steroids, Terpenes, Saponins | Shirwaikar et al. (2007) |
| 37. | *Gentiana olivieri* | Bangera | Gentian | Gentianaceae | Aerial parts | KPK, Baltistan, Kashmir | Isoorientin | Sezik et al. (2005) |
| 38. | *Ginkgo biloba* | Balkuwari, Pankha Plant | Maidenhair Tree | Ginkgoaceae | Leaf | Punjab, Karachi, | Quercetin | Lu et al. (2018) |
| 39. | *Glycyrrhiza uralensis* | Chinese mulethi | Chinese liquorice | Fabaceae | Root | Punjab, KPK | Glycyrin | Kuroda et al. (2003) |
| 40. | *Grewia asiatica* L. | Falsa | Indian phalsa | Malvacea | Leaf, Stem bark, Fruit | Sindh, Punjab, Baluchistan | Flavonoid Phenolic acid | Khattab et al. (2015) |
| 41. | *Helicteres isora* L. | Marrorr Phalli | Indian screw tree | Malvacea | Root, bark, fruit | Pakistan | Tannins | Zareen et al. (2019) |
| 42. | *Hemidesmus indicus* | Salsa, Ushba | Indian sarsaparilla | Apocynaceae | Root | Baluchistan | 2-hydroxy-4-methoxy benzoic acid | Gayathri and Kannabiran (2009) |
| 43. | *Justicia adhatoda* | Bhaker, Bansa, | | Acanthaceae | Leaf, Root | KPK (Mansehra), Punjab | Alkaloids (Vasicine and Vasicinone) | Gulfraz et al. (2011) |
| 44. | *Lagerstroemia speciosa* | Legestomia tree, jarul | Queen crape myrtle, Queen of flowers | Lythraceae | Leaf | Punjab | Gallotannin (Penta-*O*-galloyl-glucopyranose) | Klein et al. (2007) |

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| 45. | *Lantana camara* L. | Panch phuli, | Lantana weed | Verbenaceae | Leaf, Fruit | Punjab, dried area of Baluchistan | Stearoyl Glucoside of Ursolic acid | Kazmi et al. (2012) |
| 46. | *Lawsonia inermis* L. | Mehndi | Henna tree | Lythraceae | Leaf | Baluchistan, Punjab, KPK | Alkaloid, Flavonoids, Glycosides, Saponin, Steroid, Triterpenoids, Tannins | Widyawati et al. (2019) |
| 47. | *Mallotus philippensis* | Kambila | Monkey Face Tree | Euphorbiacea | Bark | KPK, Punjab | Phenolics | Nandhini and Doss (2013) |
| 48. | *Mangifera indica* L. | Aam | Mango | Anacardiaceae | Leaf, Stem bark | Sindh, Punjab | Mangiferin | Dineshkumar et al. (2010) |
| 49. | *Medicago sativa* L. | Lucerne | Alfalfa | Fabaceae | Leaf, Seed | Punjab, KPK, Gilgit, Baluchistan (Quetta) | - | Salih and Azeez (2019) |
| 50. | *Melia azedarach* | Bakain, Dhareek | Persian lilac | Meliaceae | Leaf, Fruit pericarp, Seed | Punjab, Sindh, Baluchistan | - | Seifu et al. (2017) |
| 51. | *Momordica charantia* | Karella | Bitter gourd | Cucurbitaceae | Unripen Fruit | Pakistan | Triterpenoid (Charantin) | Joseph and Jini (2013) |
| 52. | *Morus alba* L. | Safaid toot | White mulberry | Moraceae | Leaf, Fruit, Root, Bark | KPK (Hazar, Hunza, Peshawar), Gilgit, Punjab and Baluchistan | Phenolic compounds | Wang et al. (2013) |
| 53. | *Morus rubra* L. | Shah Toot | Red mulberry | Moraceae | Leaf | Upper Punjab, KPK | Phenolic compounds | Sharma et al. (2010) |
| 54. | *Musa paradisiaca* L | Kela | Banana | Musaceae | Leaf, Stem juice, Immature/green Fruit | Sindh, Punjab | Ferulic acid, Gallic acid | Nguyen et al. (2017) |
| 55. | *Nelumbo nucifera* | Kanwal | Indian lotus | Nelumbonaceae | Leaf, Seed, Rhizome | Punjab, Sindh | Tryptophan | Lee et al. (2001) |
| 56. | *Nigella sativa* L. | Kalonji | Black seed, Black cumin | Ranunculaceae | Seed | Punjab, KPK | Thymoquinone | Abdelrazek et al. (2018) |
| 57. | *Psidium guajava* L | Amrood | Guava | Myrtaceae | Leaf | Punjab, KPK, Sindh | Phenolic content | Díaz-de-Cerio et al. (2017) |
| 58. | *Senna tora* | Panwar | Wild senna | Fabaceae | Leaf, Seed | Punjab, Sindh | Phenolic Glycosides | Kumar et al. (2015) |
| 59. | *Sida cordifolia* L. | Beejband | fFlannel weed, Country mallow | Malvaceae | Arial part | KPK (Hazara) | Alkaloids, Flavonoids | Ahmad et al. (2015) |
| 60. | *Silybum marianum* | Oont Katara | Milk Thistle | Asteraceae | Seed | KPK (Swat, Hazara) Punjab (Rawalpindi, Lahore) | Silymarin | Kazazis et al. (2014) |
| 61. | *Swertia chirayita* L | Chirata | Indian balmony, Bitter stick | Gentianaceae | Root | Punjab, KPK (Galyat region) | Swerchirin | Kavitha and Dattatri (2013) |
| 62. | *Syzygium cumini* | Jamun | Malabar plum, Java plum | Myrtaceae | Leaf, Seed, Whole fruit | Plain area of Pakistan | Mycaminose | Kumar et al. (2008) |
| 63. | *Tamarindus indica* L. | Imli | Tamarind | Fabaceae | Seed, Stem bark | Sindh, Southern Punjab, lower Baluchistan (Sibi) | Flavonoids, Polyphenolic Compounds. | Maiti et al. (2014) |
| 64. | *Terminalia arjuna* | Arjun | Arjun tree | Combretaceae | Leaf, Stem bark, | Punjab, KPK (Peshawar) Sindh, lower Baluchistan | Alkaloids, Flavonoids, Tannins, Triterpenoids | Biswas et al. (2011) |
| 65. | *Terminalia chebula* | Hareer | Bedda nuts, Black myrobalan | Combretaceae | Dried fruit | Sindh | Polyphenolic compounds | Iwai (2008) |
| 66. | *Urtica pilulifera* L. | Kumaon | Roman nettle | Urticaceae | Seed | Azad Kashmir, Gilgit, KPK | Lectin | Kavalalı et al. (2003) |
| 67. | *Ziziphus jujuba* | Beri | Chinese date tree | Rhamnaceae | Fruit | Punjab, Sindh | Flavonoids, Phenolic compounds, Triterpenes | Stoilova et al. (2017) |

it has been used in Unani and Ayurvedic medicines for the treatment of adenopathy, burning sensations, syphilis, leprosy, erysipelas, malaria, fever, rheumatism, leprosy, ulcer, abdominal pain, skin diseases and heart diseases. It contains different phytochemicals such as alkaloids, terpenoids, saponins, tannins, steroids, anthraquinones, flavonoids and reducing sugars. Different parts of *Cassia fistula* like leaves, fruit, seeds, flowers and bark have antidiabetic, hypolipidemic, hepatoprotective, antioxidant, antipyretic, anti-inflammatory, antileishmanial, antimicrobial, antitumor, larvicidal, antiparasitic, anti-itching, antiulcer and wound healing activities (Ali 2014). A comparative study of different parts of *Cassia fistula*, for the evaluation of antidiabetic activities was conducted by Einstein et al. (2013). Methanolic and aqueous extract of different parts like leaves, bark, flowers and pods along with two doses (250mg/kg and 500mg/kg) was investigated on STZ-nicotinamide-induced DM rats. Among different treatments, results indicated that 500mg/kg dose of bark and leaves have hypoglycemic and antilipidemic activity than 250mg/kg dose. Malpani and Manjunath (2012) concluded that *Cassia fistula* stem bark is useful for the treatment of diabetes. Ethyl acetate extract of *Cassia fistula* bark showed decrease in blood glucose and cholesterol level in diabetic Wistar albino rats. Antidiabetic activity of *Cassia fistula* bark may be due to presence of flavonoids in ethyl acetate extract (Table 3). Dose of 2000mg/kg, petroleum ether extract of *Cassia fistula* fruit pulp showed antidiabetic activity and found safe without any mortality and sign of toxicity in diabetic rat (Akhila and Aleykutty 2015). Jangir and Jain (2017) also reported that 70% ethanolic extract of *Cassia fistula* pods extract lower the fasting blood glucose level and improve glycemic control in STZ-induced diabetic rats.

### 1.7. *Cichorium intybus*

It is herbaceous perennial, belongs to family Asteraceae and commonly called as chicory. It is native to temperate regions of the world and cultivated in UK, Netherlands, Germany, South Africa USA and India {Punjab, Jammu and Kashmir} (Bais and Ravishankar 2001). In Pakistan, it is found in Azad Jammu and Kashmir (Table 3). Different parts of the *Cichorium intybus* contain inulin, tennis, hydroxycoumarins, flavonoids, alkaloids, steroids, terpenoids, coumarins, vitamins and phenolic acid (Al-Snafi 2016a). It has antiulcer activity (Saxena et al. 2011), antioxidant activity (Shad et al. 2013), antibacterial activity (Nandagopal and Kumari 2007), hepatoprotective activity (Cha et al. 2010), cardioprotective effects, antidiabetic activity, antimalarial activity, immunomodulatory activity (Tousch et al. 2008), antifungal activity (Mares et al. 2005), anti-inflammatory activity (Cavin et al. 2005) anti-tumor activity (Hazra et al. 2002) and antiallergic activity (Kim et al. 1999a). Tousch et al. (2008) stated that a compound, chicoric acid present in *Cichorium intybus* that is responsible for its anti-diabetic activity. Methanolic

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extract of *Cichorium intybus* roots has antihyperglycemic activity in streptozocin persuaded diabetic rat by lowering blood glucose level along with correction of triglycerides and cholesterol (Singh 2013). Chicory leaves decrease blood glucose level and improves lipid profile in diabetic rats, also increase internal oxidant enzymes, show antidiabetic effects reported by Emam et al. (2016). A natural chicoric acid extract from the *Cichorium intybus* roots showed antidiabetic effect by increase insulin secretion from the pancreatic β-cells and glucose uptake by muscles cells in Wistar rats (Azay-Milhau et al. 2013). Among the different extract of chicory for antidiabetic activity, alcohol soluble extract is more effective via reduce blood glucose level, total cholesterol and triglycerides in hyperglycemic mouse model (Yunyan et al. 1999).

### 1.8. *Eclipta alba*

*Eclipta alba* belongs to the family Asteraceae and commonly known as bhringraj and false daisy. It is perennial herb, found in moist warm temperate to tropical region of the worlds. It is widely grown in China, Thailand, Brazil, India, Indonesia, Nepal, Sri Lanka, Malaysia, Philippines and Pakistan. In Pakistan, it is widely grown in Punjab and Azad Jammu and Kashmir (Table 3). Traditionally, it has been used to improve growth, strength and black color of hairs. In ayurvedic medicine, it has been used as powerful liver tonic, antivenom and also used for athlete foot, scorpion stings, eczema and dermatitis. *Eclipta alba* contain wide range of phytochemicals like alkaloids, glycosides, flavonoids, triterpenoids, polyacetylene phytosterol nicotine and nicotinic acid. Its leaves contain a-terthienlmethanol, stigmasterol, wedelolactone, demethylwedelolactone-7-glucoside and demethylwedeloactone. Its root has heptacosanol and polyacetylene. Extract of *Eclipta alba* has analgesic activity, anti-aggression activity, antibacterial activity, anticancer activity, antidiabetic activity, anti-helminthic activity, anti-inflammatory activity, hair growth promoting effects, memory enhancing activity and anti-hepatotoxic properties (Sharma et al. 2012b).

Nivedita and Vijay (2015) reported that ethanolic leaf extract of *Eclipta alba* contains carbohydrates, lactones, steroids, terpenoids glycosides, esters flavonoids and tannins, which are responsible for antidiabetic effect and beneficial for abnormalities in alloxan induced diabetic mice. Ananthi et al. (2003) reported that *Eclipta alba* has been used in traditional medicine for hypoglycemic activity. Hexokinase catalyzed the glucose into glucose-6-phosphate. In alloxan diabetic rats, insulin deficiency occurred which decrease the activity of hexokinase. *Eclipta alba* extract stimulate the insulin production which increase the activity of hexokinase, which increase the glucose utilization and lead to reduction of blood sugar level. Sazia et al. (2015) showed a trial to evaluate the outcome of *Eclipta alba* against blood glucose level in diabetic patient. Results exposed significant decrease in blood glucose level. Jaiswal et al. (2012) evaluated the antidiabetic effects of two doses (100mg/kg and 250mg/kg) of ethanolic extract of *Eclipta alba* in STZ-treated diabetic rat and concluded that 250mg/kg dose reduced blood glucose more than 100mg/kg dose which is comparable to the standard antidiabetic drug.

### 1.9. *Eucalyptus globulus*

*Eucalyptus globulus* is the evergreen tree, native plant of Australia, belongs to myrtaceae family. It is also called Tail parn, Gum tree and Neelgiri. But in Pakistan, it is locally known as Safaida. It has four subspecies which are distributed in Australia from Victoria, Tasmania to New South Wales. It is widely planted from the cool tropical to the world's subtropical areas. In Pakistan, it is present in different localities of Punjab and KPK (Table 3). Traditionally, its roots have been used as folk medicine in Unani, Siddha, Tibetan, Ayurvedic and Homeopathic medicinal systems. Its leaves, flowers and bark are used for the treatment of different diseases. Its different parts have different phytochemicals like bark contains sterols, steroid ketons, sterol esters, fatty acids, hydrocarbons mono and di glycerides. Volatile oil of its leaves contains monoterpenes (α-pinene and β-pinene), oxygenated monoterpenes (1, 8-eucalyptol, linalool, terpinen-4-ol and α-terpineol) and oxygenated sesquiterpenes (α-eudesmol, epiglobulol and globulol). While its fruit contain beta-sitosterol, stigmasterol, 2a-hydroxybetulinic acid, betulinic acid, euscaphic acid, marcrocarpal A, nacrocarpal B, oleanolic acid, 3,4,3-O-trimethylellagic acid, 4-O-(2"-O-acetyl)-alpha-L-rhamnopyranoside, $-O-alpha-L-rhamnopyranoside, 3-O-methylellagic, camaldulenside, gallic acid and ellagic acid. Extract of different parts of *Eucalyptus globulus* have antibacterial, antifungal, wound healing, anthelmintic, antidiabetic, antiplaque, antiviral, anti-inflammatory, antitumor, antihistaminic, larvicidal, antimalarial, antioxidant activities. Beside this it has potential for the curing of respiratory diseases (Kumar and Laxmidhar 2011).

Gray and Flatt (1998) evaluated the effect of liquid extract of *Eucalyptus globulus* leaves on diabetic mice. Results indicated that *Eucalyptus globulus* extract has more than one active constitution which is responsible for hypoglycemic activity by stimulating insulin secretion and increasing glucose uptake and metabolism through muscles. Jouad et al. (2004) stated that the liquid extracts of leaves of *Eucalyptus globulus* at two levels (150mg/kg and 300mg/kg) did not show any proper decrease in blood glucose level in normal rats but plasma insulin was enhanced by concentration in diabetic rats and reduce blood glucose by stimulating insulin secretions. Nakhaee et al. (2009) did a trial to check the antioxidant activity of *Eucalyptus globulus* in STZ-induced diabetic rats and it was resulted that liquid (Aqueous) extract of *Eucalyptus globulus* leaves has antihyperglycemic and antioxidant activity.

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**Table 4:** Indigenous plants of Pakistan being used for Type 1 and 2 diabetes mellitus

| Sr. No. | Botanical Name | Vernacular Name | English Name | Family | Part Used | Location | Active Ingredient | References |
|---|---|---|---|---|---|---|---|---|
| **1.** | *Allium cepa* L. | Piaz, wasal | Onion | Amarylldaceae | Bulb | Throughout the Pakistan | S-methyle cysteine sulphoxide, Quercetin | Kumari et al. (1995), Kim et al. (2011) |
| 2. | *Bombax ceiba* | Simbal | Silk cotton tree | Bombacaceae | Leaf, Stem bark, Young Root, | Punjab, | Triterpenoid compound | Bhavsar and Talele (2013) |
| 3. | *Carum carvi* L. | Zeera siah | Persian cumin | Apiaceae | Seed | Punjab, KPK (Swabi) | Carvone, Limonen, γ-Terpinene | Abou El-Soud et al. (2014) |
| 4. | *Cassia auriculata* L. | Avaram | Avaram senna | Fabaceae | Flower | Sindh, Punjab | Flavonoids | Surana et al. (2018) |
| 5. | *Coriandrum sativum* L. | Dhania | Coriander | Apiaceae | Leaf, Seed | Central Punjab, KPK, Baluchistan | Linalool, Terpenes | Kajal and Singh (2019) |
| 6. | *Emblica officinalis* | Amla | Indian gooseberry | Phyllanthaceae | Leaf, Fruit, Seed | KPK, Punjab and Kashmir | Flavonoids, Gallic Acid | Mehta et al. (2009) |
| 7. | *Glycyrrhiza glabra* | Mulathi | Liquorice | Fabaceae | Rhizome, Roots | Sindh, Punjab and Baluchistan | Glabridin | Abd-El-Ghffar (2016) |
| 8. | *Murraya koenigii* | Curry patta | Curry leaf | Rutaceae | Leaf | Punjab | Carbazole Alkaloids, Quercetin | Chakrabarty et al. (1997) |
| 9. | *Ocimum gratissimum* L. | Tukhm faranjmushk | Clove basil, African basil | Lamiaceae | Leaf | Punjab | Alkaloids, Flavonoids, Saponins, Tannins | Okoduwa et al. (2017) |
| 10. | *Ocimum sanctum* L. | Tulsi | Holy basil | Lamiaceae | Leaf, Whole plant | Punjab, Lower hilly areas of KPK | Phenolic compound (Eugenol) | Prakash and Gupta (2005) |
| 11. | *Phyllanthus amarus* | Bahupatra, Bhui aonla | Indian phyllanthus | Phyllanthaceae | Leaf | KPK, Punjab | Triterpenoid compounds (Oleanolic acid and Ursolic Acid) | Ali et al. (2006) |
| 12. | *Plantago ovata* | Ispaghol | Psyllium husk | Plantaginaceae | Husk | Punjab, KPK, Sindh | Fiber content | Ziai et al. (2005) |
| 13. | *Stevia rebaudiana* | Stevia | Sweet leaf | Asteraceae | Leaf | KPK, Punjab | Stevioside | Ahmad and Ahmad (2018) |
| 14. | *Tinospora crispa* | Gulancha | Bitter grape, Heartleaf moonseed | Menispermaceae | Stem | Different area of Pakistan | Furanoditerpenoids (Borapetoside A, Borapetoside C, Borapetol B) | Ahmad et al. (2016) |
| 15. | *Withania coagulans Dunal* | Paneer doda, Chitta verino | Vegetable rennet, Indian rennet | Solanaceae | Flower, Fruit | Punjab (Bahawalpur) | Flavonoids, Triterpenoids, And Alkaloids, Phenolic acids | Shukla et al. (2012b) |
| 16. | *Zingiber officinale* | Adrak | Ginger | Zingiberaceae | Rhizome | Sindh, Punjab, Islamabad | Gingerol (6-gingerol) | Singh et al. (2009a) |
| 17. | *Eriobotrya japonica* | Loquat | Japanese plum | Rosaceae | Leaf Seed, Flower | KPK, Baluchistan Central Punjab | Tormentic acid, Ursolic acid | Lin et al. (2018) Xu et al. (2019) |
| 18. | *Urtica dioica* L. | Bichu buti | Common nettle, Stinging nettle | Urticaceae | Leaf | KPK (Hazara, Naran and Kagan), Gilgit Baltistan and Baluchistan | Flavonoids, Polyphenols, Sterols, Triterpenes, Lectin | El Haouari and Rosado (2019) |
| 19. | *Gymnema sylvestre* | Gurmar booti | Cowplant | Apocynaceae | Leaf | Azad Jammu and Kashmir (Widely grow) | Gymnemic acid, Gymnemagenin, Gymnestrogenin | Reddy et al. (1989), Persaud et al. (1999) |
| 20. | *Ficus racemosa* L | Gularrh | Cluster fig | Moraceae | Leaf, Fruit, Root, Stem bark | Punjab | Alkaloids, Flavonoids, Beta-sitosterol, Lupeol, Saponins, Tannins, Polyphenolic compounds | Amin et al. (2015) |

Mahmoudzadeh-sagheb et al. (2010) described that leaves extract of *Eucalyptus globulus* partially restores and repairs the pancreatic beta cells in STZ-induced diabetic rats and is beneficial for the treatment of diabetes. Saka et al. (2017) conducted a study on alloxan induced diabetic rats to check antidiabetic and antioxidant activities of *Eucalyptus globulus* leaves and determined that aqueous extract of *Eucalyptus globulus* leaves has antihyperglycemic and antioxidant activities by decreasing the blood glucose level and preventing lipid peroxidation and ketoacidosis respectively.

### 1.10. *Ficus benghalensis*

It is perennial tree belonging to family Moraceae (Table 3). It was originated from Asia and discovered in India, Pakistan Burma, Southeast Asia, Southern China, Malaysia and Thailand. In Pakistan, it is located across the Punjab province. It is commonly called banyan, Bargad (Unani medicine) and Bohar in Urdu, Pakistan (Khare 2008). It has antidiabetic activity (Edwin et al. 2008), antihyperlipidemic and hypocholesterolemic activity (Shukla et al. 1995), antibacterial, antifungal activity (Ogunlowo et al. 2013), anti-inflammatory activity (Patil et al. 2009), antioxidant activity (Sharma et al. 2009), anti-diarrheal activity (Mukherjee et al. 1998), anti-arthritic activity (Thite et al. 2014), antiallergic potential (Taur et al. 2007) and wound healing potential (Garg and Paliwal 2011). Khaliq (2017) reported that *Ficus benghalensis* leaves contain alkaloids flavonoids, glucoside, terpenoids, saponins, phenols and tannins, and stem bark has glucoside, terpenoids, saponins, tannins, phenols and flavonoids. Its root is the source of alkaloids, flavonoids glycoside, terpenoids, phenols, tannins and saponins. Aqueous extract of *Ficus benghalensis* stem bark lowered the blood glucose level at 5 hours in streptozotocin induced diabetic rats (Gayathri and Kannabiran 2008). Singh et al. (2009b) described that arial roots of *Ficus benghalensis* contain a compound alpha-amyrin acetate, which showed significant antihyperglycemic activity in the experiment. Aqueous extract of

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*Ficus benghalensis* stem bark also showed significant hypoglycemic and hypocholesterolemic effect on diabetic rabbits (Gupta et al. 2002).

### 1.11. *Glycyrrhiza glabra*

*Glycyrrhiza glabra*, a perennial medicinal plant belongs to the fabaceae family (Table 4). It is native to central and southwest regions of Asia including Pakistan, Iran, Australia, South America, Afghanistan, Russia, India and China. In Pakistan, it is found in Sindh, Punjab and Baluchistan. It is commonly called liquorice or licorice. In Pakistan, it is known as Mulathi. Useful parts of this plant are rhizome and roots which are sweet in taste, used as spice and flavoring agent. Glycyrrhizin (an oleanane type triterpene saponin) is the major constituent of phytochemicals of *Glycyrrhiza glabra* roots. Other constituents are flavonoids (Liquiritin apioside, glychionide A, glychionide B, glabrone, isoviolanthin, glabraisoflavanone A, glabraisoflavanone B, 5,7-dihydroxyflavanone, galbrene and rhamnoliquiritin), phenolic compounds (hispaglabridin A, hispaglabridin B, liquiritigenin, glabridin, isoprenylchalcone, isoliquiritigen, 4-O-methylglabridin and formononetin), coumarins (glycyoumarin), saponins (licorice saponin A3, licorice saponin C2, licrorice saponin G2 and licorice saponin J2) and chalcones (licochalcone B, isoliquiritin, nelicuoside). *Glycyrrhiza glabra* leaves contain fatty acids, phenols (guaiacol, phenol), derivatives of stilbene and derivatives of caffeic acid esters. It is useful for anemia, fever, skin diseases, acidity, cough, swelling, diarrhea, jaundice, paralysis, epilepsy and hemorrhagic diseases. It has many pharmacological properties like antiulcer, antioxidant, anti-inflammatory, antibacterial, antifungal, antidiabetic, anticancer, and hepatoprotective activities (Karkanis et al. 2018).

Peroxisome proliferation activated receptors adjust the expression of a gene group which metabolize the glucose and lipid. Gupta et al. (2011) reported that the ethanolic extract of *Glycyrrhiza glabra* roots reduce the glucose by metabolism through peroxisome proliferator activated receptor ligand binding activity due to presence of prenylflavonoids (glycerin, dehydroglyasperin D, dehydroglyasperin C and glycycoumarin). Glabridin is flavonoid compound found in *Glycyrrhiza glabra* which is commonly utilized for curing of CNS and cardiovascular diseases. Abd-El-Ghffar (2016) conducted a study to check the effect of glabridin on the streptozotocin-induced diabetic rat and concluded that high dose of glabridin increase the body weight gain, HDL cholesterol and antioxidants. Glabridin showed anti-inflammatory and antioxidant activity, which is beneficial against complications in STZ induced diabetic rats. Ethanolic extract of *Glycyrrhiza glabra* root contains the polyphenolic compounds which showed α-amylase and α-glucosidase inhibitory activities in *in-vitro* study. Results indicated that *Glycyrrhiza glabra* roots have antidiabetic and antioxidant activities (Karthikeson and Lakshmi, 2017). *Glycyrrhiza glabra* root has antidiabetic activity like *Syzygium cumini*. But the combination of *Glycyrrhiza glabra* root and *Linum usitatissimum* seeds extracts showed more decrease in blood glucose level in type 2 diabetic rats as compare to glimepiride drug. Combination of these two herbs, manage the diabetes by decreasing glucose level, total cholesterol, LDL-C, serum amylase level, triglycerides and improving insulin, HDL-C level in diabetic rats. It indicated that combination of *Glycyrrhiza glabra* root and *Linum usitatissimum* seeds extract has antihyperlipidemic and antihyperglycemic activities in type 2 diabetic rats (Qureshi et al. 2018).

### 1.12. *Gymnema sylvestre*

It is woody perennial vine belongs to Asclepiadaceae family (Table 4). It is commonly called gymnema, Australian cowplant and Madhunashini. But in Pakistani traditional medicinal system it is known as "Gurmar booti". It is grown in different temperate and subtropical regions of world but in Pakistan, it widely grows in Azad Jammu and Kashmir. It is used for the treatment of allergies, cough, dental caries, eye diseases, constipation, stomach ailments, obesity and viral infection. Its leaves are rich in triterpenoid saponins, flavonols, and gurmarin. Gymnemic acid is a compound in its leaves that is responsible for antidiabetic effect. *Gymnema sylvestre* has antidiabetic properties due to presence of gymnemic acid, which reduces the blood glucose level through stimulating the insulin from insulin store (Reddy et al. 1989). Persaud et al. (1999) reported that Gymnemic acid releases insulin through cell permeability instead of stimulating exocytosis pathways. Yackzan (1969) reported that Gurmarin reduces the sweet taste sense ability of tough for sweet substances from 15 minutes to 24 hours.

### 1.13. *Justicia adhatoda*

It is perennial evergreen shrub belongs to family Acanthaceae (Table 3). It is commonly called Malabar nut, adulsa, adhatoda, vasa or vasaka, and in Pakistan it is known as adotodai, baikar, pavettia. It was originated from Asia and discovered in Nepal, India, Sri Lanka, Indonesia, Bangladesh, Malaysia, China and Pakistan (Thal, Punjab and North-east). Phytochemicals have been found in *Justicia adhatoda* leaves are alkaloids (vasicine and vasicinone), phenolic acid, tannins, saponins, anthraquinone, flavonoids (Pathak 1970) and roots contain alkaloids, steroid, alkanes and flowers contain triterpenes, flavonoids and alkanes (Dhankhar et al. 2011). Leaves and roots of *Justicia adhatoda* are used for the treatment of diabetes because these parts contain alkaloids (vasicine and vasicinone) which have antihyperglycemic effects (Gulfraz et al. 2011). Traditionally it is used for cold, fever,

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cough, pneumonia, jaundice, whooping cough and asthma (Asolkar et al. 1992) and mainly used as antimicrobial (Shinwari et al. 2009), anti-inflammatory (Chakrabarty and Brantner 2001), anti-diabetic, antispasmodic, anti-bleeding, disinfectant, anti-jaundice and oxytocic (Maurya and Singh 2010). Gulfraz et al. (2011) stated that ethanolic extract of leaves and roots of *Justicia adhatoda* have antihyperglycemia and antihyperlipidemic properties which decrease blood glucose level, reduce tissue lipids and urine in alloxan diabetic rats. Chloroform and methanolic extracts of *Justicia adhatoda* leaves have hypoglycemic effects due to antioxidant activity of its phytochemicals, in the alloxan diabetic model (Ilango et al. 2009).

**1.14. *Momordica charantia***

It is an herbaceous vine of tropical and subtropical climate belongs to the cucurbitaceae family. It is known as bitter gourd and locally called karella in Pakistan (Table 3). It is grown in Africa, Asia and South America. In Pakistan, it is cultivated in Punjab, Sindh and KPK. Different parts of *Momordica charantia* contain many phytochemicals like alkaloids, saponins, glucosides, steroids, triterpenes and fixed oils. Its fruit is rich in momordicine, charantin, ascorbigen, Amino acids like glutamic acid, aspartic acid, alanine, pipecolic acid, luteolin serine, threonine, g-amino butyric acid and fatty acids (palmitic, lauric, oleic, myristic, palmitoleic, stearic, linolenic acid and linoleic). From a long time, it has been used in traditional medicine, for the curing of fever, HIV, cough, wounds, respiratory diseases, rheumatism, skin diseases, gout and ulcer. Traditionally, its fruit and fruit juice are used to cure the diabetes in the Pakistan. Two bioactive compounds are present in unripen fruit (charantin, polypeptide-p) which are responsible for antidiabetic effects (Joseph and Jini 2013). A triterpenoid known as charantin, found in *Momordica charantia* which cure the diabetes without the side effects and is alternative to insulin (Pitiphanpong *et al.* 2007). Polypeptide-p is a hypoglycemic protein found in *Momordica charantia* fruit, which reduces blood glucose level in humans when injected under the skin (Tayyab et al. 2012). Polypeptide-p is work like human insulin in the body and used as plant-based insulin in the Type 1 diabetic patients (Paul and Raychaudhuri 2010).

**1.15. *Murraya koenigii***

It is small spreading shrub or small tree belongs to the family Rutaceae (Table 4). It was originated from India and found in Malaysia, Sri Lanka, South Africa, Bangladesh, China and Pakistan (Komal et al. 2018). In Pakistan, its distributed from River Ravi toward Assam India (Singh et al. 2014). Its leaves have more quantity of oxalic acid, koenigin, glycosides, carbazole alkaloids and resins (Kumar et al. 2013). Usually, it is known as curry tree or curry leaf. But in Urdu it's known as Kari patta (Komal et al. 2018). It has antidiabetic activity (Arulselvan et al. 2006), antimicrobial activity (Shivkanya et al. 2009), antioxidative property (Arulselvan and Subramanian, 2007a), hypocholesterol property, cytotoxic activity, antidiarrheal activity and antiulcer activity (Syam et al. 2011). Leaves of plant *Murraya koenigii* are consumed for curing of diabetes because leaves contain antioxidant carbazole alkaloids (Chakrabarty et al. 1997) and Baynes and Thorpe (1999) reported that these drugs may prevent diabetes due to antioxidant properties. Ethanolic extract of *Murraya koenigii* leaves stimulate the insulin production from pancreas of streptozotocin brought diabetic rates and results showed its anti-hyperglycemic activity (Arulselvan and Subramanian 2007b). El-Amin et al. (2013) reported that aqueous extract of *Olea europaea* and *Murraya koenigii* leaves had hypolipidemic and antihyperglycemic effect due to occurrence of antioxidants like polyphenols and carbazole alkaloids respectively. Aqueous extract of *Murraya koenigii* significant hypoglycaemic activity by reducing glucose level upto 56% in diabetic rats and more effective than standard drug Glibenclamide (49%) as reported by Chaturvedi and Chowdhary (2014). Yadav et al. (2002) also reported antidiabetic activity of *Murraya koenigii* leaves in diabetic rats.

**1.16. *Phyllanthus amarus***

It is annual herb belongs to the family Phyllanthaceae (Table 4). It is found in tropical and subtropical areas of the world. In Pakistan, it was originated from Dir Kohistan valleys, KPK province (Jan et al. 2009). It is commonly known as Gale-o-Wind, Hurricane weed. In Pakistan's traditional medicinal system, it is called Bhui-amla. Chandewar and Dhongade (2013) reported that *Phyllanthus amarus* leaves contain different phytochemicals like alkaloids, flavonoids, glycosides, steroids, tannins, phenols and saponins. It has antiseptic, hypotensive, antiviral, diuretic, anti-diabetic, and antipyretic properties (Eweka and Enogieru 2011). In addition, it is used for the treatment of jaundice, wound, diarrhea, ulcers, dysentery and urogenital disease (Santos et al. 1995). A combination of compounds oleanolic acid and ursolic acid present in *Phyllanthus amarus* hexane extract is responsible for its antidiabetic activity (Ali et al. 2006). Aqueous and hydroalcoholic extracts of *Phyllanthus amarus* decrease blood glucose level in alloxanised rats by increasing serum insulin level (Lawson-Evi et al. 2011). Raphael et al. (2002) reported that methanolic extract of *Phyllanthus amarus* Schum & Thonn has antioxidant potential that reduces blood sugar in alloxan diabetic rats. Hydroalcoholic extract of *Phyllanthus amarus* has been reported toincrease insulin activity during liver regeneration in partially hepatectomized albino rats (Chattopadhyay et al. 2007).

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**1.17. *Silybum marianum***

It belongs to the family "Asteraceae" with thorny leaves and it is a biennial or annual herb. Commonly, it is known by different names like *cardus marianus*, milk thistle, variegated thistle and Scotch thistle. In Pakistan, it is known as "Oont katara" (Table 3). It is found throughout the world, in Pakistan, it is found in KPK province as a weed. It has place in curing liver disease, prevention from cancer and cancer treatment and helpful for treatment of poisoning from death cap mushrooms (Rainone 2005). Its fruit contains compounds like Silymarin, fixed oils, amines, betaine and trimethylglycine. While its seeds have fixed oil, flavone lignans, palmitic acid, oleic acid, tocopherol, protein, sterols, sitosterol, cholesterol, mucilage, stigmasterol and campesterol (Kaur et al. 2011). Flavonolignans compounds (Silimarin) is present in *Silybum marianum* seeds, which are responsible for its antidiabetic activity (Kazazis et al. 2014). Ahmad and Abbasi (2014) reported that milk thistle seeds and leave decrease the blood fasting glucose levels and mean daily blood glucose level in induced diabetes type 2 rabbits.

**1.18. *Syzygium cumini***

It is evergreen perennial fruit tree found in subtropical and tropical climates. It is commonly grown in plain areas of the Pakistan (Table 3). Its common names are jambolan, Java plum but in Indo-Pakistan region it is called jaman. It is rich source of glycoside, ellagic acid, anthocyanins, isoquercetin, kaemferol and myrecetin. Its leave contains acylated flavonol glycosides, triterpenoids and tannin. Its stem bark is rich in ester flavonoids and tannins. The roots are source of flavonoid glycosides and isorhamnetin 3-O-rutinoside. Its seeds are the source of phytochemicals including alkaloid, flavonoids, jambosine and glycoside jambolin or antimellin anthocyanins. The extracts of barks, leaves and seeds of *Syzygium cumini* contain antibacterial, anti- inflammatory and anti-diarrheal effects (Chandhuri et al. 1990). But traditionally, its seeds are used in the medicines for the treatment of diabetes in Pakistan. Seeds of *Syzygium cumini* contain a compound "Mycaminose" that is responsible for the reduction of blood glucose level (Kumar et al. 2008). Jaman seeds reduce blood glucose level by increasing insulin excretion from b-cells of pancreas in bound form (Kumar et al. 2008). Ethanolic extract of *Syzygium cumini* showed hypoglycemic activity and hypolipidemic activity in diabetic rats (Schoenfelder et al. 2010). *Syzygium cumini* fruit extract has high potential of antidiabetic activity (Gajera et al. 2017). Sharma et al. (2012a) also reported that aqueous extract of jaman seeds lowers the glucose level to the normal level in STZ-induced type 2 diabetic rats.

**1.19. *Terminalia chebula***

It is deciduous tree growing up to 30 m tall belonging to Combretaceae family. It is known as chebulic myrobalan and Harad. But in Pakistan, it's called "Hareer". Hereditary practitioners (Hakims) use its fresh fruit to make to a product "Muraba" and in dried from in medicine (Table 3). It is present throughout the tropical and some subtropical regions like Bhutan, Bangladesh, Cambodia, Malaysia, Pakistan, China, Indonesia, Nepal, Sri Lanka India, Thailand and Vietnam. It widely grows in Pakistan (Table 3). It contains tannins, flavonol glycosides, triterpenoids, coumarin and phenolic compounds (Chattopadhyay and Bhattacharyya 2007). Its fruit is a mild laxative, stomachic, tonic and antispasmodic. It is useful in ophthalmic, dental caries, hemorrhoids, oral cavity ulcers, bleeding gums and cosmetic use like melanin inhibition (Jin et al. 2006), anti-inflammatory activity (Hsu et al. 2007), cellular aging (Nam et al. 2004) and astringent (Thomas et al. 2000). Yet it is not found that which compound is present in *Terminalia chebula* fruit that is responsible for its anti-diabetic properties. But studies showed that antidiabetic effects are due to poly phenolic compounds that reduce the glucose level and antioxidant activity (Iwai 2008). Other studies showed that C-peptide present in *Terminalia chebula*, increases glucose utilization (Johansson et al. 1992). But recent studies showed that chloroform extract of *Terminalia chebula* seeds reduces the blood sugar level by increasing the insulin production from beta cells in STZ-induced diabetic rats (Rao and Nammi 2006).

**1.20. Trigonella foenum-graecum**:

It is annual herbaceous plant belong to family Fabaceae. It is grown worldwide. In Pakistan, it is cultivated in the plain areas of Punjab (Kasur is famous for its quality cultivation). It is commonly known as fenugreek. In Pakistan, it is commonly called Maithi (Table 2). It has multiple medicinal activities like antibacterial, anti-diabetic, anti plasmodic, anti-inflammatory, antioxidant anthelmintic, hypolipidemic and immunologic (Yadav and Kaushik 2011).

It contains phytochemicals such as alkaloids (betain, carpaine, choline, trigonelline, trimethylamine and neurin), amino acids (argenine, histidine, isoleucine, leucine, lysine, L-tryptophan and 4-Hydroxyisoleucine), saponins (frnugrin B, fenugreekine, graecunins, trigofoenosides A-G), steroidal sapinogens (diosgenin, neotigogenin, gitogenin, saponaretin, neogitogenin, smilagenin, sarsasapogenin, yamogenin and yuccagenin) (Mehrafarin et al. 2010). Moorthy et al. (2010) reported that GII is an anti-hyperglycemic compound obtained by aqueous extraction of fenugreek seeds which is different from nicotinic acid and trigonelline. GII has potential as an oral anti-diabetic drug. In recent studies, Chou et al. (2017) reported that N55 compound present in fenugreek lowers plasma glucose by increasing the response of physiological levels of GLP-1. It is not too much similar to disrupt tight regulation of GLP-1R signaling as compare to GLP-1 analogues.

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**1.21. *Ocimum sanctum***

It is annual/perennial aromatic herbaceous plant belonging to family Laminacea. It is widely found in tropical to subtropical areas of the world, native to Iran and India, cultivated in Egypt, Italy, Hungary, Morocco, France, and USA (Madal et al. 1993). In Pakistan, it is found in Punjab, KPK and Azad Jammu Kashmir (Table 4). It is known as Queen of herbs, commonly called Holy basil/sacred basil and locally its name is "Tulsi" (Sai Krishna et al. 2014). Its leaves and stem contain flavonoids, triterpenoids, saponins, tannins (Jaggi et al. 2003) and phenolic acid (Kelm et al. 2000). While, its seeds contain a compound sitosterol. It has anti-diabetic properties (Hannan et al. 2006), wound healing activity (Shetty et al. 2006), cardiac activity (Sood et al. 2005), hypolipidemic (Sarkar et al. 1994), antioxidant (Trevisan et al. 2006), anticancer (Prashar et al. 1998), antimicrobial (Singh et al. 2005), immunomodulatory effect (Mediratta et al. 2002) and anti-inflammatory activity (Kelm et al. 2000). Utsav et al. (2016) reported that methanol extract of *Ocimum sanctum* whole plant is antidiabetic due to presence of different kinds of phytochemicals in it. Kelm et al. (2000) reported that leaves of *Ocimum sanctum* contain eugenol. Prakash and Gupta (2005) also reported that *Ocimum sanctum* contains a phenolic compound (Eugenol) which is responsible for its anti-diabetic activity. Alcoholic extract of leaves of *Ocimum sanctum* lowers the blood sugar level in the streptozotocin induced diabetic rats (Chattopadhyay 1993). Narendhirakannan et al. (2006) described that ethanolic extracts of *Ocimum sanctum* have significant effect in lowering the levels of blood glucose, haemoglobin and glycosylated in streptozotocin-induced diabetes rats. Leaf extracts of *Ocimum sanctum* have antidiabetic action by effecting physiological pathways of insulin secretion. *Ocimum sanctum* leaf powder (1% level) fed to normal and diabetic rats, reduces fasting blood sugar, total lipids and total amino acids, results indicate the hypoglycemic and hypolipidemic effect of *Ocimum sanctum* in diabetic rats (Rai et al. 1997).

**1.22. *Zingiber officinale***

It is herbaceous perennial with annual pseudostem belong to the zingiberaceae family. It is commonly known as Ginger but in Pakistan, it is called Adrak (Table 4). It is originated from tropical rainforests of the Indian subcontinent. It is grown in tropical to subtropical areas of China, India, Hawaii, Japan, Australia, and Malaysia. In Pakistan, it is cultivated in Sindh province. Fresh rhizome of *Zingiber officinale* is used for cooking purpose and dried form (known as Sonth) is used in medicines. Its extract has antibacterial, antimicrobial, nephroprotective, antioxidant and hepatoprotective activities (Adel and Prakash 2010). *Zingiber officinale* contains alkaloids, tannins, flavonoids, saponins, steroids, glycosides and carotenoids (Otunola et al. 2010). *Zingiber officinale* rhizome contains an active compound "[6]-gingerol" that is responsible for antidiabetic properties. [6]-gingerol contains anti-diabetic properties, which increases sensitivity of cells toward insulin along with reduced hyperlipidemia in type 2 diabetic animals (Singh et al. 2009a). *Juice of Zingiber officinale* has potential of hypoglycemic activity by increasing insulin level in type 1 diabetic rats (Akhani et al. 2004).

**Conclusion:** Published research proved that indigenous plants of Pakistan have potential for the treatment of diabetes. Published results showed that traditionally used medicinal plants in many areas of Pakistan by local people and Unani Practitioner have truly antidiabetic properties. Pakistan has huge raw material for the production of medicine for its local demand as well as to export the other countries to increase economy. It is an opportunity for Pakistan to make new medicines from the indigenous plants by extraction of the secondary metabolites through various extraction methods according to the nature of these secondary metabolites.

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