TRADITIONAL MEDICINAL SYSTEMS FOR TREATMENT OF DIABETES MELLITUS: A REVIEW

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ABSTRACT

Diabetes mellitus (DM) is a chronic disease which has clinched the world. More than 300 million people of the world are suffering from this disease and the number is still increasing at a rapid rate as modern medical science has no permanent solution for the disease. Current scenario of the nutraceuticals has increased patient's faith on the traditional medicinal system and world nutraceutical industry is estimated to reach $285.0 billion by 2021. The increasing trend of nutraceuticals in diabetes treatment makes it important to collect the traditional knowledge of medicines under one heading as it can help researchers to formulate new functional foods and nutraceuticals which can either lower down the risk or cure DM. In addition, the discussion of market available food products, their active components and possible health benefits can help the patients to understand the herbal medicines in a better way.

Keywords: Diabetes mellitus (DM), Herbal medicines, Traditional systems, Herbs

INTRODUCTION

World health organization (WHO) has defined diabetes mellitus (DM) as a chronic disease caused by inherited and/or acquired deficiency in the production of insulin by the pancreas, or by the ineffectiveness of the insulin produced [1-3]. It is a metabolic disorder of endocrine system which is characterized by hyperglycemia or hypoglycemia. Diabetes is categorized into two types i.e. insulin-dependent (type 1) and insulin independent (type 2). Type 1 diabetes (insulin dependent) is caused due to the failure of the pancreas to produce insulin. This form develops most frequently in children and adolescents. On the other hand, Type 2 diabetes (insulin independent) results from the impaired action of insulin in the body. This type is more prevalent in adults in comparison to type 1 diabetes [4] and contributes to about 90 percent of the adult cases worldwide. Diabetes is a major risk factor for morbidity like blindness, kidney failure, heart attacks and limb amputation. It was the direct cause for 1.2 million deaths in 2015 [5]. In India, the number of diabetic patients has increased from 31.7 million in 2000 to 69.1 million in 2016 [6]. A record increase of 117% has been noticed in diabetic patients in last 16 years and India has now been declared as “Diabetic Capital” of the world [7]. Diabetes also increases the incidents of hypertension and approximately 70% of diabetic patients suffer from this side effect. Hypertension is related to increased risk of cardiovascular diseases (CVD) in diabetic patients [8]. Diabetes has no permanent cure but can be controlled or suppressed with the help of chemical or natural ways. Various chemical drugs like miglitol, acarbose, metformin etc. are used in the management of diabetes [9] whereas traditional medicinal systems rely on herbs to suppress diabetes. Researchers are still trying to find a medicine or product which can eradicate the disease from the roots [3]. Due to the lack of any solid claimant for the treatment of diabetes till date, many people continue to trust the indigenous medicinal systems. Hence, it is important to review the various traditional medicinal systems, important herbs, their bioactive compounds and mechanism of treatment to generate useful information to carry future studies and develop drugs for the treatment of DM.

Search criteria

The review included articles until 2018. Articles related to indigenous herbal systems like Ayurveda, Chinese traditional medicines system, African medicinal system, Unani herbal system, the Greek-Arab herbal system were reviewed for the study. Studies were included from Research gate, Google Scholar, Science Direct, Scopus, Pubmed, SciElo by using several keywords for search: world diabetes status, traditional medicinal systems for diabetes, herbs for diabetes, herbal drugs for diabetes, phytochemicals as hypoglycemic agents. An attempt was made to review all the important literature from the ancient time to modern era. The scenario for the current herbal medicines was added by searching the online retail stores like Amazon and Indiamart. Google Scholar was used for citation and bibliography.

Blood glucose concentrations

Glucose is considered as a source of energy and an essential nutrient for the body. Normal blood sugar level varies from person to person and normal range of blood sugar (fasting) and after eating (postprandial) has been reported to range within 70-100 mg/dl and 130-150 mg/dl, respectively [10]. A person having blood sugar level above this limit is said to be diabetic (table 1). In normal condition, insulin keeps blood glucose in a normal range but under diabetic conditions, insulin function is damaged and hence a high blood sugar level is observed. Not only the high blood sugar level but low blood sugar is also considered as a major health problem [11].

Table 1: Different concentrations of blood glucose levels in different conditions

| Categories       | Blood glucose levels | References |
|------------------|----------------------|------------|
| Normal (fasting) | 70-100 mg/dl         | [10]       |
| Normal (post prandial) | 130-150 mg/dl | [12]       |
| Hyperglycaemia   | Below 70 mg/dl       | [13]       |
| Mild             | Below 40 mg/dl       |            |
| Severe           | Below 20 mg/dl       |            |
| Hyperglycaemia   | Above 250 mg/dl      | [14]       |
| Mild (fasting)   | >109 mg/dl           |            |
| Severe (fasting) | >165 mg/dl           |            |
Different traditional medicinal systems for the treatment of diabetes mellitus

Every civilization has developed indigenous medicinal systems to treat or cure diseases with the help of locally available materials. The age-old experience of thousand years in medical therapy has made these systems more reliable. Majority of the population trusts the traditional medicinal systems over allopathic system due to its lesser-known health implications. Among the traditional medicinal systems, Indian, Chinese, Arab and African systems are world renowned and a crisp review of these medicinal systems has been presented here. A variety of herbal plants and trees used for the treatment of DM, their bioactive components, mode of action and related animal studies have been discussed here.

Traditional medicinal system prevalent in India

Ayurveda is the major traditional system practised in India. Three elemental substances (doshas) are mentioned in Ayurveda, namely, Vata, Pitta and Kapha. An imbalance in these elements results in disease. This traditional system primarily relies on plants and herbs to treat diseases. A separate ministry of Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy (AYUSH) has been constituted under the government of India with a purpose to develop education and research in the indigenous medicinal system. By seeing the popularity of indigenous medicinal systems, All India Institute of Ayurveda has been established in national capital Delhi by the government of India [15].

Many herbs have been employed traditionally to treat diabetes in India (table 2). A list of indigenous flora i.e. Neem (Azadirachta indica), Babul (Acacia arabica), Kawar (Aloe barbadensis), Peepal (Ficus religiosa), Jamun (Eugenia jambolana), Karela (Momordica charantia), Lahsun (Allium sativum) etc. are used to treat DM [16]. These herbs are rich in antioxidants and phytochemicals. Phytochemicals increase antioxidant enzymes like catalase and glutathione, which suppress the high glucose levels and hence increase the insulin production in the body [17]. Amongst these, bitter melon is one of the most popular herbal plants used by hakims for preparation of anti-diabetic medicines in India. Bitter melon juice has been reported to be more effective than other forms as it reacts faster than any other formulation [18]. The beneficial effect of bitter melon has been reported due to its ability to maintain the structural integrity of the pancreatic islets and regulating the synthesis and release of pancreatic hormones [19]. It has also been reported to maintain blood cholesterol. Bitter melon is highly hypoglycaemic, so it has been advised to avoid its consumption with other medicines having a similar effect as it can immediately lower blood glucose level which leads to other health problems [20]. Nutraceutical industry has also knocked the door of medicinal systems and many ready to serve beverages and capsules like Health karte Karela, Diabeta, Neem Tea are commercially available in India. These herbal products claim to suppress the conditions like hepatic and renal problems which arise due to diabetes. Anti-stress properties have also been reported for such products [15]. In spite of commercially available herbal products, people have more faith in local hakims/vaids and hence, a large chunk of the traditional medicinal system is still unorganised.

Table 2: Popular Indian herbs used for the treatment of diabetes mellitus

| Plant name (botanical name/Family) | Parts used | Bioactive compounds | Related animal studies | References |
|-----------------------------------|------------|---------------------|-----------------------|------------|
| Peepal (Ficus religiosa/Moraceae) | Leaves, bark, fruits, roots, seeds | Saponins, steroids, methanol extract, gingerol, eugenol, cedrane, vanillin, zingerone | Aqueous extracts of bark of peepal (50 and 100 mg/kg body weight) showed hypoglycemic effect in streptozotocin-induced diabetic rats. | [21] |
| Blackberry (Syzygium cumini or Eugenia jambolana/Myrtaceae) | Leaves, roots, bark, stem, seeds | Saponins, flavonoids, tannins, saponins, sterols, carbohydrates, phenolic alcohols, ellagic acid, salicylic acid, fibres, polyphenols, flavonoids, cardiac glycosides, terpenes, steroids, and resins | Aqueous extracts of seeds of Syzygium cumini (2.5 g and 5 g/kg body weight) showed a hypoglycemic effect in alloxan-induced diabetic rats. | [22] |
| Fenugreek (Trigonella foenum graecum/Fabaceae) | Seeds and leaves | Saponins, steroids, methanol extract, gingerol, eugenol, cedrane, vanillin, zingerone | Aqueous extract of fenugreek (60 mg/kg body weight) showed hypoglycemic activity in streptozotocin-induced hyperglycemic rats. | [23] |
| Bitter melon (Momordica charantia/Cucurbitaceae) | Pulp, seeds and leaves | Triterpene, protein, steroid, alkaid, inorganic lipids and phenolic compounds, saponins, charantin, resins | Aqueous extract of bitter melon lowered the glycemic response to both oral and intraperitoneal glucose load in normal mice without altering the insulin response. | [24] |
| Onion (Allium cepa/Amaryllidaceae) | Whole | Alkaloids, flavonoids, cardiac glycosides, terpenes, steroids, and resins | A mixture of minerals and vitamin extract of onion juice (1 ml/100 g body weight) showed hypoglycemic activity in alloxan-induced rats. | [25] |
| Holy basil (Ocimum sanctum/Lamiaceae) | Leaves | Volatile oil, carislineol, cirmaratin, isothymusin, rosmarinic acid, apigenin, campestrol | Ethanolic extracts of basil leaves (200 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced male albino rats. | [26] |
| Gum Arabic (Acacia nilotica/Fabaceae) | Bark, pods, leaves | Tannins, gallic acid, alkaloids, saponins | Aqueous extracts of leaves of gum arabic showed hypoglycemic effects in alloxan-induced diabetic mice. | [27] |
| Aloe vera (Barbadensis mill/Asphodelaceae) | Leaves extract | Anthraquinones, glycosides, vitamins (A, C, E), lipids, sterols, gibberlins, pseudototinosaponin AII and prototinosaponins AII | A mixture of minerals and vitamin extract of leaf pulp of aloe vera (300 mg/kg body weight) showed hypoglycemic effect in streptozotocin-induced adult male albino rats. | [28] |
| Gooseberry (Ribes uva-crispa/Grossulariaceae) | Whole | Tannins, phenols, alkaloids, flavonoids, gallic acid, corilagin, geraniin, ellagic acid | Phenol extracts of gooseberry (13.5 mg/kg body weight) showed hypoglycemic activity in type 2 diabetic rat models. | [29] |
| Plant | Parts Used | Active Constituents | Effects |
|-------|------------|---------------------|---------|
| Mulberry (Morus alba) | Leaves, stems, flowers | Rutin, isoquercitrin, astragalin, caffeic acid, ethanolic extract | Aqueous extract (300 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced diabetic rats. [40] |
| Guava (Psidium guajava) | Fruits | Oxalic acid, malic acid, ammonia, phenylpropanol amide, butenyl acetate, tannins, resins, calcium oxalate, tannic acid, flavonoids, phenolic acid | Methanol extracts of guava leaves (250 mg/kg body weight) showed hypoglycemic effects in streptozotocin and alloxan-induced diabetic mice. [38] |
| Coriander (Coriandrum sativum) | Leaves, roots and stems | Flavonoids, sterols, amino acids, saponins and tannins | A Dose of 200 mg/kg and 400 mg/kg body weight of a methanolic extract of coriander showed a significant dose-dependent decrease in blood glucose level. [42] |
| Cumin (Cuminum cyminum) | Seeds | Flavonoids, anthraquinones, phytosterol, saponins, steroids, tannins, triterpenoids | Normal rats maintained on 1.25% cumin powder for 8 weeks showed reduction in hyperglycaemia and glucosuria. [44] |
| Cinnamon (Cinnamomum cassia) | Stems, seeds | Methylhydroxycalcohol, tannins, flavonoids, glycosides, terpenoids, coumarins, anthraquinones | Streptozotocin-induced diabetic rats showed positive effects with cinnamon methanol extracts (3 g/kg body weight). [46] |
| Olives (Olea europaea) | Leaves, fruits, roots | Alkaloids, terpenoids, secoiridoids, ethanolic, oleosides, tyrosol | Aqueous extract of olive leaves (200 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced diabetic rats. [48] |
| Stinging nettle (Urtica dioica) | Leaves, stems, flowers | Ethanol, aluminum chloride, flavonoids, acetylcholine, histamine, phenylpropanol amide, caffeic acid, chlorogenic acid, fatty acids | Acetate extracts of nettle leaf (100 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced diabetic rats. [51] |
| Periwinkle (Catharanthus roseus) | Leaves, roots, flowers | Alkaloids, bisphosphatase, fructose, superoxide dimitase, peroxidase, catalase, dichloromethane, methanol | Methanolic extracts of periwinkle (500 mg/kg body weight) showed hypoglycemic activity in alloxan diabetic rats. [53] |
| Garlic (Allium sativum) | Whole | Alkaloids, saponins, steroids, carbohydrates, tannins, flavonoids, terpenoids, phenolics | Minerals and vitamin extract of garlic juice (1 ml/100 g body weight) showed hypoglycemic effects in alloxan-induced diabetic rats. [56] |
| Ginseng (Panax quinquefolius) | Leaves, flowers and berries | Triterpenes, saponins, polyacetylenes, polysaccharides, nitrogen-containing compounds, ubiquitins, phenolic compounds | Ethanol extract of ginseng root (500 mg/kg body weight) showed a hypoglycemic effect in streptozotocin-induced diabetic rats. [61] |
| Lilac (Syringa vulgaris) | Stems, flowers, leaves | Isocoumarin, nimbinflavone, nimbolinol, nimbinene, nimbolide, quercetin, quercitrin | Ether extracts of neem seed (2 g/kg body weight) showed antidiabetic effects in streptozotocin-induced diabetic rats. [63] |
| Curry leaves (Murraya koenigii) | Leaves | Carbohydrates, alkaloids, phytosterols, alcohol, flavonoids, saponins, tannins, glycosides, carbohydrates | Aqueous extract of curry leaves (300 mg/kg body weight) showed antidiabetic activity in alloxan-induced diabetic rats. [65] |
| Gymnema (Gymnema sylvestre) | Leaves | Steroids, terpenoids, alkaloids, flavonoids, coumarins, saponins, tannins | Ethanol extract of Gymnema sylvestre (800 mg/kg body weight) showed hypoglycemic activity in Otsuka Long-Evans Tokushima fatty (OLETF) mice. [70] |
| Loquat (Eriobotrya japonica) | Fruits, dried leaves | Triterpenes, flavonoids, glycosides, sesquiterpenes, uronic acid, oleic acid, precuscin B1, chlorogenic acid | Leaf extracts of loquat (800 mg/kg body weight) showed hypoglycemic activity in Otsuka Long-Evans Tokushima fatty (OLETF) mice. [68] |

**Note:** The effects listed are based on the in vivo studies conducted on various animal models. The results are indicative of the potential efficacy of the plant extracts in managing diabetes-related parameters. Further research is needed to ascertain their clinical efficacy and safety.
Traditional medicinal system prevalent in China

In traditional Chinese medicinal system, diabetes is categorised as Xiaokezheng and Xiaodanzheng. The predominance of yin deficiency explains the syndrome differentiation of the disease. According to the religion of China, yin deficiency means negative forces which are present in the food and the universe. There should be a positive balance between yin (negative forces) and yang (positive forces).

According to Chinese theory, these forces regulate the life of their people. Even if one of these forces is lacking, it results in the symptoms of DM. Inflammation in the stomach, deficiency of kidney yin, deficiency of yin or yang and yin yang has been described as the symptoms of DM. The yin-deficiency may be due to emotional disorders, overstrain, improper diet and excessive sexual activities.

Chinese doctors suggest the use of integrated treatment for diabetes. The treatment includes nourishing yin, moistening of dryness and increasing fluid production. They usually mix two or more herbs together to make one formula which shows hypoglycemic activity as well as suppresses the symptoms caused by the DM [81].

Chinese herbs (table-3) are reported to be most effective for type 2 DM, when they are consumed in mixture form. Chinese doctors always provide 2 or 3 types of medicines after examining the symptoms to reduce the effects. Indian Ayurveda and Chinese traditional system have many herbs (peepal, blackberry, onion, garlic etc.) in common [82]. Berberine is the most commonly found bioactive compound in major Chinese herbs used for the treatment of diabetes [83]. Rhizoma pumipidis is the richest source for this bioactive compound [84]. There are 30 anti-diabetic herbal formulas in China which are chemically approved by the Chinese State Food and Drugs Administration (SFDA). This system is being practised for hundred years and is still followed [3].

| Chinese name/English name | Botanical name/family | Parts used | Bioactive compounds | Related animal studies | Reference |
|--------------------------|-----------------------|------------|---------------------|-----------------------|-----------|
| Shu di Huang/Rehmania root | Rehmannia glutinosa/Scrophula riacae | Roots | Catalpol, phenethyl alcohol, leucosceptoside, glycosides, monoterpene sesquiterpenes, pinelleic acid, mannitol, ajugal, uracil, raffinose, terpenoids | Oligosaccharide in rehmanniaceae (100 mg/kg body weight) showed hypoglycemic effects in alloxan-induced diabetic rats. | [85] |
| Guang fang ji/Hang fang ji | Stephania tetranda moore/Menipperm aceae | Roots | Alkaidoids, tetrandrine, protoberbine, morphinane, phenanthrene, steroids, terpenoids, lignans, coumarins | Alkaidoids present in Stephania tetranda S. Moore has been reported to cause anti-hyperglycemic effects in streptozotocin diabetic animals at a dosage of 1 mg/kg body weight. | [86] [87] |
| Huang lian/Coptis goldthread | Rhizoma coptidis/Ranuncula la | Roots, stems, seeds, leaves | Isoquinoline, alkaloids, berberine, palmatine, jateorhizine, epiberberine, coptisine | Berberine extract of coptis (200 mg/kg body weight) showed the hypoglycemic activity in alloxan-induced diabetic rats. | [84] [88] |
| Huang Qi/Milk vetch root | Radix astragali/Fabaceae ae | Roots | Isoflavones, iso-flavonoids, saponins, gaskodes 2, astragalside, polysaccharides | Ethanollic extracts (2 g/kg body weight) showed hypoglycemic activity in db/db induced diabetic mice. | [89] [90] |
| Bai guo/Maidenhair tree | Ginkgo biloba/Ginkgoace ae | Leaves | Flavonoid glycosides, terpene lactones, ginkgolic acids | Ginkgo protein extracts (200 mg/kg body weight) showed hypoglycemic activity in pregnant rats and effect on their reproductive outcome. | [91] |
| Wuweizi/Five flavor berry | Fructus schisandraei/Schis andreae | Fruits | Lignans, polysaccharides | Flavonoids extracts showed hypoglycemic activity in streptozotocin-induced rats. | [92] |
| Pueraria /Gegen | Pueraria lobata/Fabaceae | Dried roots | Isoflavonoids, triterpenoids | Isoflavins extract of pueraria (100 mg/kg body weight) acted on skeletal muscles and improve insulin levels in the body of type 2 diabetic male sprague dawley rats' model. | [93] |
| Shan zhu yu/Cornelian cherry | Cornus mas/Cornacea | Carp | Ethanol, ursoic acid, glycosides, loganic acid, olea nolic acid, mevaloside | Ethanollic extract of cornelian cherries showed hypoglycemic activity and directly affected the insulin levels in the pancreas in alloxan-induced rats. | [94] |
Unani medicinal system

Unani system of medicine deals with various conditions of health and provides preventive, curative and curative health care. Scientific principles and holistic concepts of healing and health are the basis of Unani treatment system [95]. This system is practiced in India, Bangladesh, Pakistan, Sri Lanka, Nepal, China, Iran, Iraq, Malaysia, Indonesia, Central Asia, Middle Eastern countries, some African and European countries [96]. Arabs developed the Unani medicinal system into elaborate medical sciences and its teaching was started in Greece. So, Unani medicinal system is also known as Greco-Arab medicinal system [97]. Unani medicinal system is based on four humors. These are 4 fluids of body i.e. blood, phlegm, yellow bile, and black bile which are related to mental, emotional, spiritual and physical causes of any disease. The humors are assigned such characteristics as body heat, urine and stool examination, observation and palpitation. The prescriptions of medicines given by Unani medicinal system contains detailed instructions about the dosage of the medicine [99]. This system was introduced to India in eighth century by Arabs and Iranians [95]. Herbs used for treatment of DM under Unani system are bitter apple, virgin’s mental, cape liliac, spiny gourd, hisawarg, marshmallows, malabar nut, senna, fennel, licorice root etc. [table 4] [99].

Although the Unani system is known as a Greco-Arab system but with time Greco-Arab system has created a new identity and new system is somewhat different from Unani. In the Greco-Arab medicinal system, a mixture of four herbal plants is prepared. These medicinal plants are leaves of walnut (juglans regia), olive (Olea europaea), nettle (Urtica dioica) and saltbush (Atriplex). The mixture is known as ‘Glucolevel’. It has been reported to enhance the insulin production in the body and thus maintaining blood glucose level. Medicines prepared from these herbs or their products are used clinically [100]. Along with herbs, mineral extracts from animals are also used to prepare traditional medicines for the treatment of DM [100, 101]. The use of common Indian herbs like garlic and onion has been also reported in this medicinal system.

| Herb name               | Botanical name/family | Parts used          | Bioactive compounds                                                                 | Related animal studies                                      | References |
|-------------------------|-----------------------|---------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------|------------|
| Bitter apple            | Citrullus colocynthus/Cucurbitaceae | Fruits, leaves, roots | Glycosides, alkaloids, flavonoids, carbohydrates, phenolic acids, tocopherols, carotenoids | Saponin extracts of the rind of bitter apple (50 mg/kg body weight) showed a hypoglycemic effect in alloxan diabetic rats and rabbits. | [102, 103] |
| Virgin’s mantle         | Fagonia indicura brum or Fagonia cretica/Zygophyllaceae | Whole plant         | Glycosides, saponins, tannins, alkaloids, flavonoids, anthraquinones, coumarins, phenols | Methanol extracts of rind of virgin’s mantle (500 mg/kg body weight) showed hypoglycemic effects in alloxan-induced diabetic rabbits. | [104, 105] |
| Cape liliac             | Melia azedarach/Meliaceae | Fruits, leaves, stem, bark | Flavonoids, phenolic, linoleic acid, saponins, terpenoids, glycosides, rutins, alkaloids | Methanolic leaf extract showed an increase in wound healing capacity in alloxan diabetic rats. | [106, 107, 108] |
| Spiny gourd             | Mimordica dioca/Cucurbit | Fruits, seeds       | Phytic acid, alkaloids, flavonoids, saponins, steroids, saponins, triterpenoids, lectin | Methanol extracts of spiny gourd (300 mg/kg body weight) showed anti-diabetic activities in streptozotocin-induced diabetic rats. | [109, 110] |
| Hisawarg                | Rhyza stricta decne/Apocynaceae | Fruits, seeds, flowers, leaves | Alkaloids, flavonoids, b-carboline | Rhaza (2-4 g/kg body weight) showed anti-diabetic properties in alloxan-induced diabetic rats. | [111, 112] |
| Malabar nut             | Justicia adhatoda or Adhatoda zeylanica/Anacanthaceae | Leaves, roots       | Carbohydrates, proteins, steroids, alkaloids | Ethanolic extracts of leaves (50-100 mg/kg body weight) and roots (100 mg/kg body weight) showed anti-diabetic properties in alloxan-induced diabetic rats. | [114, 115] |
| Senna                   | Senna didymobotrya or Senna auriculata/legumes | Leaves             | Flavonoids, steroids, phenols, tannins, alkaloids, terpenoids, glycosides, saponins | Ethanol extracts of leaves of senna (150 mg/kg body weight) showed hypoglycemic activity in streptozotocin-induced diabetic mice. | [116, 117] |
| Fennel                  | Foeniculum vulgare/Umeliifers | Leaves, flowers     | Tannins, saponins, flavonoids, alkaloids, terpenoids | Aqueous extracts (300 mg/kg body weight) showed anti-diabetic activity in streptozotocin-induced diabetic rats. | [118, 119] |
| Licorice root           | Glycyrrhiza glabra/legumes | Leaves, fruits, stem, roots | Flavonoids, sterols, amino acids, saponins, triterpene, tannic acid, isoflavonoids, coumarins, saponins | Flavonoid extract of licorice root oil showed anti-diabetic effects in obese diabetic rats. | [120, 121] |

Traditional medicinal system prevalent in Africa

In Africa, the traditional medicinal system is ritually followed in Guinea [122] and nearly 45000 species of medicinal plants are used in the treatment of various diseases [123]. Herbal medicines used in Africa are very effective and most of them have been approved chemically. According to 2005 data, about 80% of the people in Africa followed herbal treatments and had positive results [124]. Many surveys have been conducted in Africa which proved the effectiveness of traditional medicines. Tsabang et al. conducted a survey on 116 diabetic patients in Cameroon, Africa in 2016 and reported that Allium cepa, Momordica charantia, Persea americana and Phyllanthus amarus were the principal plants used for the treatment of DM. Authors concluded that herbal medicine played an important role in the management of diabetes in Cameroon [125].
Table 5: Important herbs used in African medicinal system for the treatment of diabetes mellitus

| Name of the herb                                            | Parts used | Bioactive compounds                                      | Related animal studies                                                                 | Reference |
|-------------------------------------------------------------|------------|----------------------------------------------------------|----------------------------------------------------------------------------------------|-----------|
| Riboss tea plant                                            | Leaves, stem, seeds | Aspalathin, dibydroachalcone, orientin, flavones, isovitexin, tannins, flavanols | Alkaline extracts of rooibos tea (500 mg/kg body weight) showed hypoglycemic activity and reduced the oxidative stress in streptozotocin-induced diabetic rats. | [126]     |
| *Gota kola* (Centella asiatica/Apocynaceae)                | Leaves    | Alkaloids, flavonoids, phenols, tannins, glycosides, steroids, saponins | Ethanolic and methanolic extracts of leaves of this plant (250 mg/kg body weight) showed anti-diabetic effects in alloxan-induced diabetic rats. | [128]     |
| Honey bush/kustee/herbal tea (Cyclopia intermedia/Fabaceae) | Leaves    | Xanthone, magnifierin, flavone, glycoside, flavanones, lutecin, isomagniferin, hesperetin, eriocitrin | Hot water aqueous honey bush extract (5 mg/kg body weight) showed anti-diabetic activities in streptozotocin-induced diabetic rats as well as in diet-induced diabetic rats. | [130]     |
| Wood spider or devil’s claw (Harpagophyllum procumbens/Pedaliaceae) | Leaves, roots | Flavonoids, phytosterols, glycosides, acetoside, isoacetoside | The secondary aqueous root extract of devil’s claw plant (800 mg/kg body weight) showed hypoglycemic activity in streptozotocin induced diabetic rats. | [131]     |
| Um'akalaabo (Pelargonium graveolens/Geraniaceae)            | Leaves    | Terpenoids, flavonoids, phenolics, cinnamic acids, tannins, coumarins, isomenthone | Essential oil of leaves of *Pelargonium graveolens* (two doses of 75 mg/kg and 150 mg/kg body weight along with reference drug glibenclamide) showed hypoglycemic activity in alloxan-induced diabetic rats. | [133]     |

**Herbal formulations available in the market, their dosage and health claims**

The traditional herbal medicine system has entered a new era of nutraceuticals. Many formulations of these herbal plants are available in the market in the form of pills, capsules, oils and syrups. These products may either be a preparation of single herb or formulation of two or more herbs. Health claims for many disorders like obesity, DM, CVD and sex irregularities have been reported for these products [135-171]. These are known to control diabetes either by controlling glycemic index or enhancing the effectiveness of insulin. Major herbal products available in the market have been discussed in table 6.

Table 6: Herbal medicines available in Indian market, their dosage and their health claims

| Medicines/Dosage | Herb present | Health claims                                                                 | References |
|------------------|--------------|-------------------------------------------------------------------------------|------------|
| Stream CP3 Capsules/1 in a day | Peepal | Helps to cure diabetes, constipation treats ear infections, prevents arthritis, and heals wounds, treat skin conditions and show antimicrobial properties. | [135] |
| Herbal Hills Methi Seed Powder/once in a day | Fenugreek | Helps to treat diabetes and in proper digestion, helps to detoxify the body, supports uterine health. | [136] |
| Pitambari Karela Tablets/2 in a day | Bitter melon | Helps to treat diabetes, fever, common cold, cough, sore throat, kidney stone and heart disorders. | [137] |
| Himalaya Karela Tablets/2 in a day | Aloe vera | Helps to treat diabetes, hypertension, skin problems, rashes, wounds and hyperlipidemia. | [138] |
| Gloco Care Karela Medicine/2 in a day | Onion | Helps to cure DM, slower the rate of occurrence of cancer, CVDs. | [139] |
| Deemark Diaba Amrit/50 mg in a day | Garlic | Helps to cure diabetes, CVD, hyperlipidemia, hypertension, helps in cancer, fungal infections, have antimicrobial effects. | [140] |
| Reese Fresh Onion Juice/50 g a day | Holy basil | Helps in diabetes fever, common cold, cough, sore throat, kidney stone and heart disorders. | [141] |
| Durkee Garlic Oil/2-5 mg | Aloe vera juice/10-20 ml daily | Helps to treat diabetes, hypertension, skin problems, rashes, wounds and hyperlipidemia. | [142] |
| Bhumijs Tulsi Capsules/2 in a day | Triphala Aloe vera Juice/1 cap twice a day | Helps to cure diabetes, constipation, insomnia, bloating and blood pressure. | [143] |
| Shivalik Tulsi Capsules/1 in a day | Patanjali Aloe vera/20-30 ml daily | Helps to cure diabetes, improve digestion problems, good for hair health and also helps to cure respiratory problems. | [144] |
| Patanjali Amla Juice/20-30 ml daily | Holy basil Amla Capsules/1 in a day, Cure Garden Gluco Balance/2 in a day (added cumin) | Helps to cure diabetes, prevent atherosclerosis, suppress effects of cancer and enhances immunity. | [145] |
| Best Naturals Mulberry Leaf Extract/1g in a day | Mulberry | Helps to cure diabetes, prevent atherosclerosis, suppress effects of cancer and enhances immunity. | [146] |
| Shri ji Neem Tablets/1-2 tablets daily | Lilac | Helps to cure diabetes, treat skin infections, helps in heart diseases, in fever, breathing conditions, cure malaria. | [147] |
| Ayurvedic Neem Capsules/1 d, Gold 350 Raw Coriander Seeds/In meal time vegetables we can add | Coriander | Helps to cure diabetes, high blood pressure, cholesterol and in urinary infections also. | [148] |
| Health Thru Nutrition Black Cumin Seed Oil/once in a day, Raw jeera seeds/In meal we can use | Cumin | Helps to cure diabetes, constipation, insomnia, bloating and blood pressure. | [149] |
| The vitagreen Cinnamon/1 capsule in a day, Gluco care/1 capsule in a day, Nutri flair Ceylon Cinnamon Capsules/2 in a day | Cinnamon, bitter melon | Helps to cure diabetes, allergies, relieve cold and flu, boost energy and improves digestion. | [150] |
| Livestamin Ashwagandha Capsules/2 in a day, Herbal Hills Dia Care Churna/2 spoons in morning in empty stomach | Ginseng | Helps to cure diabetes, to treat stress, boost the immune system, enhance stamina, and reduces high cholesterol, prevention of heart disease. | [151] |
| In life Diastan/2 capsules in a day | Gymnema basil | Helps to cure diabetes, maintain lipid levels in the body. | [152] |
CONCLUSION
Increase in the number of diabetic patients, high cost for medical treatments, unsatisfactory treatment response and mistrust of people in present-day health care facilities signifies the still incomplete nature of the modern medicinal system. These factors are the major reasons for the continuous trust of people in the traditional medicinal systems. All the major traditional medicinal systems, viz., Indian, Chinese, African and Unani medicinal systems provide strong evidence for their effectiveness and the rationale for why people continue to trust traditional knowledge. It can be concluded that important constituents of Ayurveda and other traditional medicinal systems can provide a base for development of more effective drugs in modern medicinal system.

AUTHORS CONTRIBUTIONS
All the authors have contributed equally

CONFLICT OF INTERESTS
Declared none

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