

Review Article

TRADITIONAL MEDICINAL SYSTEMS FOR TREATMENT OF DIABETES MELLITUS: A REVIEW

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Received: 19 Feb 2018 Revised and Accepted: 14 Apr 2018

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

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DOI: <http://dx.doi.org/10.22159/ijpps.2018v10i5.25374>

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 morbidities 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 y 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 Greeco-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 hypoglycaemic 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. CAS source index search tool was used for the abbreviation of journals.

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]
Hypoglycaemia	Below 70 mg/dl	
Mild	Below 40 mg/dl	[13]
Severe	Below 20 mg/dl	
Hyperglycaemia	Above 250 mg/dl	
Mild (fasting)	>109 mg/dl	[14]
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, bittermelon 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 kart 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 (<i>Ficus religiosa</i> /Moraceae)	Leaves, bark, fruits, roots, seeds	Flavonoids, glycosides, alkaloids, steroids, saponins, vitamin C in non-enzymatic, enzymatic constituents are catalase, peroxidase etc.	Aqueous extracts of bark of peepal (50 and 100 mg/kg body weight) showed hypoglycemic effect in streptozotocin-induced diabetic rats.	[21] [22]
Blackberry (<i>Syzygium cumini</i> or <i>Eugenia jambolana</i> /Myrtaceae)	Leaves, roots, bark, stem, seeds	Alkaloids, flavonoids, tannins, saponins, sterols, carbohydrates, polyphenols, ellagic acid, salicylic acid, fibre	Aqueous extract of seeds of <i>Syzygium cumini</i> (2.5 g and 5 g/kg body weight) showed a hypoglycemic effect in alloxan-induced diabetic rats. Ethanol extract of seeds of <i>Eugenia jambolana</i> (100 mg/kg body weight) showed hypoglycemic activity in alloxan-induced diabetic rats.	[23] [24]
Fenugreek (<i>Trigonella foenum graecum</i> /Fabaceae)	Leaves and seeds	Saponins, steroids, methanol extract, gingerol, eugenol, cedrane, vanillin, zingerone.	Alkaloid extracts of fenugreek (60 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced hyperglycemic rats.	[25] [26]
Bitter melon (<i>Momordica charantia</i> /Cucurbitaceae)	Pulp, seeds and leaves	Triterpene, protein, steroid, alkaloid, 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. Aqueous extract powder of fresh unripe whole fruits at a dose of 20 mg/kg body weight reduced fasting blood glucose by 48%.	[19] [27]
Onion (<i>Allium cepa</i> /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.	[28] [29]
Holy basil (<i>Ocimum sanctum</i> /Lamiaceae)	Leaves	Volatile oil, cirsilineol, circimaritin, isothymusin, rosmeric acid, apigenin, campesterol	Ethanol extracts of basil leaves (200 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced male albino rats.	[30]
Gum Arabic (<i>Acacia nilotica</i> /Fabaceae)	Bark, pods, leaves	Tannins, gallic acid, alkaloids, saponins	Aqueous extracts of leaves of gum arabic showed hypoglycemic effects in alloxan-induced diabetic mice.	[31]
<i>Aloe vera</i> (<i>Barbadensis mill</i> /Asphodelaceae)	Leaves extract	Anthraquinones, glycosides, vitamins (A, C, E), lipids, sterols, gibberlins, pseudoprotinosaponin AIII and prototinosaponins AIII	Anthraquinone extract of leaf pulp of <i>aloe vera</i> (300 mg/kg body weight) showed hypoglycemic effect in streptozotocin-induced adult male albino rats.	[32]
Gooseberry (<i>Ribes uva- crispa</i> /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.	[33] [34]

Mulberry (<i>Morinda citrifolia/Moraceae</i>) And white mulberry (<i>Morus alba</i>)	Leaves, fruits	Rutin, isoquercitrin, astragalinal, caffeic acid, ethanol, methanol, kaempferol	Terpenoids and flavonoid extract of white mulberry solids showed hypoglycemic effects in type 2 diabetic murine models of mice. Protein extracts of leaves of mulberry (35 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced diabetic rats. Methanol extracts of guava leaves (250 mg/kg body weight) showed hypoglycemic effects in streptozotocin and alloxan-induced diabetic mice.	[35] [36] [37]
Guava (<i>Psidium guajava/Myrtaceae</i>)	Leaves, flowers, bark, roots, buds, twigs, fruits skin	Oxalic acid, malic acid, amylase, phenylpropyl acetate, butenyl acetate, tannins, resins, calcium oxalate, tannic acid, flavonoids, phenolic acid		[38] [39]
Radish (<i>Raphanus sativus/Brassicaceae</i>)	Roots and leaves	Acetone, acetic acid, trifluoroacetic acid, anthocyanidin, phenols, anthocyanin, potassium chloride, sodium acetate	Aqueous extract of root juice (300 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced diabetic rats.	[40] [41]
Coriander (<i>Coriandrum sativum/Umbellifers</i>)	Leaves, roots and seeds	Flavonoids, steroids, 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] [43]
Cumin (<i>Syzygium cumini</i> or <i>Cuminum cyminum/Umbellifers</i>)	Seeds	Flavonoids, anthraquinones, phytosterol, saponins, steroids, tannins, triterpenoids	Normal rats maintained on 1.25% cumin powder for 8 w showed reduction in hyperglycaemia and glucosuria.	[44] [45]
Cinnamon (<i>Cinnamomum cassia/lauraceae</i>)	Stems, seeds	Methylhydroxychalcone, tannins, flavonoids, glycosides, terpenoids, coumarins, anthraquinones	Streptozotocin-induced diabetic rats showed positive effects with cinnamon methanol extracts (3 g/kg body weight).	[46] [47]
Olives (<i>Olea europaea/Oleaceae</i>)	Leaves, fruits, roots	Alkaloids, terpenes, secoridoids, ethanol, oleosides, tyrosol	Aqueous extracts of olive leaves (200 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced diabetic rats. Polyphenol extracts of olive leaves (500 mg/kg body weight in form of a tablet) showed a hypoglycemic effect in streptozotocin-induced diabetic rats.	[48] [49] [50]
Stinging nettle (<i>Urtica pilulifera</i> or <i>Urtica dioica/Urticaceae</i>)	Leaves, stem, flowers	Ethanol, aluminium chloride, flavonoids, acetylcholine, histamine, phenylpropane, caffeic acid, chlorogenic acid, fatty acids	Acetate extracts of stinging nettle (100 mg/kg body weight) showed hypoglycemic effects in streptozotocin diabetic rats.	[51] [52]
Periwinkle (<i>Catharanthus roseus</i> or <i>Vinca rosea/Apocynaceae</i>)	Leaves, roots, flowers	Alkaloids, bisphosphatase, fructose, superoxide dismutase, peroxidase, catalase, dichloromethane, methanol	Methanolic extracts of periwinkle (500 mg/kg body weight) showed hypoglycemic activity in alloxan diabetic rats. Organic extracts of the juice of fresh leaves of periwinkle (100 mg/kg body weight) showed hypoglycemic effects in alloxan diabetic rats.	[53] [54] [55]
Garlic (<i>Allium sativum/Amaryllidaceae</i>)	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. Garlic oil (50 mg/kg body weight) showed a hypoglycaemic effect in streptozotocin-induced white male albino rats.	[56] [57] [58]
Ginseng (<i>Panax quinquefolius/Araliaceae</i>)	Leaves, flowers and berries	Triterpene, saponins, polyacetylenes, polysaccharides, nitrogen-containing compounds, ubiquitous, phenolic compounds	Improvement in renal damage was observed in streptozotocin-induced diabetic rats with ginseng due to heat processing aqueous extracts of ginseng (100 mg/kg body weight).	[59] [60]
Ginger (<i>Zingiber officinale/Zingiberaceae</i>)	Whole	Flavonoids, saponins, tannins, terpenoids, phenols	Ethanol extract of ginger garlic powder (500 mg/kg body weight) showed a hypoglycemic effect in streptozotocin-induced diabetic rats.	[61] [62]
Lilac/Neem (<i>Azadirachta indica/Meliaceae</i>)	Leaves, root, stem, flowers, seeds, bark	Isozadriolide, nimbaflavone, nimbandiol, nimbinene, nimbolide, quercetin, quercitrin	Ether extracts of neem seed (2 g/kg body weight) showed antidiabetic effects in streptozotocin-induced diabetic rats.	[63] [64]
Curry leaves (<i>Murraya koenigii/Rutaceae</i>)	Leaves	Carbohydrates, alkaloids, phytosterols, alcohol, flavonoids, saponins, tannins, glycosides, carbohydrates	Aqueous extracts of curry leaves (300 mg/kg body weight) showed antidiabetic activity in alloxan-induced diabetic rats. Dried powdered curry leaves (35 mg/kg body weight) showed hypoglycemic effects in streptozotocin-induced diabetic rats.	[65] [66] [67]
Gymnema (<i>Gymnema slyvestre/Asclepiadaceae</i>)	Leaves	Steroids, terpenoids, alkaloids, flavonoids, coumarins, saponins, tannins	Leaf ethanolic extracts showed hypoglycemic activity in streptozotocin-induced diabetic rats.	[68] [69]
Loquat (<i>Eriobotrya japonica/Rosaceae</i>)	Fruits, dried leaves,	Triterpenes, flavonoids, glycosides, sesquiterpenes, ursolic acid, oleanolic acid, procyanidin B2, chlorogenic acid,	Ethanol extracts of seeds of loquat (8000 mg/kg body weight) showed hypoglycemic activity in Otsuka Long-Evans Tokushima fatty (OLETF)	[70]

Cardamom (<i>Elettaria cardamomum/Zingiberaceae</i>)	seeds Leaves, fruits, seeds	epicatechin Flavonoids, tannins, saponins, quinone, glycoside, terpenoids, phenol, coumarins, steroids, alkaloids, anthocyanin	rats and mice. Flavonoid extract of cardamom, ginger and cinnamon (250 mg/kg body weight) showed hypoglycaemic activity in alloxan-induced diabetic rats.	[71] [72]
Sesame seed (<i>Sesamum indicum/Pedaliaceae</i>)	Seeds, leaves	Flavonoids, protein, triterpenes, ethanol, polyphenols	Ethanol extract of sesame seeds (500 mg/kg body weight) showed hypoglycaemic activity in streptozotocin-induced diabetic rats.	[73] [74]
Celery seeds (<i>Trachyspermum ammi/Apiaceae</i>)	Seeds, leaves	Alkaloids, flavonoids, steroids, tannins, saponins, glycosides, quinones, proteins, coumarins	Flavonoid extract of seeds (400 mg/kg body weight) showed anti glycaemic activity in streptozotocin-induced diabetic rats.	[75] [76]
Black pepper (<i>Piper nigrum/Piperaceae</i>)	Seeds	Alkaloids, flavonoids, terpenes, steroids, lignans, phenolics	Aqueous extracts (300 mg/kg body weight) showed effect on antioxidant pathways in streptozotocin rats.	[77] [78]
Peppermint (<i>Mentha piperita/lamiaceae</i>)	Leaves,	Flavonoids, phenols, terpenes	Juice of peppermint (0.29 g/kg body weight) showed anti glycaemic effects in streptozotocin induced male diabetic wistar rats.	[79] [80]

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 and *yin* or *yin* and *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 doctor suggests 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 hypoglycaemic 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 coptidis* 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].

Table 3: Important Chinese herbs for treatment of diabetes mellitus

Chinese name/English name	Botanical name/family	Parts used	Bioactive compounds	Related animal studies	Reference
<i>Shu di huang/Rehmania root</i>	<i>Rehmannia glutinosa/Scroph ula riaceae</i>	Roots	Catalpol, phenethyl alcohol, leucosceptoside, glycosides, monocyclic sesquiterpenes, pinelllic acid, mannitol, ajugol, uracil, raffinose, terpenoids	Oligosaccharide in <i>rehmanniae</i> (100 mg/kg body weight) showed hypoglycaemic effects in alloxan-induced diabetic rats.	[85]
<i>Guang fang ji/Hang fang ji</i>	<i>Stephania tetrandra moore/Meniper maceae</i>	Roots	Alkaloids, tetrandrine, protoberberine, morphinane, phenanthrene, steroids, terpenoids, lignans, coumarins	Alkaloids present in <i>Stephania tetrandra S. Moore</i> has been reported to cause anti-hyperglycaemic effects in streptozotocin diabetic mice at a dosage of 1 mg/kg body weight.	[86] [87]
<i>Huang lian/Coptis goldthread</i>	<i>Rhizoma coptidis/Ranuncu la</i>	Roots, stem, seeds, leaves	Isoquinoline, alkaloids, berberine, palmatine, jateorrhizine, epiberberine, coptisine	Berberine extract of coptis (200 mg/kg body weight) showed the hypoglycaemic activity in alloxan diabetic rats.	[84] [88]
<i>Huang Qi/Milk vetch root</i>	<i>Radix astragali/Fabace ae</i>	Roots	Isoflavones, isoflavonoids, saponins, galoside 2, astragaloside, polysaccharides	Ethanol extracts (2 g/kg body weight) showed hypoglycaemic activity in db/db induced diabetic mice.	[89] [90]
<i>Bai guo/Maidenhair tree</i>	<i>Ginkgo biloba/Ginkgoace ae</i>	Leaves	Flavonoid glycosides, terpene lactones, ginkgolic acids	<i>Ginkgo</i> protein extracts (200 mg/kg body weight) showed hypoglycaemic activity in pregnant rats and effect on their reproductive outcome.	[91]
<i>Wuweizi/Five flavor berry</i>	<i>Fructus schisandrae/Schis andreae</i>	Fruits	Lignans, polysaccharides	Flavonoids extracts showed hypoglycaemic activity in streptozotocin-induced rats.	[92]
<i>Pueraria /Gegen</i>	<i>Pueraria lobate/Fabaceae</i>	Dried roots	Isoflavonoids, triterpenoids	Isoflavin extracts of <i>pueraria</i> (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]
<i>Shan zhu yu/Cornelian cherry</i>	<i>Cornus mas/Cornaceae</i>	Carp	Ethanol, ursolic acid, glycosides, loganic acid, oleanolic acid, mevaloside	Ethanol extract of cornelian cherries showed hypoglycaemic activity and directly affected the insulin levels in the pancreas in alloxan diabetic rats.	[94]

Unani medicinal system

Unani system of medicine deals with various conditions of health and provides promotive, preventive and curative health care. Scientific principles and holistic concepts of health and healing are the basis of Unani treatment system [95]. This system is practiced in India, Bangladesh, Pakistan, Srilanka, 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 temperament such as blood is hot and moist, phlegm is cold and moist, yellow bile is hot and dry, black bile is cold and dry [98]. Procedure of diagnosis of any disease in Unani medicinal system includes 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 lilac, spiny gourd, hisawarag, 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 '*Glucoselevel*'. 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.

Table 4: Herbs used for the treatment of diabetes mellitus in Unani system

Herb name	Botanical name/family	Parts used	Bioactive compounds	Related animal studies	References
Bitter apple	<i>Citrullus colocynthus/Cucurbitaceae</i>	Fruits, leaves, roots and stem	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	<i>Fagonia indica</i> brum or <i>Fagonia cretica/Zygophyllaceae</i>	Whole plant	Glycosides, saponins, tannins, alkaloids, flavonoids, anthraquinones, coumarins, phenols	Methanolic extracts of juice of virgin's mantle (500 mg/kg body weight) showed hypoglycemic effects in alloxan-induced diabetic rabbits.	[104] [105]
Cape lilac	<i>Melia azedarach/Meliaceae</i>	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	<i>Mimordica dioca/Cucurbits</i>	Fruits, seeds	Phytic acid, alkaloids, flavonoids, 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	<i>Rhazya stricta decne/Apocynaceae</i>	Fruits, seeds, flowers, leaves	Alkaloids, flavonoids, b-carboline	<i>Rhazya</i> (2-4 g/kg body weight) showed anti-diabetic properties in alloxan-induced diabetic rats. Lyophilized extracts (2.36 g/kg body weight) showed anti-diabetic effects in streptozotocin-induced diabetic rats.	[111] [112] [113]
Malabar nut	<i>Justicia adhatoda</i> or <i>Adhatoda zeylanica/Acanthaceae</i>	Leaves, roots	Carbohydrates, proteins, steroids, alkaloids	Ethanol 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]
<i>Senna</i>	<i>Senna didymobotrya</i> or <i>Senna auriculata/legumes</i>	Leaves	Flavonoids, steroids, phenols, tannins, alkaloids, terpenoids, glycosides, saponins	Ethanol extracts of leaves of <i>senna</i> (150 mg/kg body weight) showed hypoglycemic activity in streptozotocin-induced diabetic mice.	[116] [117]
Fennel	<i>Foeniculum vulgare/Umbellifers</i>	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	<i>Glycyrrhiza glabra/legumes</i>	Leaves, fruits, stem, roots	Flavonoids, sterols, amino acids, saponins, triterpene, tannic acid, isoflavonoids, coumarins, still benoids	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 (Botanical name/Family)	Parts used	Bioactive compounds	Related animal studies	Reference
Roiboss tea plant (<i>Aspalathus linearis/Fabaceae</i>)	Leaves, stem, seeds	Aspalathin, dihydrochalcone, orientin, flavones, isovitexin, flavanones, 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] [127]
<i>Gotu kola</i> (<i>Centella asiatica/Apiaceae</i>)	Leaves	Alkaloids, flavonoids, phenols, tannins, glycosides, steroids, saponins	Ethanollic and methanolic extracts of leaves of this plant (250 mg/kg body weight) showed anti-diabetic effects in alloxan-induced diabetic rats.	[128] [129]
Honeybush/kustee/herbal tea (<i>Cyclopia intermedia/Fabaceae</i>)	Leaves	Xenthone, magniferin, flavone, glycoside, flavanones, luteolin, 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 (<i>Harpagophytum procumbens/Pedaliaceae</i>)	Leaves, roots	Flavonoids, phytosterols, glycosides, acteoside, isoacteoside	The secondary aqueous root extract of devil's claw plant (800 mg/kg body weight) showed hypoglycemic activity in streptozotocin induced diabetic rats.	[131] [132]
Umckalaabo (<i>Pelargonium graveolens/Geraniaceae</i>)	Leaves	Terpenoids, flavonoids, phenolics, cinnamic acids, tannins, coumarins, isomenthone	Essential oil of leaves of <i>Pelargonium graveolens</i> (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] [134]

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]
Pitambri Karela Tablets/2 in a day, Himalaya Karela Tablets/2 in a day, Gluco Care Karela Medicine/2 in a day, Deemark Diaba Amrit/50 mg in a day	Bitter melon	Used in the treatment of DM, kidney stones, fever, reducing obesity, hypertension, cancer, improving immune functions.	[137] [138] [139] [140]
Reese Fresh Onion Juice/50 g a day,	Onion	Helps to cure DM, slower the rate of occurrence of cancer, CVDs.	[141]
Durkee Garlic Oil/2-5 mg,	Garlic	Helps to cure diabetes, CVD, hyperlipidemia, hypertension, helps in cancer, fungal infections, have antimicrobial effects.	[142] [143]
Bhumija Tulsi Capsules/2 in a day, Shivalik Tulsi Capsules/1 in a day, Patanjali Aloe vera Juice/10-20 ml daily, Triphala Aloe vera Juice/1 cap twice a day	Holy basil <i>Aloe vera</i>	Helps in diabetes fever, common cold, cough, sore throat, kidney stone and heart disorders. Helps to treat diabetes, hypertension, skin problems, rashes, wounds and hyperlipidemia.	[144] [145] [146] [147] [148]
Patanjali Amla Juice/20-30 ml daily, Himalaya Amla Capsules/1 in a day, Cure Garden Gluco Balance/2 in a day(added cumin)	Gooseberry	Helps to cure diabetes, improve digestion problems, good for hair health and also helps to cure respiratory problems.	[149] [150] [151]
Best Naturals Mulberry Leaf Extract/1g in a day	Mulberry	Helps to cure diabetes, prevent atherosclerosis, suppress effects of cancer and enhances immunity.	[152] [153]
Shri ji Neem Tablets/1-2 tablets daily, Ayurleaf Neem Capsules/1 d,	Lilac	Helps to cure diabetes, treat skin infections, helps in heart diseases, in fever, breathing conditions, cure malaria.	[154] [155]
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.	[156]
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.	[157]
The vitagreene Cinnamon/1 capsule in a day, Glucocare/1 capsule in a day, Nutri flair Ceylon Cinnamon Capsules/2 in a day	Cinnamon, bitter melon and turmeric	Helps to cure diabetes, allergies, relieve cold and flu, boost energy and improves digestion.	[158] [159] [160]
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.	[161] [162]
In life Diastan/2 capsules in a day	Gymnema, basil,	Helps to cure diabetes, maintain lipid levels in the body,	[163]

Sunergetic Olive Leaf Extract/once in a day, Disano Olive Oil/can be taken with salads or in foods	peepal, fenugreek Olives	promotes healthy functioning of pancreatic cells. Helps to cure diabetes, maintain healthy heart, helps in weight loss, improve brain health, improve skin health and helps in hormone balancing.	[164] [165]
Planetary Herbals <i>Rehmannia Endurance</i> 150 Tabs/1 tablet 3 times a day	Rehmania root	Helps to cure DM, treat menopause, impotence, hair loss and other hormone deficiencies.	[166]
Radiant Natural Whole Herb Berberine 900 mg/2 capsules daily	Coptis goldthread	Helps to cure diabetes, maintain healthy cholesterol levels, manage triglycerides and support healthy lipid levels.	[167]
Pure Mountain Botanicals Immuno Well RX Capsules/1 capsule twice daily	Milk-vetch root, mushroom, garlic	Helps to cure diabetes, fight ageing signs, CVD and sometimes cancer.	[168]
Herbal Hills Dhamasa Powder/3 gms, 1 to 2 times daily	Dhamasa	Helps to cure diabetes, heart problems, support healthy liver functions, have antioxidant and thrombolytic properties.	[169]
Shri ji Herbal Spenai Bitter Powder Anidiabetic Medicine/2-3 teaspoons a day	Spiny gourd	Helps to cure diabetes, reduces weakness, controls excessive hunger, excessive thirst, maintains functions of organs, improves digestion and clears the bowel.	[170]
Piping Rock Licorice Root Liquid Extract (alcohol and sugar free)/2 ml, 2-3 times a day	Licorice root	Helps to cure diabetes, has antibacterial properties, beneficial for digestion, sooth irritation and helps relieve stomach ulcers.	[171]

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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