

## A comprehensive Review: Effect of antidiabetic drugs with respect to microbiota

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### Abstract

Diabetes mellitus is a disease that affects all organ systems in human body if left untreated. Various treatment modalities have been tested in all branches of medicines i.e, western, Indian, Chinese, Unani etc. However, due to conflicting and lesser amount of knowledge regarding traditional Medicine it has not been used to its fullest potential. Besides, Western medicines are closely associated with various side-effects. Hence, it is important that traditional herbal medicines are used for treating this disease. Also, diabetic state is associated with alterations in microbiota in human body. Hence, some of the anti-diabetic extracts also act by managing the microbial population within human body. Thus review paper provides with an insight into anti-microbial nature of some of the herbal extracts used for treating diabetes.

**Key words:** diabetes, plants, microbiota, metabolic disorder, medicine

### Introduction

Diabetes mellitus is metabolic disease which is characterized by genetic predisposition towards development of a clinical condition manifested by significant increase in blood glucose. First recorded history of diabetes mellitus can be dated in Ebers papyrus of Egypt in 1500 B.C. This disease has written documentation in Vedic, Arabic, Chinese and Mediterranean cultures.

Diabetes is a big public health issue because it affects large numbers of population worldwide. Individuals suffering from diabetes have been found to suffer greater health issues and tend to die at a young age. Symptoms associated with diabetes mellitus are- increase in thirst, increase in frequency as well as volume of urine passed. <sup>1,2</sup>

If this condition is not treated, health related complications such as- dehydration and/or acidosis may develop. Elevated levels of blood glucose cause organs damage such as- eyes, nervous system, kidneys and blood vessels. A disorder in regulation of metabolism of glucose is mainly due to insulin deficiency or lack of response towards insulin. <sup>1, 2, 3, 4</sup>

### Plants with anti-diabetic activity:

Following are plants which have a role in controlling diabetes and which also possess anti-microbial activity.

**1) Actinodaphne hookeri** Meissn. (**Synonym:** *A. angustifolia* Nees.): This plant belong to the Lauraceae family. It is an inhabitant of western Ghats, Orissa and Sikkim in India. It is known by a diversity of names such as- Thali (**Siddha**), Paratathali (**Tamilnadu**) and Pisaa (Maharashtra). Infusion of its leaves have a disinfectant activity in urinary tract, has anti-diabetic and spasmolytic properties. Its leaves contain minute amount of an alkaloid which consist of  $\beta$ -sitosterol, hentriacontanol,

hentriacontanone, and quercetinrhamnoside and hydrocarbons. The bark contains actinodaphnine alkaloid. This plant exhibits no effect on microbiota.<sup>5</sup>

**2. Allium cepa** Linn.: This plant belongs to *Liliaceae* (also known as, *Alliaceae* family. It is cultivated annually across India. States which commonly grow *Allium cepa* (commonly known as onion in English, Palaandu or Durgandh in Ayurvedic language, Piyaz in Unani Medicine and Venkaayam in Siddha or Tamil language ) include- Tamil Nadu, Karnataka, Andhra Pradesh, Maharashtra and Madhya Pradesh. Its biological action includes- Antibiotic, anti-bacterial, anti-sclerotic, anticoagulant, hypotensive, anti-inflammatory, antispasmodic, anti-asthmatic, expectorant, carminative, diuretic and anti-diabetic.<sup>5</sup>

Other important areas of application include- preventing atherosclerosis, changes associated with ageing in blood vessels and decrease in appetite.<sup>5</sup>

Onion bulbs have been found containing volatile oils along with sulphur contents. These include allylpropyl disulphide along side sulphur containing compounds such as- alliin; phenolic acids, allicin, flavonoids and sterols.<sup>5</sup>

The hypoglycemic activity of onion has been attributed to its two constituents- allylpropyl disulphide along with allicin. Di-phenylamine which is isolated from mature onion bulbs has been found to exhibit anti-hyperglycemic action. Both alliin as well as allicin have been found to exert inhibition of aggregation of platelets. The antibiotic action of *Allium cepa* can be attributed to allicin. It has been seen that regular usage of onion can reduce requirement of insulin in diabetic patients. Thiosulphinates which have been isolated from juice of onion has been found to exhibit anti-asthmatic function.<sup>5</sup>

However, this plant also exhibits no efficacy on microbial population.

**3. Balanites aegyptiaca** (Linn.) (Synonym- *B. roxburghii* Planch). This plant belongs to the *Simaroubaceae* or *Balanitaceae* family. It is grown in Dry areas in India, specially Rajasthan, Madhya Pradesh Gujarat and Deccan. Other common names used are- Desert Date, Taapasadrum, Taapasa vrksha, Ingudi, Angaar Vrksa, Dirghkataka (in Ayurveda); Hingan or Hanguul (in Unani) and Nanjunda (in **Tamilian language**).<sup>6</sup>

Various activities include- expectoration (from seed extract), spasmolytic anti-bacterial, anti-fungal, for treating whooping cough, leucoderma besides diseases of skin.<sup>6</sup>

Diosgenin, an important ingredient in oral contraceptive drugs is derived from *Balanites* fruit and it has been shown to have spermicidal action. Long term administration of its fruit extract has been shown to have hyperglycaemia induced testicular dysfunction. Its aqueous fruit extract exhibits anti-diabetic role in streptozotocin induced diabetes in mice. Its seed contains a compound known as balanitins that plays cytostatic role. This plant has no effect on microflora in body.<sup>6</sup>

**4. Caesalpinia bonduc** (L.): This plant belongs to *Caesalpinaceae* family and is found to grow all around the year. It is commonly found in West Bengal and Southern parts of India as a hedge plant. Other commonly used names include- Nikkar Nut, Fever Nut, Kantaki Karanja, Lataakaranja, Karanjin, Puutikaranja, Bonduc Nut, Kuberaakshi in **Ayurvedic** language, Karanjwaa in Unani language and Kazharchikkaai in Tamil Nadu.<sup>7,8</sup>

This plant exhibits anti-periodic, anti-rheumatic activity, anti-diabetic activity, febrifuge, emmenagogue, diuretic, Anthelmintic and anticalculous activity. Its seeds are found to contain an alkaloid, caesalpinine along with saponins and bonducin. There is no effect on microbial population.<sup>7,8</sup>

**5. Ceiba pentandra** (Linn.): Its synonym is *Eriodendron anafractuosum*. It belongs to

*Bombacaceae* Family. Its habitat in India are its Western and Southern parts of India. Other common names are- Kapok, White Silk Cotton. The Ayurvedic terminologies are- Kuuta-Shaalmali and ShvetaShaalmali.<sup>7,8</sup>

Its actions are- laxative, astringent, vertigo, migraine and as demulcent in painful conditions associated with micturition. It acts as a diuretic, anti-spasmodic and anti-diabetic agent.

This plant comprises of linarin, fatty acids, di-glycerides and phospholipids. Extract of *Ceiba pentandra* derived from its stem and bark exhibits anti-microbial activity.<sup>7,8</sup>

**6. *Cinnamomum zeylanicum*:** This plant belongs to the *Lauraceae* family. This plant grows in Western Ghats at lower altitudes in Kerala. Commonly used names are- Cinnamon. In traditional Ayurvedic medicine, this plant is known as- Daaruchini, Varaanga, Tvak, Daarusitaa, Choncha and Utkata. In Unani medicine, it is known as Daarchini.

Its medicinal activities have been demonstrated differently by its various parts of the plant. Its bark has anti-spasmodic, carminative, expectorant, astringent, haemostatic and antiseptic properties. Its leaves have “anti-diabetic” activity. Ground form of cinnamon has been used for managing diarrhea, dysentery; stomach pain, gastric irritation, nausea, vomiting; toothache, neural pain and rheumatism. It exerts no effect on microbiota.<sup>7,8</sup>

**7. *Coptis teeta*:** This plant belongs to ‘*Ranunculaceae*’ family. It is found wide spread in Mishmi Hills in Arunachal Pradesh and China.

Its synonyms used in Ayurvedic medicine are- Mamira, Maamiraa and Tiktamuulaa. In Unani medicine, it is known as- Maamisaa.<sup>8</sup>

It is found to contain alkaloid constituents such as- berberine, coptin, coptisin and jatrorrhizine.

This herb has an anti-diabetic; hypoglycaemic as well as hypotensive roles.<sup>8</sup>

**Activity against micro-flora:** Its antimicrobial activity is due to its activity on reticuloendothelial cells by means of an increase in leucocytic phagocytosis. Its role is in treating stomach, anti-periodic, anti-bacterial and anti-fungal activity. It can be prescribed for conditions such as- convalescence, debility, dysentery, intermittent fever, dyspepsia, intestinal catarrh and oral thrush.<sup>8</sup>

It has been found to inhibit erythrocytic haemolysis, decrease in peroxidation of lipids, decrease in generation of superoxide peroxidation as well as a decrease in hydroxyl radicals.<sup>8</sup>

**8. *Emblica officinalis* (*Phyllanthus emblica* Linn.):** This plant belongs to the ‘*Euphorbiaceae*’ Family. It is found native in tropical Southeastern Asian countries with wide distribution in India. Commonly used name is- Indian gooseberry.<sup>9,10</sup>

In traditional Indian medicine system, it is known by the numerous names such as- Amla, Aamalaki, Aamalaka, Amoghaa, Amritaphala, Nelli, Dhaatri, Kaayasthaa, Nellikkaai, Vrshya, Dhaatriphala, Vayasyaa, Shiva and Hattha. In Unani medicine, it is known as- Aamalaa or Amlaj.<sup>9,10</sup>

Various beneficial effects of *Emblica officinalis* fruit are- antioxidant, anti-anemic, anti-emetic, astringent, diuretic, anti-hemorrhagic, bronchitis, anti-diarrhoeal, anti-diabetic and carminative activities.<sup>9,10</sup>

It is used in disease conditions such as- dyspepsia, vomiting, jaundice, bacillary dysentery, eye problems, peptic ulcer and gastro-intestinal tonic. Combination of amla juice along with turmeric and honey has been used for treating diabetes. Its seed has anti-bile, anti-asthmatic.<sup>9,10</sup>

*Emblica officinalis* fruit contain cytokinine associated factors such as- zeatin, zeatin riboside, zeatin nucleotide and phyllembin. Phyllembin has been shown to exhibit depression of CNS along with spasmolytic function. It acts by potentiating activity of adrenaline.<sup>9,10</sup>

Its leaves has gallic acid (an anti-oxidant) and ascorbic acid which play a role in inflammation. Its bark has proanthocyanidin, a tannin. Anti-oxidative activity is exhibited by superoxide dismutase which has anti-senescent or anti-aging action. Its aqueous fruit extract has been found to increase cardiac glycogen levels and cause decrease in serum SGOT, SGPT and LDH levels.

It lowers serum level of LDL cholesterol, triglycerides, phospholipids however, without any affect on HDL levels. This plant has no anti-microbial action.<sup>9,10</sup>

9. **Garuga pinnata** Roxb.: This plant belongs to the family '*Burseraceae*'. It is found growing all across India till hills. It is commonly known as- Grey Downy Balsam. Other local Indian terms used are- Paaranki, Arunelli, Kharpata, Karre Vembu, Ghogar and Toon.<sup>11</sup>

Its various action include- a) Its fruit can be used to treat stomach; its leaves have been shown to possess astringent action, anti-asthmatic properties anti-inflammatory and anti-allergic activities. The extract from its bark has anti-diabetic properties.<sup>11</sup>

Leaves as well as bark of its stem have been found to contain phytochemicals such as- sterols, stigmasterol, sitosterol, campesterol, aliphatic compounds, various fatty acids, long-chain esters, tannins and waxes. Its leaves contain phytochemicals like- garugarin along with amentoflavone. Its gum resinous derivative has been found to contain  $\alpha$ -amyrin, butyrospermol and dammarandiol.

However, it has no activity on microflora.<sup>11</sup>

10. **Geranium robertianum** Linn.: This herbaceous plant belongs to the *Geraniaceae* family. Its habitat is Western Himalaya region from Kashmir till Garhwal in Uttarakhand hills. It is commonly known as- 'Robert Geranium'.<sup>11</sup>

Its activities include- haemostatic, styptic, astringent, anti-diarrhea and anti-diabetic function. This herbaceous plant has strong odor and bitter, saline as well as astringent taste. It is applied on external surface to resolve tumors. It has a tonic action for improving functioning of liver as well as gallbladder for preventing calculus formation.<sup>11</sup>

This herb is found to contain phytochemical compounds such as- flavonoids like- Rutin. **Anti-Microbial Activity:** Ethanolic extract of this herb has been found to inhibit *E. coli*, *P. aeruginosa* and *S. aureus* growth.<sup>11</sup>

11. **Glycyrrhiza glabra** Linn.: This plant belongs to family *Papilionaceae* or *Fabaceae*. This plant is found native to Mediterranean countries. In India, it is cultivated in Punjab, Southern parts of India and Jammu and Kashmir. It is known as Licorice or Liquorice in common English Vernacular. It is also known as- Mulethi, Yashtimadhu, Madhuli, Madhuyashtyaahva, Madhurasaa, Atirasaa, Madhuka, Yashtika, Madhuyashtikaa, Yastikaahva, Yashtyaahva, Yashti, Klitaka and Yashtimadhuka, Athimathuram, Asl-us-soos and Rubb-us-soos.<sup>12</sup>

Its biological activities include- Demulcent, expectorant, anti-allergic, anti-biological action include- anti-inflammatory, anti-stress, spasmolytic, laxative, anti-depression, anti-ulcerative, emmenagogue, hepatoprotective, estrogenic and predominantly anti-diabetic. It is useful in conditions such as- Respiratory infections, catarrh, bronchitis, dry cough, tuberculosis, genitor-urinary disorders, urinary tract infections, pain in abdomen, oral, gastric as well as duodenal ulcerations, it is used for treatment of adreno-corticoid insufficiency.<sup>12</sup>

Its primary phytochemical compound is- glycyrrhizin (triterpene saponin having lowered hemolytic index), Glycyrrhetic acid and aglycone (found in root), iso-flavonoids, triterpenoids, chalcones, coumarins, lignans, amines, sterols, amino acids, gum and volatile oils.<sup>12</sup>

One of the disadvantages or adverse effect of administering liquorice at high glycyrrhizin concentration is hypokalemia which leads to retention of fluid. Deglycyrrhizinated liquorice is a type of extract of liquorice which is used for treating peptic ulcers.<sup>12</sup>

**Anti-microbial activities:** Oral preparations of liquorice that contain glycyrrhetic acid can be for treating viral origin infections for example, herpes, viral hepatitis and common cold.<sup>12</sup>

Its preparations intended for topical application contain glycyrrhetic acid. These can be used in management of eczema and psoriasis.<sup>12</sup>

12. **Gymnema sylvestre** Br.: This plant belongs to *Asclepiadaceae* family of plant kingdom. It is found in natural habitat such as Central Peninsular parts of India. It is commonly known as- Australian Cow Plant and Ipecacuanha. In traditional Ayurvedic medicine, it is also known as- Passaam, Meshavalli, Shirukurinja, Chhaagalshringi, Meshashringi and Meshavishanika. In **Unani** literature, it is known as- Gurmaar Buuti.<sup>11, 12</sup>

**Biological activity:** Its leaves have anti-diabetic activity and act by stimulation of cardiovascular system and uterus. Its leaf extract is used for treatment of paraesthesia as well as furunculosis.

The entire plant has diuretic and antibilious role. Its roots have expectorant, emetic, astringent and can ease stomach pain.<sup>11, 12</sup>

Phytoconstituents of this plant are- Gymnemagenin (a sapogenin) and Gymnemic acid that causes inhibitory effects on plasma glucose levels.<sup>11, 12</sup>

In homeopathic practice, a medication that is obtained from its leaves as well as roots is routinely prescribed in diabetes mellitus as well as diabetes insipidus.<sup>11, 12</sup>

**Antimicrobial efficacy:** Its antimicrobial activity can be seen by inhibition of formation of dental biofilm which has microbial origin.<sup>11, 12</sup>

13. **Ocimum canum** Sims.: It is also known as- *O. americanum* Linn. And it belongs to the family *Labiatae* or *Lamiaceae*. This herb is found widely distributed in Plains as well as lower hilly areas of India. It is commonly known as Holy Basil in English language. Other traditional terms are- Kaali Tulsi, Vana-Tulsi, Nai-Tulsi and Ganjamkorai.<sup>13, 14</sup>

**Phytochemical constitution:** Phytochemical constitution includes various components like- citral, camphor, Methylheptenone, methylnonylketone,  $\beta$ -sitosterol, betulinic acid, nevadensin, flavonoids, pectolarigenin-methylether and ursolic acid.<sup>13, 14</sup>

**Biological activities:** This plant has stimulatory, carminative and diaphoretic activity. It is used for treating cold, catarrh, leucorrhoea, diseases affecting urino-genital system and bronchitis along side diseases of skin. It has hypoglycaemic action.<sup>13, 14</sup>

**Microbial activity:** This plant has anti-fungal activity.<sup>13, 14</sup>

14. **Rhus parviflora** Roxb.: This herb belongs to the plant family, *Anacardiaceae*. It has been found to be distributed on dry and hot slopes of Himalayas extending from Punjab till Nepal and in hilly areas of Madhya Pradesh and Southern India.<sup>14</sup>

Other synonyms are- Sumach, Tintidi, Tintindeeka and Sumaaq.<sup>14</sup>

**Biological Activities:** The juice of its fruit have a vermifuge activity. It has astringent as well as diuretic action. It has anti-diabetic activity. Its root is used in treating irritable bladder and urinary incontinence.<sup>14</sup>

**Phytochemical constitution:** This plant contains flavonoids, quercetin, myricetin, kaempferol and its O-rhamnosides, beta-sitosterol, hentriacontane, hentriacontanol, lignoceric acid and iso-rhamnetin-alpha-L-arvinoside.<sup>14</sup>

**Microbial activity:** This anti-diabetic plant has no microbial activity.<sup>14</sup>

15. **Schweinfurthia sphaerocarpa** Br.: The synonym for this plant is *S. papilionacea*. It belongs to the *Scrophulariaceae* family. This plant grows in arid areas in Gujarat and Rajasthan.

It is commonly known in India as- Nepaal-Nimba.<sup>15</sup>

This plant is used for treating enteric fever. It has anti-diabetic activity and diuretic action.<sup>15</sup>

**Phytochemistry:** This plant has phytoconstituents like- schweinfurthin (hydrocarbon), *epi*-ephedradine and schweinine.<sup>15</sup>

**Anti-microbial activity:** *Epi*-ephedradine A has been mutagenic action on *Salmonella typhimurium*.<sup>15</sup>

16. **Scoparia dulcis** Linn.: This plant belongs to *Scrophulariaceae* family of plant kingdom. It is indigenous found in tropical parts of America. In India, it is found as weed in west Bengal, Tamil Nadu and some parts of India.<sup>15</sup>

In English Vernacular language, it is known as Sweet Broomweed. In local language in India it is known as-Jastimadhu, Ghodaa-tulasi and Madhukam.<sup>15</sup>

**Medicinal uses:** This plant is used for treatment of variety of renal diseases, fever, bronchitis and cough. Its roots are used as febrifuge. Its stem and leaves are used for treating anemic conditions, albuminuria, ketonuria and similar complications of diabetes mellitus.<sup>15</sup>

**Phytochemistry:** Amellin, its anti-diabetic component is found to occur in leaves and stems of this green plant. Flavonoids- scutellarein and O-methylscutellarein are other important phytochemicals compounds. Other phytochemicals are- triterpenoids, friedelin, scopadol, dulcitol, betulinic acid, dulcitolic acid, dulciolone, Benzoxazolinone, tritriacontane, beta-sitosterol, D-mannitol, and hexacosanol.<sup>15</sup>

**Antimicrobial activity:** This plant has no anti-microbial activity.<sup>15</sup>

17) **Strychnos potatorum** Linn.f. belonging to *Loganiaceae* or *Strychnaceae* family. This plant is inhabitant of West Bengal, Central and Southern Indian forests. Its biological action are its anti-diabetic, epilepsy, emetic, expectorant and anti-dysenteric properties.<sup>16</sup>

**Phytochemistry:** Biological principle of this plant is- Mannogalactan which causes reduction of cholesterol and triglyceride levels. Other biological constituents are- diabolin, acetyldiabolin, gavagebrucine, novacine, strychnine, icajine, oleanolic acid and its derivatives, isomotirol, campesterol, stigmaterol, and sitosterol.<sup>16, 17, 18</sup>

However, this plant extract does not exhibit any anti-microbial activity.<sup>16, 19</sup>

### Conclusion

Management of diabetes mellitus can be done by using certain herbal based extracts which have usually no side-effects on one's general physical health. Some of these agents also exhibit anti-microbial activity along with anti-diabetic effects. This review paper provides an insight into anti-diabetic and anti-microbial effect of some of the commonly used medicinal agents in routine patient management. <sup>12, 13, 20</sup>

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