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A SYSTEMATIC REVIEW OF SOME POTENTIAL ANTI-DIABETIC HERBS USED IN INDIA CHARACTERIZED BY ITS HYPOGLYCEMIC ACTIVITY

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A SYSTEMATIC REVIEW OF SOME POTENTIAL ANTI-DIABETIC HERBS USED IN INDIA CHARACTERIZED BY ITS HYPOGLYCEMIC ACTIVITY

T. K. Ujwala, Shawn Tomy, Sandra Celine and J. Sam Johnson Udaya Chander *

Pharm D Interns, RVS College of Pharmaceutical Sciences, Coimbatore, TN, India.

ABSTRACT: In the last few years, there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world. In this study, we intend to do a systematic search to identify the most potent antidiabetic herbs that are available in India. Relevant medical databases and websites were searched. To qualify for inclusion, the herbs should have excellent antidiabetic potential confirmed with biomarker (reduction in HbA1c) and the herbs should also possess limited adverse effects if at all any. Eligible studies must also meet the following criteria: published in English and peer-reviewed journals. We also used related keywords like diabetes mellitus, plant (herb), India, patient, glycemic control, clinical trial, RCT, natural or herbal medicine, Ayurvedic plants, hypoglycemic plants, and individual herb names from popular sources, as keywords or combination of them.

Keywords:

Diabetes Mellitus; Ayurveda, Hba1c, Randomized Controlled Trial, Glycemic Control

INTRODUCTION: Diabetes mellitus is a group of chronic metabolic disorder associated with error in the metabolism of carbohydrate, lipid and protein and it became the third "killer" of the health of mankind along with cancer, cardiovascular and cerebrovascular diseases. The present century has progressed towards naturopathy and thus, medical plants have an ever emerging role to play in treatment or management of lifelong prolonging diseases like diabetes mellitus [1, 2, 3]. It is estimated that there are approximately 33 million adults with diabetes in India

This number is likely to increase to 57.2 million by the year 2025 and India will become The Diabetic Capital of the world soon. Diabetes is a multifactorial disease leading to several complications, and therefore demands a multiple therapeutic approach.

In the last few years, there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects [4]. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these, 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world [5]. Ayurvedic literatures like Charak Samhita has already reported the use of plants, herbs and their derivatives for treatment of diabetes mellitus. More than 400 plants have been incorporated in approximately 700 recipes which are used to treat diabetes mellitus in almost two thirds of the world population [2].

METHODS:

A systematic search strategy was developed to identify the most potent antidiabetic herbs that are available in India. Various relevant medical databases and websites were searched. To qualify for inclusion, the herbs should have excellent antidiabetic potential confirmed with biomarker (reduction in HbA1c) and the herbs should also possess limited adverse effects if at all any. Eligible studies must also meet the following criteria: published in English and peer-reviewed journals. We searched Medline, Science Direct, EMBASE, Scopus, and Google Scholar using diabetes mellitus, plant (herb), India, patient, glycemic control, clinical trial, RCT, natural or herbal medicine, Ayurvedic plants, hypoglycemic plants, and individual herb names from popular sources, as keywords or combination of them. In addition, experts in the field were contacted to select studies that meet the criteria and we also looked up references of key articles. We limited studies to those articles published in English and restricted our search to herbs (Indian plants) for changes in glycemic indexes.

All articles were read in full and data were extracted in a standardized fashion. Hence, this review presents 15 antidiabetic herbs below with references to their scientific name, vernacular names, the family, the morphological description, chemical constituents, and other uses. These plants can be best used only as a preliminary screening of potential antidiabetic herbs and not as a definitive or complete hypoglycemic plant. We have not reviewed the original data behind the studies listed here. We have, in all cases, took original author's representations as true and evidence-based.

Hemidesmus indicus:

Family: Periplocacea

Vernacular Names:

Arabic : Zaiyana, Ausaba lunnara

Marathi : Anantmool, Upalsari, Dudhasali

Oriya : Onontomulo

Punjabi : Anantmool

Sanskrit : Anantamula, sariva, naga jihva

Tamil : Nannari

Telugu : Gadisugandhi, Sugandhipala

Malayalam : Naruninti, Nannari

Bengali : Anantmool

English : Indian Sarsaparilla

Konkani : Dudvali

Kannada : Sogadeberu, Namadaberu

Hindi : Magrabu, Salsa, Kapooree

Gujarati : Sariva

Morphology:

The stems and branches which twine anticlockwise are profusely lactiferous, elongate, narrow and wiry of a deep purple or purplish brown colour with the surface slightly ridged at the nodes. Leaves: Simple, petioled, exstipulate, opposite, entire, apiculate acute or obtuse, dark green above but paler and sometimes pubescent below. Leaves of the basal parts of the shoots are linear to lanceolate. Flowers: Greenish yellow to greenish purple outside, dull yellow to light purplish inside, calyx deeply five lobed, corolla gamopetalous, about twice the calyx, Stamens five, inserted near base of corolla with a thick coronal scale. Stamens five, inserted near base of corolla with distinct filaments and small connate oblong anthers ending in inflexed appendages. Pistil bi carpellary, ovaries free, many ovuled with distinct styles. Fruit two straight slender narrowly cylindrical widely divergent follicles. Seeds many, flat, oblong, with a long tuft of white silky hairs[1].

Chemical Constituents:

The entire plant from India contain indicusin steroid[8]. Six new pentacyclic triterpenes including two oleanenes identified as olean-12-en-21 beta-yl acetate, and olean-12-en-3 alpha-yl acetate, three ursenes characterized as 16(17)-seco-urs-12,20(30)-dien-18 alpha H-3 beta-yl actetate, urs-20(30)-en-18 beta H-3 beta-yl acetate and 16(17)-seco-urs-12,20(30) dien-18-alpha H-3 beta-ol and a lupene formulated us lup-1,12-dien-3-on-21-ol including a known compound, beta-amyrin acetate, on the basis of spectroscopic techniques and chemical means[9]. 2.50% of tannins were present in the leaves[10]. Coumarinolignoids like hemidesminine[11], hemidesrnin, hemidesmin1 and hemidesmin2 were also found[12]. Thepresence of flavonoids viz., hyperoside and rutin were also reported[13].

Uses:

The roots are used as antipyretic, anti-diarrhoeal, astringent, blood purifier, diaphoretic, diuretic, refrigerant and tonic[2-4], roots are useful in biliousness, blood diseases, dysentery, diarrhoea, respiratory disorders, skin diseases, syphilis, fever, leprosy, leukoderma, leucorrhoea, itching, bronchitis, asthma, eye diseases, epileptic fits in children, kidney and urinary disorders, loss of appetite, burning sensation and rheumatism[5-7, 2, 4], Root bark is used to cure dyspepsia, loss of appetite, nutritional disorders, fever, skin diseases, ulcer, syphilis and rheumatism[4]. Stem of H. indicus is used as diaphoretic, diuretic, laxative and in treating brain, liver and kidney diseases, syphilis, gleet, urinary discharges, uterine complaints, leukoderma, cough and asthma[6].

Vetiveria zizanioides:

Family: Poaceae

Vernacular Names:

Gujarati : Valo

Marathi : Vala

Telugu : Kuruveeru, Vettiveellu, Vettiveerum

Tamil : Vattiver

Kannada : Vattiveeru, Laamancha, Kaddu, Karidappasajje, Hullu

Malayalam: Ramaccham, Vettiveru

Ayurvedic name: Ushira

Morphology:

Vetiveria zizanioides is a densely tufted grass with the culms arising from an aromatic rhizome up to 2 m tall; the roots are stout, dense and aromatic; leaves are narrow, erect, keeled with scabrid margins; inflorescence is a panicle, up to 15-45 cm long of numerous slender racemes in whorls on a central axis. Spikelets are grey to purplish, 4-6 mm long, in pairs, one sessile the other pedicelled; 2-flowered; the lower floret is reduced to a lemma, upper bisexual in sessile, male in the pedicelled spikelet; glumes are armed with stout, tubercle-based spines, lemmas awnless, palea minute[14].

Chemical Constituents:

The chemical constituents present in the plant are Vetiverol, Vetivone[24], Khusimone, Khusimol, Vetivene, Khositone, Terpenes, Benzoic acid, Tripene-4-ol, ß-Humulene, Epizizianal, vetivenyl vetivenate, iso khusimol, Vetiver oils, vetivazulene[25], Zizaene, prezizaene, and b- vetispirene[26]. Among these, the major active constituents identified are khusimol, vetivone, eudesmol, khusimone, zizaene, and prezizaene[27] which are considered to be the fingerprint of

the oil [28-30], Among the 60 components identified to date, the sesquiterpene alpha-vetivone, beta-vetivone [31], and khusimol always occur in the oil in amounts up to 35%. As a result, they are considered to be fingerprints of the oil even though they do not possess the typical odor characteristics associated with vetiver.

Uses:

Various tribes use the different parts of the grass for many of their ailments such as mouth ulcer, fever, boil, epilepsy, burn, snakebite, scorpion sting, rheumatism, fever, headache[15]. Other activities it possesses are antioxidant activity[16], antifungal activity[17], antibacterial activity[18], hepatoprotective activity[19], anti-tubercular activity[20], mosquito repellent activity[21], anti hyper glycaemic activity[22], and antidepressant activity[23].

***Acacia catechu*:**

Family: Leguminoseae

Vernacular Names:

Assam : Kat, Khair, Khoira, Koir

Bengal : Khayer, Kuth

Bombay : Khaderi, Khaira, Khera

Gujarat : Kher, Kherio, Kheriobaval

Hindi : Katha, Khair, Khairbabul,

Khyar

Central Provinces: Khair

Ceylon : Karangall, Kashukutta

Deccan : Katha, Khair, Khairbabul

English : Black Catechu, Cutch

Catechu

Sanskrit : Bahushalya, Balapatra

Tamil : Kadiram, Karangalli

Telugu : Kasu, Khadiram,

Mallasandra

Morphology:

It is a medium-sized, thorny deciduous tree grows up to 13 meters in height. Leaves are bipinnately compound, leaflets 30-50 paired, main rachis pubescent, with large conspicuous gland near the middle of the rachis. Flowers are pale yellow, sessile, found in axillary spikes. Fruits show flat brown pods, with triangular beak at the apex, shiny, narrowed at base. There are 3-10 seeds per pod. The gummy extract of the wood is called katha or cutch[32].

Chemical Constituents: Catechin, epicatechin, epicatechin gallate, procatechinic acid, tannins, alkaloids quercetin and kaempferol. Porifera sterol glucosides and afzelechin gum are also present in minor quantity[60].

Uses: Anti-bacterial activity[33-38], anti mycotic activity[39-41], antioxidant activity[42-46], immuno modulatory activity[47], antipyretic activity[48], hepato-protective activity[48-51], antidiarrheal activity[48, 52, 53], antidiabetic activity[54-58], antisecretory and antiulcer activity[59].

Salacia reticulate:

Family: Hippocrateaceae

Vernacular Names:

English : Marketing nut tree

Kannada : Ekanayakam

Malayalam : Eknayakam, Ponkoranti

Sanskrit : Vairi ekanayakam

Tamil : Ekanayakam, Koranti, Ponkoranti

Telugu : Anukunda chettu

Morphology: A large woody climbing shrub[61]. The greenish grey color bark of the plant is smooth, with white inside. The average dimension of a leaf is 3 – 6 inches long and 1 – 2 inches broad[62]. They are opposite and elliptic-oblong, base acute, apex abruptly acuminate, margin toothed with minute rounded teeth, leathery, hair-less, shiny, lateral nerves about seven pairs, prominent beneath. S. reticulata produces greenish white to greenish yellow color flowers as clustered (2-8) in leaf axils[63]. Flowers are bisexual, calyx lobes entire, anthers dehiscing transversely. Fruits are globose, tubercular, pinkish orange when ripe. They contain 1-4 seeds[63, 64]. The plant flowers in December under Indian conditions[62], whereas in Sri Lanka, flowering starts in late November and seeds are available from March to June[64].

Chemical Constituents:

Presence of mangiferin, kotalanol and salacinol have been identified to have antidiabetic properties[0-72]. Other chemical constituents such as 1,3-diketones, dulcitol and leucopelargonidin (a linear isomer of natural rubber), iguesterin (quinonemethides), epicatechin, phlobatannin and glycosidal tannins, triterpenes, and 30-hydroxy-20(30) dihydroisoiguesterin, hydroxyferruginol, lambertic acid, kotalagenin 16-acetate, 26-hydroxy-1,3-friedelanedione, and maytenfolic acid have also been detected in the root of S. Reticulate[70, 71, 73, 74].

Uses:

Itching and swelling, asthma, thirst, amenorrhea and dysmenorrhea[65]. The roots are acrid, bitter, thermogenic, urinary astringent, anodyne, anti-[66] [67, 68]

inflammatory[66]. The roots and stem of S. *reticulata* have been widely used in treating diabetes and obesity[67, 68], gonorrhea and rheumatism, skin diseases[67] and haemorrhoids[66]. In addition, the water extracts of leaves of S. reticulata could be beneficial for the prevention of diabetes and obesity as it has multiple effects such as the ability to increase the plasma insulin level and lower the lipid peroxide level of the kidney[69].

Strychnos potatorum:

Family: Loganaceae

Vernacular Names:

English : Clearing nut tree

Sanskrit : Ambuprasadanaphala,

Ambuprasadani, Chakshushya,

Chhedaniya.

Hindi : Nirmali

Marathi : Chilbing, Chilhara, Gajara, Nirwali

Bangal : Nirmali

Malalyalam : Katakam, Tettamparap,

Titramparala

Punjabi : Niemali

Tamil : Akkolam, Kadali,

Tettankottai

Urdu : Nirmali

Morphology: *Strychnos potatorum* is a medium-sized, glabrous tree of height 1213 m. Stem is fluted and covered with black, thick, square to rectangular scales. Bark is 1.32 cm thick, black or brownish-black, corky, with very deep and narrow vertical thin ridges, which easily break off. Branches are swollen at nodes. Leaves are about 57.5 cm long, nearly sessile, subcoriaceous, ovate or elliptic, acute, glabrous and shining, spuriously three or five nerved, with lateral nerves springing from the lower part of the mid rib, nearly reaching the tip. The base rounded or acute, petioles 2.5 mm long, flowers large for the genus, in short almost glabrous nearly sessile axillary cymes; peduncles 0.5 mm long; and pedicels very short. Caly ×2 mm long, five lobed; lobes 2.5 mm long, oblong, acute with a tuft of hair inside towards the base of each lobe. Ovary ovoid, glabrous, tapering into a long glabrous style; and stigma obscurely two lobed. Fruit is a berry, black when ripe, globose, 12 cm in diameter, whitish, shining, with short addressed yellow silky hairs.

Seeds are globose in shape. Population of nirmali is depleting fast due to self non-generative mechanism in fruits. They are often decayed and are prone to fungal attack as soon as they fall. Flowering occurs in September-October, while fruiting occurs in December[75-79].

Chemical constituents:

Diaboline (major alkaloid) and its acetate, brucine[84], loganin, mannose, sucrose, arachidonic, lignoceric, linoleic, oleic, palmitic, and stearic acids[85]. β-sitosterol, stigmasterol (also in leaves and bark along with campesterol); oleanolic acid and its 3β acetate, saponins containing acid oleanic, galactose and mannose (seeds) and triterpenes and sterols mannogalactans[86]. alkaloids, flavonoids, glycosides, lignins, phenols, saponins, sterols, and tannins. The lignan glycosides vanprukoside, strychnoside, and glucopyranoside isolated from Strychnos vanprukii have shown significant antioxidant property. Among the five groups of phytochemicals determined from the root, stem bark, and seeds of *Strychnos potatorum*, tannins were found to be the most abundant one followed by saponins and alkaloids. While phenols and flavonoids were low in concentration, quenching and fluorescing alkaloids were reported from the various parts of the plant. However, more number of alkaloids were found in the root and stem bark[87].

Uses: According to Ayurveda, seeds are acrid, alexipharmic, lithotriptic, and cures strangury, urinary discharges, head diseases etc., Roots cure leukoderma whereas fruits are useful in eye diseases, thirst, poisoning, and hallucinations. The fruits are emetic, diaphoretic, alexiteric, etc., According to Unani system of medicine, seeds are bitter, astringent to bowels, aphrodisiac, tonic, diuretic, and good for liver, kidney complaints, gonorrhea, colic, etc. Powdered stem bark mixed with lime juice can be given in cholera. Leaves: As poultice over maggot infected ulcers. Seed: Tonic stomachic demulcent, emetic and used in acute diarrhea, diabetes, gonorrhea, and eye diseases like conjunctivitis, lachrymation, or copious watery of eyes. The paste of seed is reported to be consumed internally along with little tender coconut milk in urinary disorder and retention of urine[80]. It can be used for clarification of turbid water[81]. It also has metal binding properties[82] and antimicrobial properties[83].

Holarrhena antidycentrica:

F**amily**: Apocynaceae

Vernacular names:

Kannada : Koodsaloo, korchie

Konkani : Kudo

Malayalam : Kutakappaala

Punjabi : Keor, kewar

Sanskrit : Indrayava, sakraparyaaya,

sakraasana

Tamil : Kirimllikai

Telugu : Girimallika

Morphology:

It is a large tree of 30 to 40 feet in height. Its flowers are colored white and fruits are half inch in size. A large to small-sized deciduous tree, yielding milky latex. The stem bark is grayish-brown and rough. The stem is white and soft. The leaves are simple, large, arranged opposite to each other, oval shaped,

papery, and smooth or hairy. The flowers are white, small and arranged in a cluster which looks like flattened top. The petals are salver shaped and overlap towards right side. The fruits are long follicles, which look like two slender pencils arising from a node. The follicles have white warty spots on the surface. Dried fruits break open releasing numerous flat seeds with brown hairs. The hairs are short lived[88].

Chemical constituents:

Around 30 alkaloids have been isolated from the plant, mostly from the bark. These include conessine, kurchine, kurchicine,holarrhimine, conarrhimine, conaine, conessimine, iso-conessimine, conimine, holacetin and conkurchin[91]. The bark contains the alkaloids, regholarrhenine-A, -B, -C, -D, -E and -F; pubescine, norholadiene, pubescimine, kurchinin, kurchinine, kurchinidine, holarrifine, holadiene, kurchilidine, kurchamide, kurcholessine, kurchessine, conessine and isoconessimine, and the steroidal compounds kurchinicin and holadyson. The alkaloid conessine is used as a therapeutic drug for the treatment of dysentery and helminthic disorders. Conessine and conimine inhibited the growth of *Shigella sonnei, S. flexneri* and *Salmonella enteritidis* strains in vitro. The plant possesses potent immune stimulant property[90].

Uses: The bark is used as an astringent, anthelmintic, antidontalgic, stomachic, febrifuge, antidropsical, diuretic, in piles, colic, dyspepsia, chest affections and as a remedy in diseases of the skin and spleen. It is a well-known drug for amoebic dysentery and other gastric disorders. It is also indicated in diarrhea, indigestion, flatulence and colic[89]. Root and bark is used in amoebic dysentery. Bark is astringent, anthelmintic, amoebicidal, diuretic. Used in colic, dyspepsia, piles, diseases of the skin and spleen. Seed is anti-bilious. Used for promoting conception, also for toning up vaginal tissues after delivery[90].

***Trigonella foneum greacum* linn.**

Family: Fabaceae

Vernacular Names:

Hindi : Methi

English : Fenugreek seeds

Telugu : Mentulu

Kannada : Mentita

Malayalam : Ventiyam

Punjabi : Metha

Morphology:

Stems 20-23 cm long, straight, rarely ascending, branching rarely, simple, sparsely pubescent, usually hollow, anthocyanin tinged at base or all the way up, rarely completely green. First leaf simple, sometimes weak trifoliate, oval or orbicular with entire margin and long petiole. Stipules fairly large, covered with soft hair. Leaf petiole thickened at the top, attenuate beyond point of attachment of lateral leaflets. The petioles are very small, cartilaginous. The petioles and the blade of the leaflets are anthocyanin-tinged to a varying degree of green. Flowers in leaf axils, more rarely solitary. Calyx 6-8 mm, soft hairy with teeth as long as the tube, half as long as the corolla. Corolla 13-19 mm long pale yellow (white at the end of flowering period). Sometimes is lilac coloured at the base. Standard tend backwards oblong emarginated at apex with bluish spots (these spots are absent from some genotypes), wings half as long as the standard: keel obtuse, split at base. Pods are 10-18 cm long and 3.5 x 5.0 cm broad, curved, rarely straight, with transient hairs. Before ripening, the pod is green or reddish coloured. When ripe, turn into light straw or brown containing 10-20 seeds. Seeds vary from rectangular to rounded in outline with a deep groove between the radical and cotyledons, the length is 3.5-6.0 mm and the width 2.5-4.0 mm, light greyish, brown, olive green or cinnamon coloured, with a pronounced radical that is half the length of the cotyledons[92].

Chemical Constituents:

95. *foenum graecum* leaf is a good source of calcium, iron, β-carotene and several vitamins[95]. A T. *foenum graecum* seed is good source of protein (20-30%) high in tryptophan and lysine; free amino acids (4-hydroxyisoleucine, arginine, lysine, histidine); (25.8%), fat (6.53%), ash content (3.26%), crude fibre (6.28%), energy (394.46 Kcal/100 g seed) and moisture (11.76%)[96]. It contains lecithin, choline, minerals, B. Complex, iron, Phosphates, PABA (Para-Amino Benzoic Acid) and vitamins A and D. In addition, its main chemical compounds are saponins, coumarin, fenugreekine, nicotinic acid, phytic acid, scopoletin and trigonelline[97]. The significance of T. *foenum graecum* seeds is due to the defatted part with high quality fibre including steroidal saponins and protein comparable to those of soybean[98]. The important chemical constituents are saponins, coumarin, fenugreekine, nicotinic acid, phytic acid, scopoletin and trigonelline. The seeds also have the alkaloid trigonelline with mucilage, tannic acid, yellow colour substance, fixed and volatile oils and a bitter extractive diosgenin and gitogenin, a trace of trigogenin[99].

Use:

The seeds are hot, with a sharp bitter taste; tonic, antipyretic, anti-helminthic, increase the appetite, astringent to the bowels, cure leprosy, " vata", vomiting, bronchitis, piles; remove bad taste from the mouth, useful in heart disease (Ayurvedic). The plant and seeds are hot and dry, suppurative, aperient, diuretic, emmenagogue, useful in dropsy, chronic cough, enlargement of the liver and the spleen. The leaves are useful in external and internal swellings and burns; prevent the hair falling off (unani). Fenugreek seeds are considered carminative, tonic and aphrodisiac. Several confections made with this are recommended for use in dyspepsia with loss of appetite, in the diarrhea of puerperal women, and in rheumatism.[93, 94] The seeds being toasted and afterwards infused are used by native practitioners in southern India for dysentery. In the konkan, the leaves are used both externally and internally on account of their cooling properties. An infusion of the seeds is given to small-pox patients as a cooling drink.[93]

***Cassia auriculata* Linn.**

Family: Caesalpinaceae

Vernacular names:

English name : Tannre's cassia

Sanskrit : Charmaranga

Gujarati : Aawa

Hindi : Tarwar

Marathi : Tarota

Morphology:

It is also known as Avaram tree, The leaves are alternate, stipulate, paripinnate compound, very numerous, closely placed, rachis 8.8-12.5 cm long, narrowly furrowed, slender, pubescent, with an erect linear gland between the leaflets of each pair, leaflets 16-24, very shortly stalked 2-2.5 cm long 1-1.3 cm broad, slightly overlapping, oval, oblong, obtuse at both ends, mucronate, glabrous or minutely downy, dull green, paler beneath, stipules very large, reniform-rotund, produced at base on side of next petiole into a filiform point and persistent. Its flowers are irregular, bisexual, bright yellow and large (nearly 5 cm across), the pedicels glabrous and 2.5 cm long. The racemes are few-flowered, short, erect, crowded in axils of upper leaves so as to form a large terminal inflorescence (leaves except stipules are suppressed at the upper nodes). The five sepals are distinct, imbricate, glabrous, concave, membranous and unequal with the two outer ones much larger than the inner ones. The petals also number five, are free, imbricate, crisped along the margin, bright yellow, veined with orange. The anthers number ten are separate, with the three upper stamens barren; the ovary is superior, unilocular, with marginal ovules. The fruit is a short legume, 7.5–11 cm long, 1.5 cm broad, oblong, obtuse, tipped with long style base, flat, thin, papery, undulately crimpled, pilose, pale brown. 12-20 seeds per fruit are carried each in its separate cavity[100].

Chemical Constituents:

Glycerine, Thymine, 1-Butanol, 3 Methyl-, formate, 4H-pyran-4-one; 2,3-dihydro-3,5-dihydroxy-6-methyl, benzaldehyde, 4-methyl-, pentyl ester, Resorcinol, Sucrose, Levoglucosan, D-glucopyranoside, 3-O-methyl-d-glucose; 1,2- Benzenedicarboxylic acid, Benzenamide, n-Hexadecanoic acid, ethyl ester, 1-Tridecyne, Phytol, 1-E,11,Z-13-octadecatriene, 13-Octadecenal, Octadecenoic acid; 1,2,3,4-Tetrahydroisoquinoline-6-ol-1-carboxylic acid, a-Tocopherol, N-acethyramine[106].

Use:

This plant has described to be useful against skin diseases, liver troubles, and tuberculosis and is used in the treatment of hematemesis, pruritus, leukoderma and diabetes. The leaves are laxative and are useful in skin diseases. The shrub is especially famous for its attractive yellow flowers, which are used in the treatment of skin disorders and body odour. It is widely used in traditional medicine for rheumatism, conjunctivitis and diabetes. Its bark is used as an astringent, leaves and fruits as anthelminthic, seeds used to treat eye troubles and root employed in skin diseases[101]. It is also used as hypolipidemic[102] and antioxidant[103], used in skin disease and has hepatoprotective effect[104]. It was also observed that flower and leaf extract of Cassia is shown to have antipyretic activity[105].

Santalum Album:

Family: Santalaceae

Vernacular names:

Bengali : Chandan, sufaid-chandan

Burmese : Santagu

English : Sandal, cendana, sandal tree, east

Indian sandalwood

French : Santal blanc

German : Weisser Sandel

Gujarati : sukhad, sukhet.

Hindi : Chandal, srikhanda, chandan, talia-

parnam, sandal

Italian : Sandalo bianco

Sanskrit : Ananditam, chandana, taliaparnam

Spanish : Sandalo blanco

Tamil : Kulavuri, sandanam, santhanam,

srigandam,ulocidam

Morphology:

The plant was mainly exploited for fragrant sandalwood oil obtained by steam distillation. A small evergreen glabrous tree with slender drooping branches the sapwood white and odorless. The heartwood is yellowish brown and strongly scented. Leaves of dimension 3.8 – 6.3 by 1.6 to 3.2 cm; are elliptic, lanceolate, subacute glabrous, and entire thin base acute; petioles 1 – 1.3 cm long slender flowers, brownish purple induorous, in terminal and auxiliary paniculate cymes shorter than leaves. Perianth campanulated limb of four, valvate triangular segments stamens 4, exerted, alternating with 4 rounded obtuse scales. Drupe globose 1.3 cm diameter. Purple black; endocarp hard ribbed fruit concealed about size of a pea, spherical crowned by rim like remains of perianth tube, smooth, rather flesh, nearly black, seed solitary[107].

Chemical Constituents:

Palmitone (44%) and d-10- hydroxypalmitone[110], Santalol (a-santalol, b-santalol), Hydrocarbons (santene, a and b santenes and nor-tricycloekasantalene), Alcohols (teresantalol and santenol), Acids (teresantalic acid and a-and ß-santalic acid), Ketones (santalone and l-santenone), Tannins, Terpenes, Resins[111], Aldehydes (nor-tricycloekasantalal and isovaleraldehyde), Ketosantalic, Tricyclosantalal, α-santalene, trans-β- bergamotene, β-santalene (S & E), α-curcumine, α- santalol, beta-santalol (S&E), nuciferol, α-santalal and β- santalal in Santalum album[112, 113].

Use:

Sandalwood is mainly used as coolant, and also sedative effect and has astringent activity, making it useful as disinfectant in genitourinary and bronchial tracts, diuretic, expectorant and stimulant. The sweet powerful and lasting odor makes Sandalwood oil useful in perfume industry. The same is also used as tonic for heart, stomach, and liver, anti-poison, fever, memory improvement and as a blood purifier. Various uses mentioned in Ayurveda system about sandalwood are in treatment of various other ailments like diarrhea with bleeding intrinsic hemorrhage bleeding piles, vomiting, poisoning, hiccoughs initial phase of pox, urticaria, eye infections and inflammation of umbilicus[108, 109].

Withania somnifera:

Family: Solanaceae

Vernacular names:

Sanskrit : Ashwagandha

Hindi : Asgandha

English : Winter cherry

Arabian : Bahman

Bengali : Ashwagandha

Japanese : Ashwangandha

Nepalese : Aasoganda

Pusta : Kutilad

Tamil : Amurkkurale Kizhangu

Morphology:

Withania *somnifera* is an evergreen, erect, branching, tomentose shrub, 30-150 cm in height. Leaves are simple, ovate, glabrous, and up to 10 cm long. Flowers are greenish or lurid yellow, small about 1 cm long; few flowers (usually about 5) born together in axillary, umbellate cymes (short axillary clusters). Fruits are globose berries, 6 mm in diameter, orange red when mature, enclosed in the inflated and membranous persistent calyx. Seeds are yellow, reniform and 2.5 mm in diameter[114]. The stout fleshy roots when dry are cylindrical, gradually tapering down, straight, unbranched, 10-17.5 cm long and 6-12 mm in diameter. The main roots bear fiber-like secondary roots. The outer surface of the roots is brownish white and interior is creamy white when broken. They have a short and uneven fracture, a strong odour and mucilaginous biter and acrid taste[115].

Chemical Constituents:

The roots are reported to contain alkaloids, amino acids, steroids, volatile oil, starch, reducing sugars, glycosides, hentriacontane, dulcitol, withaniol, an acid and a neutral compound. The total alkaloidal content of the Indian roots has been reported to vary between 0.13 and 0.31%, though much higher yields (up to 4.3%) have been recorded[114, 115]. The leaves of the plant (Indian chemotype) are reported to contain 12 withanolides, 5 unidentified alkaloids (yield, 0.09%), many free amino acids, chlorogenic acid, glycosides, glucose, condensed tannins, and flavonoids[116, 121]. The green berries contain amino acids, a proteolytic enzyme, condensed tannins, and flavonoids. They contain a high proportion of free amino acids which include proline, valine, tyrosine, alanine, glycine, hydroxyproline, aspartic acid, glutamic acid, and cysteine. The tender shoots are rich in crude protein, calcium and phosphorous, and are not fibrous. They are reported to contain scopoletin. The stem of the plant contains condensed tannins and flavonoids. The bark contains a number of free amino acids[136].

Use: Anti-inflammatory , sedative, hypnotic, narcotic, general tonic, diuretic, aphrodisiac, alterative, deobstruent[114, 116-122], uterine tonic and increases production of semen[114, 118, 119], immunomodulation, and hematopoiesis[123-130], anti-aging[126], musculotropic activity[115], antibiotic activity[115, 120, 126, 131], and antitumorous acivity[115, 120, 126, 132-135].

Aeglemarmelos.

Family: Rutaceae

Vernacular names:

English : Indian quince

Nepali : Bel

French : Oranger du Malabar

Indonesian : Majo tree

Malay : Pakok maja bhatu

Sanskrit : Bilwa

Bangali : Bel

Hindi : Sir phal

Mrathi : Kaveeth

Tamil : Vilva maram

Telugu : Maredu

Urdu : Bel

Morphology:

2. *marmelos* is a slow growing, medium-sized tree, 25 to 30 feet tall. The stem is short, thick, soft, flaking bark, and spreading, sometimes spiny branches, the lower ones drooping. Young suckers bear many stiff, straight spines. There are sharp, axial one-inch long spikes on this tree. The leaflets are oval or lancet shaped, 4-10 cm long, 2-5 cm wide. Leaves composed of 3 to 5 leaflets in it. The lateral leaflets are without petiole and the terminal one has a long one. The petiole is 1-2.5 inch long. Mature leaves emit a peculiar fragrance when bruised. Flowers occurs in clusters of 4 to 7 along the young branchlets, have our re-curved, fleshy petals. The flowers are greenish white in color with a peculiar fragrance. Flowering occurs during the month of May and June. Fruit is spherical or oval in shape with a diameter of 2 to 4 inch. Shell is thin, hard and woody in nature. It is greenish when unripe and, upon ripening, it turns into yellowish color. The pulp of the fruit has 8 to 15 segments. The pulp is yellow, soft, pasty, sweet, resinous and fragrant. Fruition occurs in the month of May and June. The seeds are embedded in the pulp. The seeds are small (nearly 1 cm in length), hard, flattened-oblong, bearing woolly hairs and each enclosed in a sac of adhesive[158].

Chemical constituents:

Different organic extracts of the leaves of A. *marmelos* have been reported to possess alkaloids, cardiac glycosides, terpenoids, saponins, tannins, flavonoids and steroids[165, 166]. A. *marmelos* fruit pulp is reported to have steroids, terpenoids, flavonoids, phenolic compounds, lignin, fat and oil, inulin, proteins, carbohydrates, alkaloids, cardiac glycosides and flavonoids[167].

Use: The different parts of Bael are used for various therapeutic purposes, such as for treatment of Asthma, Anaemia, Fractures, Healing of Wounds, Swollen Joints, High Blood Pressure, Jaundice, Diarrhoea Healthy Mind and Brain Typhoid Troubles during Pregnancy[159]. Aegle *marmelos* has been used as a herbal medicine for the management of diabetes mellitus in Ayurvedic, Unani and Siddha systems of medicine in India[160], Bangladesh[161] and SriLanka[162]. The main usage of the parts of this tree is for medicinal purposes. The unripe dried fruit is astringent, digestive, stomachic and used to cure diarrhea and dysentery[163]. Sweet drink prepared from the pulp of fruits produce a soothing effect on the patients who have just recovered from bacillary dysentery[164]. The ripe fruit is a good and simple cure for dyspepsia. The pulp of unripe fruit is soaked in gingelly oil for a week and this oil is smeared over the body before bathing. This oil is said to be useful in removing the peculiar burning sensation in the soles. The roots and the bark of the tree are used in the treatment of fever by making a decoction of them. The leaves are made into a poultice and used in the treatment of opthalmia.

The leaf part of the plants have been claimed to be used for the treatment of inflammation, asthma, hypoglycemia, febrifuge, hepatitis and analgesic. The mucilage of the seed is a cementing material. The wood takes a fine polish and is used in building houses, constructing carts, and agricultural implements. A yellow dye is obtained from the rind of the unripe fruits. The dried fruits, after their pulp separated from the rind, are used as pill boxes for keeping valuable medicines, sacred ashes and tobacco. In Homeopathic treatments, it is largely used for conjunctivitis and styes, rhinitis, coccygodynia, nocturnal seminal emission with amorous dreams, and chronic dysentery. Ayurveda prescribes the fruit of the herb for heart, stomach, intestinal tonic, chronic constipation and dysentery; some forms of indigestion, typhoid, debility, cholera, hemorrhoids, intermittent fever, hypocondria, melancholia and for heart palpitation. The unripe fruit is medicinally better than the ripe fruit. Leaf poultice is applied to inflammation; with black pepper for edema, constipation and jaundice.

Azadirachta indica.

Family: Acanthaceae.

Vernacular names:

Bengali : Nim, Nimgachh

Guajarati : Danujhada, Limbado,

Limbra, Limdo

Hindi : Nim, Nimb

Sanskrit : Arista, Nimba, Nimbah, Picumarda

English : Indian Lilac, Margosa tree, Neem

tree

Kannada : Bemu, Bevinamara, Bivu, Kaybevu

Punjabi : Bakam, Drekh, Nim.

Morphology:

It is a tree 40-50 feet or higher, with a straight trunk and long spreading branches forming a broad, round, crown with a rough, dark brown bark with wide longitudinal fissures separated by flat ridges. The leaves are compound, imparipinnate, each comprising 5-15 leaflets. The compound leaves are themselves alternating with one another. It bears many flowered panicles, mostly in the leaf axils. The selel are ovate and about 1 cm long with sweet scented white oblanciolate petals. It produces yellow drupes that are ellipsoid and glabrous, 12-20 mm long. Fruits are green, turning yellow on ripening, aromatic with garlic-like odour. Fresh leaves and flowers come in March-April. Fruits mature between April and August depending upon locality[152, 153].

Chemical constituents:

Active principles isolated from different parts of the plant include: Azadirachtin, meliacin, gedunin, nimbidin, nimbolides, salanin, nimbin, valassin, and meliacin forms the bitter principles of Neem oil, the seed also contain tignic acid responsible for the distinctive odor of the oil[155]. Neem kernels contain 30-50% of oil, mainly used by the soap, pesticide and pharmaceutical industries and contain many active ingredients, which are together called triterpene or limnoids[156]. The four best limnoids compounds are: Azadirachtin, Salannin, Meliantriol, and Nimbin. Limonoids contain insecticidal and pesticidal activity[157].

Use: Hot water extract of the bark is taken orally by the adult female as a tonic and emmenagouge. Anthraquinone fraction of dried flower, fruit and leaf is taken orally for leprosy. Hot water extract of the flower and leaf is taken orally as an anti-hysteric remedy, and used externally to treat wound. The dried flower is taken orally for diabetes. Hot water extract of dried fruit is used for piles and externally for skin disease and ulcers. Hot water extract of the entire plant is used as anthelmintic, an insecticide and purgative. Juices of bark of Andrographic *puniculata*, Azardiracta *indica*, Tinospora *cardifolia*, are taken orally as a treatment for filariasis. The hot water extract is also taken for fever, diabetes, and as a tonic, refrigerant, anthelmintic. Fruit, leaf and root, ground and mixed with dried ginger and 'Triphala" is taken orally with lukewarm water to treat common fever[153]. Leaves, due to insecticidal properties, are kept with woollen and other cloths for long time. Leaf juice is given in gonorrhoea and leucorrhoea. Leaves, flower, and leaf-based extracts respectively prompting the recommendation to use neem as a vegetable bitter tonic to promote good health[154].

Gymnema sylvestre:

Family: Asclepiadaceae

Vernacular names:

English : Sugar destroyer, Periploca of the woods

Sanskrit: Ajaballi, Ajagandini, Ajashringi, Bahalchakshu

Hindi: Gur-mar, merasingi

Bengali: Mera-singi

Marathi: Kavali, kalikardori, Vakundi

Gujarati: Dhuleti, mardashingi

Telugu: Podapatri

Tamil: Adigam, cherukurinja

Kannada: Sannager-asehambu

Malayalam: Cakkarakkolli, Madhunashini

Morphology:

It is a large woody twinning shrub growing wildly running over the tops of high trees in forests. Stem is aerial, hard, twinning and branched. The young stems, branches are smooth and cylindrical. Leaves are elliptic, base acute to acuminate, glabrous and opposite. The fruit is a capsule with 10-12 dark brown colored seed[137]. The inflorescence is umbellate cyme with small yellow colored flowers; Follicles are terete and lanceolate upto 3 inches in length. The Calyx-lobes are long, ovate, obtuse and pubescent. Corolla is pale yellow campanulate, valvate, corona single, with 5 fleshy scales. Scales adnate to throat of corolla tube between lobes; Anther connective produced into a memberanous tip, pollinia 2, erect, carpels 2, unilocular; locules many ovuled[138, 139, 140, 141].

Chemical constituents:

The leaves of G. *sylvestre* contain triterpene saponins belonging to oleanane and dammarene classes. Oleanane saponins are gymnemic acids and Gymnema saponins, while dammarene saponins are gymnemasides[144, 145]. The leaves also contain resins, albumin, chlorophyll, carbohydrates, tartaric acid, formic acid, butyric acid, anthraquinone derivatives, inositole alkaloids, organic acid (5.5%), parabin, calcium oxalate (7.3%), lignin (4.8%), cellulose (22%)[146]. The gymnemic acids contain several acylated (tiglolyl, methylbutyroyl, etc) derivatives of deacylgymnemic acid (DAGA) which is a 3-O-β-glucouronide of gymnemagenin (3β, 16β, 21β, 22α, 23, 28-hexahydroxy-olean-12-ene). The individual gymnemic acids (saponins) include gymnemic acids I-VII, gymnemosides A-F and gymnemasaponins.

The presence of gymnemic acids, (+) quercitol, lupeol, (-) amyrin, stigma sterol, etc., have been reported from G. *sylvestre*. A new flavonol glycoside namely kaempferol 3-O-beta-D-glucopyranosyl-(1à4)- alpha-L- rhamno pyranosyl-(1à6)-beta-D-galactopyranoside has also been found in aerial parts of G. *sylvestre*[147, 148]. Three new oleanane type triterpene glycosides i.e. beta-O-benzoyl sitakisogenin 3-O-beta-D-glucopyranosyl (1à3) -beta-D-glucurono pyranoside, the potassium salt of longiospinogenin 3-O-beta-D-glucopyranosyl (1à3) – beta - D-glucopyranoside and the potassium salt of 29-hydroxylongispinogenin 3 - O - beta - D-glucopyranosyl (1à3) - beta-D-glucopyranoside along with sodium salt of alternoside II were also present[149]. Four new triterpenoid saponins, gymnemasins A, B, C and D were identified as 3-O-[beta-D-glucopyranosyl(1à3) – beta - D- glucopyranosyl]-22-O-tiglyol-gymnemanol, 3 - O-[beta-D-glucopyranosyl(1à3)-beta - D - gluc uro – nopyranosyl]- gymnemanol, 3-O-beta-D-glucuronopyranosyl-22-O-tigloyl-gymnemanol and 3- O- beta – D – glucopyranosyl - gymnemanol respectively. The aglycone, gymnemanol, which is a new compound, was characterized as 3 beta-16 beta-22 alpha-23-28-pentahydroxyolean – 12 - ene. Gymnestrogenin, a new pentahydroxytriterpene from the leaves of G. sylvestre has also been reported[150, 151].

Uses:

It has been used in India for the treatment of diabetes for over 2,000 years. The leaves mainly reduce the blood sugar levels. The leaves were also used for stomach ailments, constipation, water retention and liver disease. Extracts of Gymnema is not only claimed to curb sweet tooth, but also for treatment of problems such as hyperglycemia, obesity, high cholesterol levels, anemia, digestion and eye complaints. The leaves of Gymnema are also reported to be bitter, astringent and acrid. The leaves act as anti-inflammatory, anthelmintics, laxative, cardiotonic, expectorant and antipyretic. It is useful in dyspepsia, constipation, jaundice, hemorrhoids, cardiopathy, asthma, bronchitis and leukoderma[142]. Gymnema leaf extract is also used for the treatment of snake bite[143].

Operculina turpettum.

Family: Convolvulaceae.

Vernacular names:

Latin : Ipomoea turpethum

Sanskrit : Shveta, Tribhandi, Trivruta,

Sarvanubhuti, Sarala, Nishotra,

Kalaparni, Nandi, Kalameshi,

Rechani, Kutarana, Bhandi,

Palindi, Ardhachandra

English : Turpeth root, Indian jalap,

Transparent wood-rose

French : Turbith Vegetal,

German : Turpeth Trichterwinde

Hindi : Pithori, Nakpatra, Nishut, Nishoth

Arabic : Turband, Thurbud

Chinese : he guoteng

Chemical constituents:

Root bark is rich in turpeth resin consisting of 10% 'turpethin' which is a glycoside analogue of Jalapine and Convolvulin. It also contains Turpethinic acids-A, B, C, D, & E[177], some ether soluble resin, volatile oil, albumin, starch, lignin salts, ferric oxide, Scopoleptin, Betulin, lupiol & beta-sitosterol[177, 178, 172]. Turpethin is mainly responsible for purgative action and is an excellent &relatively safer substitute for jalap.[172]

Use:

In Ayurveda, root is used internally to treat fevers, anorexia, edema, anemia, ascites, constipation, hepatosplenomegaly, hepatitis, intoxication, abdominal tumors, ulcers, wounds, worm infestation, pruritus and other skin disorders[169]. Root is also administered to treat obesity, haemorrhoids, cough, asthma[170], dyspepsia, flatulence, paralysis, gout, rheumatism, melancholia, scorpion sting, and snake bites[171]. The paste of root powder is used topically to treat vitiligo & other skin disorders, alopecia, cervical lymphadenitis, haemorrhoids, fistulas, ulcers, & chancres[172, 173]. Oil extracted from the root bark is used in skin diseases of a scaly nature[174, 175]. A processed ghee or fresh juice of leaves is dropped into the eyes to treat diseases like corneal opacity or ulcer and conjunctivitis. Root powder mixed with ghee and honey is also used to treat hematemesis, tuberculosis & herpes.[176]

RESULTS AND DISCUSSION: Among different metabolic disorders, diabetes mellitus can be considered as a major cause of economic loss, which can hinder the development of the nation as a whole. Apart from this, uncontrolled diabetes mellitus leads to many complications both macrovascular as well as microvascular including blindness, heart disease, and renal failure. To prevent this devastating health problem, the future research should focus into a new and potentially active antidiabetic agent from plant source. In the present review, the interest is focused on the profile of herbal plants which have a hypoglycemic effect. The families of plants with the most potent hypoglycemic effects include: Periplocacea, Poaceae, Leguminoseae, Hippocrateaceae, Loganaceae, Apocynaceae, Fabaceae, Caesalpinaceae, Santalaceae, Solanaceae, Rutaceae, Asclepiadaceae, and Convolvulaceae. The most commonly studied species are: *Vertivera zizanoidis, Hemidesmus indicus, Mucuna prurita*, *Acasia catechu, Astercantha*, and *Operculina turpethum*. Diverse methods were used in the experiments. The diabetic model that was most commonly used was the streptozotocin-induced diabetic mouse or rat to obtain type I diabetic models. Some authors have used transgenic mice as a model of type II diabetes with hyperinsulinemia. The majority of the articles confirmed the medicinal plants' ability to produce hypoglycemic effects in the management of diabetes mellitus. Numerous mechanism of action has been proposed in these plant extracts.

Some has activity on pancreatic ß cells (synthesis, release, and cell regeneration or reactivation) or the increase in the protective/inhibitory effect against insulinase and the increase of the insulin sensitivity or the insulin-like activity of the plant extracts. Other mechanisms may involve increase of peripheral utilization of glucose, increase of synthesis of hepatic glycogen and/or decrease of glycogenolysis acting on enzymes. Any of these actions may be responsible for the reduction and or abolition of diabetic complications.

CONCLUSION: The above review has presented comprehensive details of anti-diabetic plants used in the treatment of diabetes mellitus all over Indian subcontinent. The plants mentioned above have potent hypoglycemic effects. Plant drugs and herbal formulations are frequently considered to be less toxic and free from side effects than synthetic ones. The prevalence of diabetes mellitus continues to rise worldwide and treatment with oral hypoglycemic drugs ends with numerous side effects and huge monetary expenditure.

As the global prevalence of diabetes is estimated to increase from 4% in 1995 to 5.4% by the year 2025, phytomedicine is being looked up once again for the treatment of diabetes. This review has listed some fifteen potent anti-diabetic herbs available in the southern part of India. More investigations must be carried out to evaluate the mechanism of action and the toxic effect of medicinal plants with ant diabetic effect. We believe that the details of the plants given in this review are useful to students, researchers and practitioners.

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Authors: T. K. Ujwala, Shawn Tomy, Sandra Celine and J. Sam Johnson Udaya Chander *

Authors Address: Pharm D Interns, RVS College of Pharmaceutical Sciences, Coimbatore, TN, India

Email: mail2samjohnson@gmail.com

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