AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Comparative Review of two Anti-Diabetic Herbal Drugs - *GymnemaSylvestre*and *CostusIgneus*

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ABSTRACT

Diabetes mellitus is one of the common endocrine disorders characterized by deranged secretion of insulin and/or glucagon with extensive disturbance of carbohydrate, protein and lipid metabolism. *GymnemaSylvestre* is a woody, climbing plant of tropical forests of central and southern India and in parts of Africa. Gymnema has played an important role in Ayurvedic medicine for centuries. Its use has been confined primarily to the management of diabetes mellitus and similar hypo/hyperglycemic conditions. The first scientific confirmation of G. sylvestre use in human diabetics came almost a century back when it was demonstrated that the leaves of G. sylvestre reduce urine glucose in diabetics. *Costusigneus* Nak commonly known as fiery costus, Step ladder or Spiral flag or Insulin plant, is native to South and Central America. This is a recent introduction to India from America as an herbal cure for diabetes and hence commonly called as 'insulin plant.

Keywords: Ayurveda, Anti-Diabetic Activity, Herbal Drug, Gymnemasylvestre, Costusigneus.

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Received 06June 2014, Accepted10July2014

Please cite this article in press as: Bhatt N *et al.*,Comparative Review of two Anti-Diabetic Herbal Drugs - *GymnemaSylvestre*and *CostusIgneus*. American Journal of PharmTech Research 2014.

INTRODUCTION

'Ayurveda', which translates as "knowledge of life," dates back 5,000 years to the ancient Sanskrit texts, the Vedas. It's a system of healing that examines physical constitution, emotional nature, and spiritual outlook in the context of the universe. According to the philosophy, universal life force manifests as three different energies, or doshas, known as vata, pitta, and kapha.

We are all made up of a unique combination of these three forces. Though everyone has some of each, most people tend to have an abundance of one or two of the doshas. This unique combination is determined at the moment of conception, and is your own personal blueprint, prakriti (nature) [2,3]. As you move through life, the proportion of each of the three doshas constantly fluctuates according to your environment, your diet, the seasons, the climate, your age, and many other factors. As they move into and out of balance, the doshas can affect your health, energy level, and general mood[2,3].

Traditional Herbal Medicine, By definition, 'traditional' use of herbal medicines implies substantial historical use, and this is certainly true for many products that are available as 'traditional herbal medicines'[2]

Anti-Diabetic Activity

Diabetes mellitus is chronic metabolic disorders that affect human body in terms of physical, psychological and social health. It is defined as a group of disorders lipids, carbohydrates and proteins [1,2]. It is becoming the third "killer" of the health of mankind along with cancer, cardiovascular and cerebrovascular diseases[3]. The prevalence of diabetes mellitus is expected to reach up to 4.4% in 2030, and the occurrence was found to be high in India, China, and USA. Historical accounts reveal that as early as 200 BC, diabetes mellitus was well recognized disease in India even as distinguished in two types: a genetically based disorder and a dietary related disorder[4].

Among all the cases of diabetes, type 2 diabetes was found to be more prevalence.Knowledge about diabetes mellitus existed in ancient Egypt and Greece. The word "diabetes" is derived from the Greek word "Diab" (meaning to pass through, referring to the cycle of heavy thirst and frequent urination); "mellitus" is the Latin word for "sweetened with honey" (refers to the presence of sugar in the urine). According to ancient Hindu physicians, "Madhumeha" is a disease in which a patient passes sweet urine and exhibits sweetness all over the body, such as in sweat, mucus, breath, and blood. It was recommended that the low carbohydrate diet and almost total withdrawal of animal fats should be taken by the patients suffering from Madhumeha, whereas

obese adults should live on low calorie diet. There are two types of Diabetes mellitus: Type 1,(Insulin dependent diabetes mellitus), which is hereditary and is treated by insulin, and Type 2,"adult type"(non-Insulin dependent diabetes mellitus) which occurs in elderly people and is treated by controlling the diet andoral hypoglycemic drugs. The drugs which lower the blood sugar level or treat the symptoms of diabetes mellitus are known as hypoglycemic drugs. It can be categorized into insulin and insulin preparation, which are employed only parenterally, and oral hypoglycemic drug which can be administered orally[5]. Table 1 contains list of anti diabetic plant according to the origin of the country[21].

Table 1: List of Anti-diabetic plants from different countries

Country	Plant
Africa	Combretummicranthum, Ficuscapensis, Cassia sieberiana, Ocimum sanctum, Anacardiumoccidentale, Jatrophacurcas, Allium sativum, Citrus medica, Moringaoleifera, Catharanthusroseus, Tamarindusindica, Carica papaya, Landolphiadulcis, Mesonerumbenthamianum, Ocimumviridae, Psidiumguajava and Pterocarpusericens.
Canada	Abiesbalsamea, Acoruscalamus, Aralia racemosa, Arisaematriphyllum, Celastrusscandens, Coryluscornuta, Gaultheria procumbens, Juniperuscommunis, Kalmia angustifolia, Nupharvariegatum, Piceamariana, Populusbalsamifera, Populustremuloides, Prunusserotina, Quercus alba, Quercusrubra, Sassafras albidum, Sorbus Americana, Taraxacumofficinale, Thujaoccidentalis and Verbascumthapsus.
China	Astragalusmembranaceus, Panax ginseng, Polygonatumodoratum, Lyciumbarbarum, Ophiopogonjapocicus, Epimediumsagittatum, Lithospermumerythrorhizon, Rheum palmatum, Hordeumvulgare, Codonopsispilosula, Momordicacharantia, Punicagranatum, Dioscoreaopposita, Allium cepa, Trigonellafoenumgraecum, Prunella vulgaris and Ephedra sinica.
India	Abromaaugusta, Abutilum indicum, Aconitum palmatum, Asparagus racemosus, Berberisaristata, Catharanthusroseus, Costusspeciosus, Ficusracemosa, Ipomoea batatus, Momordicachrantia, Syzygiumcuminii, Trigonellafoenumgraecum, Urticadioica, Zingiberofficinale, Allium cepa, Allium sativum, Aloe vera, Cajanuscajan, Gymnemasylvestre, Momordicacharantia, Ocimum sanctum, Pterocarpusmarsupium and Tinosporacordifolia.
Israel	Achilleafragrantissima, Achilleafragrantissima, Allium cepa, Coridothymuscapitatus, Pinushalepensis, Salvia fruticosa, Sileneaspera and Teucriumpolium.
Jordan	Allium cepa, Artemisia vulgaris, Aloe vera , Alpiniaofficinarum, Brassica oleraceae, Cichoriumpumilium, Cinnamomumzeylanicum, Hibiscus sabdariffa, Juniperusphoenicea, Pisumsativum, Quercuscoccifera, Rheum ribes, Sarcopoteriumspinosum, Terminaliachebula, Trigonellafoenumgraecum, Varthemiaiphionoides and Zizyphusspina-christi.
Mexico	Abutilon trisulcatum, Agave atrovirens, Allium cepa, Aloe barbadensis, Ananascomosus, Argemonemexicanam, Artemisia absinthium, Bidensleucantha, Carica papaya, Cassia fistula, Catharanthusroseus, Jatrophaelbae, Musa sapientum, Piper hispidum, Plumbagoscandens, Quassiaamara,

	Quercusacutifolia, Sennamultiglandulosa, Tamarindusindica, Trigonellafoenumgraecum and Zizyphus acuminate.
Morocco	Ammivisnaga, Carumcarvi, Artemisia absinthium, Lactuca sativa, Tetraclinisarticulata, Lavanduladentata, Trigonellafoeniculumgraecum, Allium sativum, Aloe succotrina, Linumusitatissimum, Eucalyptus globulus, Myrtuscommunis, Sesamum indicum, Punicagranatum, Nigella sativ, Prunusamygdalus, Citrus bigaradia, Peganumharmala and Zygophyllum.
NorthAmerican	Abiesbalsamea, Aralia nudicaulis, Cornusstolonifera, Juniperuscommunis, Piceamariana, Prunusserotina, Quercusrubra, Solidagocanadensis, Sorbusamericana, Taraxacumofficinale and Verbascumthapsus.

GYMNEMA SYLVESTRE

GymnemaSylvestre is a woody, climbing plant of tropical forests of central and southern India and in parts of Africa. Distribution is worldwide and it is recognized in the traditional medicinal literature of many countries including Australia, Japan, and Vietnam. Gymnema has been referred to in some texts as *Asclepiasgeminata, Gymnemamelicida,* and *Periplocasylvestris*. Gymnema has played an important role in Ayurvedic medicine for centuries. Its use has been confined primarily to the management of diabetes mellitus and similar hypo/hyperglycemic conditions[6,7,8]. Despite the part used being the leaf, another common name of this species is miracle fruit, which is shared by two other species: Synsepalumdulcificum and Thaumatococcus daniellii[6].

Vernacular Name

English :Periploca of the woods

Hindi :GudmarSanskrit : Mesasrngi

Geographical Distribution

G. sylvestre is native to the tropical forests of central and southern India had wider distribution and it grows in the plains fromthe coast, in scrub jungles and in thickets at an altitude ranging from 300 - 700m. The genus Gymnema comprises 40 species distributed from Western Africa to Australia. G.acuminatum (Roxb.) Wall, G. aurantiacum, G. balsamicum, G. elegans W&A, G. hirsutum W&A, G.lactiferum, G. latifolium, G.montanumHook.f., G. sylvestre R.Br., G. tingens W&A, G. indorum, G.yunnanse and G. spartum are some of the important species of genus Gymnema.. They are mainly

distributed in the Deccan peninsula parts of northern, western India, Tropical Africa, Australia, Vietnam, Malaysia and Sri Lanka[7].

Taxonomy

Kingdom: Plantae

Subkingdom: Tracheobionta

Super division: Spermatophyta

Division: Magnoliophyta

Class: Magnoliopsida

Subclass: Asteridae

Order: Gentianales

Family: Asclepiadaceae

Genus: Gymnema

Species: sylvestre

Morphology

G. sylvestre is a slow growing, perennial, woody climber, distributed throughout the India, in dry forests upto 600 m height. It is mainly present in the tropical forest of Central and Southern India. It is also found in Banda, konkan, Western Ghats, Deccan extending to the parts of western and northern India [6-8]. The plant is a large, more or less pubescent, woody climber.

Figure 1: Photograph of *GymnemaSylvestre*

The leaves are opposite, usually elliptic or ovate (1.25 – 2.0 inch x 0.5-1.25 inch). Flowers are small, yellow, in axillary and lateral umbel in cymes; Follicles are terete and lanceolateupto 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[7].

G. sylvestre is a potent antidiabetic plant and used in folk, ayurvedic and homeopathic systems of medicine. It is also used in the treatment of asthma, eye complaints, family planning, snakebite,urinary complaints, stomach problems, piles, chronic cough, breathing troubles, colic

pain, cardiopathy, constipation, dyspepsia and haemorrhoids, hepatosplenomegally. In addition, it also possesses antimicrobial, anti-hypercholesterolemic, anti- inflammatory and sweet suppressing activities and it also acts as feeding deterrents to caterpillar[7].

Literature surveys reveal that, G. sylvestre is a popular plant used in treating various ailments and used as one of the important ingredient in several ayurvedic formulations, very little efforts have also been made to verify its efficacy through scientific screening in animal models and clinical trials. The present review highlights the various folk, ayurvedic uses and pharmacognostical, phytochemical and pharmacological studies conducted on G. Sylvestre[7,8].

Phytochemical Study

The leaves of G. sylvestre contain triterpenesaponins belonging to oleanane and dammarene classes. Oleananesaponins are gymnemic acids and gymnemasaponins, while dammarenesaponins are gymnemasides. 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%).

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, 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-(1-->4)- alpha-Lrhamnopyranosyl-(1-->6)-beta-D-galactopyranoside has also been found in aerial parts of G. sylvestre [22-25].Three new oleanane type triterpene glycosides i.e. beta-O-benzoylsitakisogenin 3-O-beta-D-glucopyranosyl (1-->3)-beta-D-glucuronopyranoside, the potassium salt of longiospinogenin 3-O-beta-D-glucopyranosyl (1-->3)-beta-D-glucopyranoside and the potassium salt of 29- hydroxylongispinogenin 3-O-beta-D-glucopyranosyl (1-->3)-beta-D-glucopyranoside along with sodium salt of alternoside II were isolated from an ethanol extract of the leaves of G. sylvestre [26]. Four new triterpenoidsaponins, gymnemasins A, B, C and D isolated from the leaves of G. sylvestre were identified as 3-O-[beta-D-glucopyranosyl(1-->3)-beta Dglucopyranosyl]-22-O-tiglyol-gymnemanol,3-O-[beta-D glucopyranosyl(1-->3)-beta-D-glucuro - 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 been reported[9-11,23].

Major Pharmacological Activity

Antidiabetic Activity

The first scientific confirmation of G. sylvestre use in human diabetics came almost a century back when it was demonstrated that the leaves of G. sylvestre reduce urine glucose in diabetics. In an animal study, Paliwal et al have investigated that gurmar leaf powder had positiveand encouraging effects over blood glucose levels. No adverse effect was observed on the healthstatus of the subjects and thus, it can thus be concluded that gurmar powder is effective in lowering the fasting as well as postprandial blood glucose levels. Moreover, Sugihar et al have investigated the antihyperglycemic action of a crude saponin fraction and five triterpene glycosides derived from the methanol extracts of G. Sylvestre[10-12].

COSTUS IGNEUS

Costusigneus Nak (syn. *Costuspictus* D. Don, *Costusmexicanus* Liebm ex Petersen or *Costuscongenitus* Rowle), commonly known as fiery costus, Step ladder or Spiral flag or Insulin plant, is native to South and Central America. This is a recent introduction to India from America as an herbal cure for diabetes and hence commonly called as 'insulin plant. It is widely grown in gardens as ornamental plant in South India and also run wild in many places. It is used in India to control diabetes, and it is known that diabetic people eat one leaf daily to keep their blood glucose low. Leaves of C. igneus were one among the plants known to be effectively used for treating diabetes by the tribal people of Kolli hills of Namakkal district, Tamilnadu. In Mexican folk medicine, the aerial part of C. pictus D. Don is used as an infusion in the treatment of renal disorders[13-15].

The plant belongs to the family Costaceae. The Costaceae was first raised to the rank of family by Nakai on the basis of spirally arranged leaves and rhizomes being free from aromatic essential oils. Before the elevation to family status, Engler and Prantl recognized Costoideal as a subfamily under Zingiberaceae. Several anatomical and morphological features support this isolated position including well developed aerial shoot with distinct, rigid, and commonly branched stems. The leaves are inserted in a low spiral with divergences. The family Costaceae consists of four genera and approximately 200 species. The genus Costus is the largest in the family with about 150 species that are mainly tropical in distribution.The present review deals with the recent research carried out in the area of phytochemistry, pharmacological, biological activities, and safety of Costusigneus Nak[14,15].

Taxonomy

Botanical name: Costusigneus

Kingdom: Plantae

Subkingdom: Viridaeplantae

Division: Tracheophyta

Super division: Euphyllophytina

Class: Liliopsida

Subclass: Commelinidae

Order: Zingiberales

Family: Costaceae

Subfamily: Asteroideae

Genus: Costus

Species: Igneus

Morphology

It is a perennial, upright, spreading plant reaching about two feet tall, with the tallest stems falling over and lying on the ground. Leaves are simple, alternate, entire, oblong, evergreen, 4-8 inches in length with parallel venation. The large, smooth, dark green leaves of this tropical evergreen have light purple undersides and are spirally arranged around stems, forming attractive, arching clumps arising from underground rootstocks. Beautiful, 1.5-inch diameter, orange flowers are produced in the warm months, appearing on cone-like heads at the tips of branches. Fruits are inconspicuous, not showy, less than 0.5 inch, and green-colored[16,17].

Figure 2: Photo graph of *CostusIgneus*

Growth and propagation

Spiral flag grows in either full sun or partial shade. It needs fertile soil and ample moisture, and is often planted near water. Propagation is by division of the clumps, cuttings, or by separating the offsets or plantlets that form below the flower heads. Mites and nematodes can be a problem, especially on light, sandy soil. The plant has no diseases are of majorconcern[18].

Phytochemical Study

Sequential screening for phytochemicals of C. igneus leaves revealed that it is rich in protein, iron, and antioxidant components such as ascorbic acid, α-tocopherol, β-carotene, terpinoids, steroids, and flavonoids. It was revealed in another study that methanolic extract was found to contain the highest number of phytochemicals such as carbohydrates, triterpenoids, proteins, alkaloids, tannins, saponins, and flavonoids. Preliminary phytochemical evaluation of Insulin plant (C. pictus) revealed that the leaves contain 21.2% fibers. Successive extracts gave 5.2% extractives in petroleum ether, 1.06% in cyclohexane, 1.33% in acetone, and 2.95% in ethanol. Analysis of successive extracts showed presence of steroids in all extracts. The ethanol extract contained alkaloid also. The major component of the ether fraction was bis (2'-ethylhexyl)-1,2-benzenedicarboxylate (59.04%) apart from α-tocopherol and a steroid, ergastanol. Stem showed the presence of a terpenoid compound lupeol and a steroid compound stigmasterol. Bioactive compounds quercetin and diosgenin, a steroidal sapogenin, were isolated from C. igneus rhizome. Trace elemental analysis showed that the leaves and rhizomes of C. pictus contains appreciable amounts of the elements K, Ca, Cr, Mn, Cu, and Zn. Steam distillation of stems, leaves, and rhizomes of C. pictus D. Don yielded clear and yellowish essential oils. The major constituents identified in the essential oil are enlisted in table below[18,19].

Table 1.2: Content of oil of *CostusIgneus*

Stem oil (%)	Leaf oil (%)	Rhizome oil (%)
Hexadecanoic acid (28.3)	Hexadecanoic acid (24.51)	Hexadecanoic acid (25.26)
9,12-Octadecadienoic acid (18.33)	2-pentanol (22.48)	9,12-octadecadienoic acid (7.74)
Dodecanoic acid (5.62)	Dodecanoic acid (3.96)	Dodecanoic acid (16.56)
Linalylpropanoate (6.03)	Farnesyl acetone (7.04)	Tetradecanoic acid (10.20)
A-eudesmol (3.55)	A-ionone (8.01)	Linalool (8.48)

Major Pharmacological Activities

Anti-diabetic Activity

A lot of research work has been conducted to evaluate the anti-diabetic effect of insulin plant. The summary of the animal experimentations done are tabulated. In a cross- sectional clinical study, patients consuming either one fresh leaf or 1 teaspoon of shade-dried powder/day of C. igneus in

conjunction with other modalities of treatment had effectively produced glycemic control in diabetics[20,21].

However, A study evaluated the ability of a tea made from the leaves of C. spicatus to alter glucose homeostasis in mice, a model of obesity-induced hyperglycemia, with progressive beta-cell depletion. Intraperitoneal (IP) insulin tolerance testing after the 10-week study period showed that C. spicatus tea consumption did not alter insulin sensitivity, which suggested that at the dose given, tea made from C. spicatus leaves had no efficacy in the treatment of obesity-induced hyperglycemia[22,24,25].

CONCLUSION

The prevalence of diabetes mellitus is expected to reach up to 4.4% in 2030, and the occurrence was found to be high in India, China, and USA. Diabetes mellitus was well recognized disease in India even as distinguished in two types: a genetically based disorder and a dietary related disorder.According to ancient Hindu physicians, “Madhumeha” is a disease in which a patient passes sweet urine and exhibits sweetness over the body, such as in sweat, mucus, breath, and blood. From this two herbal anti-diabetic drug Gymnema is a traditional drug, and Costusigneus’s activity is recently evolved.

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