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A COMPREHENSIVE REVIEW ON THE ANTI-DIABETIC ACTIVITY OF *MOMORDICA CHARANTIA* AND *SYZYGIUM CUMINI* SEEDS

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ABSTRACT

Diabetes mellitus is the most common endocrine disorders accompanied with many metabolic syndromes. Use of herbal medicines has been an option to treat a great number of diseases such as diabetes and its complications. In this article, general descriptions, traditional uses, medicinal properties and pharmacology activities of *Momordica charantia* and *Syzygium cumini* seeds have been reviewed. *Momordica charantia* (karela) is an herbal plant grown in tropical and subtropical regions, belonging to the family- Cucurbetaceae. The main phytochemical constituents of karela are tri-terpenes, proteins, steroid and phenolic compounds, which are responsible for biological and p'cological activities such as, anti-diabetic, antiviral, anti-malarial, antitumor etc. *Syzygium cumini* are also known as Jamun in India. *Syzygium cumini* (Jamun) contains various phytochemical components such as, carbohydrate, protein, vitamin, steroid, alkaloid and phenolic compound. *Syzygium cumini* are shows pharmacological activities including, anti-viral, anti-diabetic, anti-pyretic and anti-diarrheal.

Keywords – Diabetes mellitus, *Syzygium cumini* seeds and *Momordica charantia* seeds

1. INTRODUCTION:-

Diabetes mellitus is the complex group of diseases with varieties of causes. People or human beings with diabetes having high blood glucose levels, also called as high blood sugar or hyperglycemia. Diabetes mellitus are the most common metabolic syndromes. These ways, the body use digested foods for energy. The digestive tract break down of carbohydrates, sugars and starches found in many foods into

glucose, form of sugars that enters the blood stream or blood vessels. With the help of the hormones, insulin, cells throughout the body absorb glucose and it's used for energy[1]. Diabetes mellitus are developed in the body does not make enough insulin or unable to used insulin effectively, or both. Insulin is secreting in the pancreas, an organ located behind the stomach. The pancreas contains clusters of cells called as islets. β-cells within the islets make insulin and it's released into the blood.

In present investigation, we reported the types, pathophysiology, diagnosis and treatment of diabetes mellitus through the combination extract of herbal medicines.

2. TYPES AND CAUSES:-

The two main types of diabetes mellitus are; type-1 diabetes and type-2 diabetes. A third type is gestational diabetes, it's developed during pregnancy. Other type of diabetes are caused by defects in specific genes or changes in a single genes, diseases of the pancreas, certain drugs or chemicals, infection and other conditions. Some people are shows signs of both type-1 diabetes and type-2 diabetes mellitus.

2.1Type-1 diabetes(insulin- dependent diabetes mellitus):-

Type-1 diabetes is caused by a lack of insulin due to destruction of insulin and it's produces beta cells in the pancreas. In type-1 diabetes are an autoimmune disease, the body immune system attack and destroyed the β-cells. Type-1 diabetes is typically occurs in children's and young adult, though it can appear in any age. In the past, type-1 diabetes was called insulin-dependent diabetes mellitus (IDDM). Latent auto-immune diabetes in adults (LADA) may be slowly developed in much kind of type-1 diabetes mellitus[3].

2.2Type-2 diabetes (non-insulin dependent diabetes mellitus):-

Type-2 diabetes are the most common form of diabetes is caused by a combination factors, including insulin resistance, a condition in which the body muscles, fats and liver cells does not used insulin effectively. Type-2 diabetes developed when the bodies can no longer secretion of enough insulin to compensate for the impaired ability to used insulin. Symptoms of type-2 diabetes may be developed gradually and can be subtle; some patients with the type-2 diabetes [2] remain undiagnosed for years. Type-2 diabetes may developed most often in middle age and older people who are also increased body weight or obese[2].

Thesediseases, once rare in youth, are becoming more common in overweight and obese children and adolescents.

2.3 Type-3 diabetes (Gestationaldiabetes mellitus):-

Gestational diabetes mellitus is defined as the glucose intolerance, which is first recognized during pregnancy condition in women. The diagnosis of gestational diabetes mellitus can represent unidentified pre-existing diabetic conditions, the unmasking of a compensated metabolic abnormality during the pregnancy or a direct metabolic consequence of the hormonal changes. In normal conditions, the insulin secretion is increased by 1.2 to 2.5 fold during pregnancy reflecting a state of insulin resistance [3].

2.4. Other type of diabetes (Genetic defect of β-cells):-

Some relatively un-common form of diabetes known as monogenic diabetes is caused by mutations or changein single genes. These mutations are usually inherited, but sometimes the gene mutations are occurs spontaneously. Most of these gene mutations are cause diabetes by reducing beta cells ability to produce insulin. The most common type of monogenic diabetes is neonatal diabetes mellitus (NDM) and MODY. Neonatal diabetes mellitus (NDM) occurs in the first 6 months of life. MODY is usually found during adolescence or early adulthood but sometimes is does not diagnosed until later in life[3].

3. PATHOPHYSIOLOGY:-

Insulin is the principal hormone which regulates the uptake of glucose from the blood into most cells of the body, especially liver, muscles and adipose tissue. Therefore, deficiency of insulin or the insensitivity of its receptors plays a central role in all form of diabetes mellitus. The body obtains glucose from 3 main places, the intestinal absorption of foods, the breakdown of glycogen, the storage forms glucose found in the liver and gluconeogenesis, the generation of glucose from non-carbohydrate components in the body. Insulin plays a critical role in balancing glucose level in body. Insulin can be inhibited the breakdown of glycogen or the process of gluconeogenesis, it can stimulates the transport of glucose into fats and muscle cells and it can stimulates the storage of glucose in the form of glycogen. Insulin are released into the blood by β-cells, found in the islet cells of Langerhans in the pancreas, in response to rising level of blood glucose, typically after eating. Insulin is used by about two third of the

body's cells to absorb glucose from of the blood for used as fuels, for conversion to other needed molecules. Lower blood glucose levels are result in decrease insulin release from the β-cells and in breakdown of glycogen to glucose[3].

This process is mainly controlled by the hormones, glucagon, which acts in the opposite manner to insulin. The amount of insulin available are insufficient, if the cells respond poorly to the effects of insulin (Insulin insensitivity or Insulin resistance), or if the insulin itself is defective, then glucose will not be absorbed properly through the body cells that require it, and will not be stored appropriately in the liver and muscle cells. The net effects are persistently high levels of blood glucose, poor protein synthesis and other metabolic derangement, such as acidosis. The glucose concentration in the blood remains high over time. When, the kidneys will reach a threshold of reabsorption and glucose will be excreted in the urine (glucosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water throughthe kidney, resulting in increased urine production (polyuria) and increased fluid losses. Lost blood volume will be replaced osmotically from of water held in body cells and other body compartments, causing dehydration and increased thirst (Polydipsia).

4. HERBAL PLANTS USED IN TREATMENT OF DIABETES MELLITUS [4]:-

Table 1: List of some herbal plants for treatment of diabetes

Botanical Name	Common Name	Family	Part Used	Active Constituents
Curcuma Longa	Turmeric	Zingiberaceae	Rhizomes	Curcumin
Dioscorea-dumetorum	Kunth	Dioscoreaceae	Bark	Dioscoretine
Azadirachta-indica	Neem	Meliaceae	Bark	Nimbin
Areca Catechu	Supari	Arecaceae	Leaves	Arecoline
Momordica-charantia	Bitter gourd	Curcubitaceae	Fruit	Charantin
Trigonella-foenum	Methi	Fabaceae	Seed	Diosgenin
Syzygium-cumini	Jambu	Myrtaceae	Fruits, seed.	Cuminiresinol

5. ANIMAL MODELS USED IN ANTI-DIABETIC ACTIVITY [5]:-

5.1 *in-vivo* animal models for diabetes mellitus:-

5.1.1. Pharmacological induction for diabetes.

5.1.2. Surgical models for diabetes.

5.1.3. Genetic models for diabetes:-

(a) Animal strains that spontaneously developed diabetes.

(b) Genetically engineered diabetic mice/rats.

5.1.4. Other models for type-2 diabetes to identified the reduction of pancreatic β-cell mass.

5.2 *In-vitro*study for diabetes mellitus:-

5.2.1. *In-vitro* study on insulin secretion:-

(a) Studies for isolated pancreatic islet cell lines.

(b) Studies for insulin-secreting cell lines.

5.2.2. *In-vitro* study on glucose uptake.

6. GENERAL DESCRIPTION OF THE PLANT:-

6.1 *Momordica charantia:-*

Momordica charantia L. (karela) has been used as a medicines and foods. The plants are called by different names since it grown in tropical regions such as India, Malaya, China, tropical Africa, Middle East, America and Thailand. Propagated by seeds, bitter gourd vine flowers in about 30-40 days and produced mature fruits about 20 days after that. For the medical purpose, the fruits may be used fresh as pulp or juice or dry powder or in a fluid extracts. *Momordica charantia* have been used in various Asian traditional medicine systems for a long time. Like most bitter-taste food, bitter melon are stimulates digestion.While this can be helpful in human with sluggish digestion, dyspepsia, and constipation, it can sometimes make heartburn and ulcers worse. The fact that *Momordica charantia* are also a demulcent and at least mild inflammation modulator.

6.1.1 Botanical profile [6]:-

Kingdom- Plantae

Division- Magnoliophyta

Class- Magnoliopsida

Order- Cucurbitales

Family- Cucurbitaceae

Genus- *Momordica*

Species-*Momordica charantia*

Fig.1:- ***Momordica charantia*** **(Karela)**

6.1.2 Taxonomy [6]:-

Bitter gourd (Karela) is a flowering vines in the family-Cucurbitaceae. It's a slender, climbing annual vines with long stalked leaves and yellow colors, solitary male and female flowers borne in the leaves axils. Leaves aresimple; usually palmate 5-7 lobed, tendrils un-branched or two branched. It bears simple alternate leaves 4-12cm across, with 3-7 cm deeply separated

lobes. Fruits: ovoid, ellipsoid or spindle shaped, usually ridged or warty, dehiscent irregularly as a three valves fleshy capsule or indehiscent. The young fruits are emerald green colors, turning to orange-yellow when ripened. On maturity, the fruits are splits into three irregular valves that curl backwards and released numerous reddish brown to white seeds encased in scarlet arils. Bitter melons are comes in many variety of shape and sizes.

6.1.3 Biological activities[8]:- The different parts of the Bitter melons (Karela) contains following various biological activities such as:-

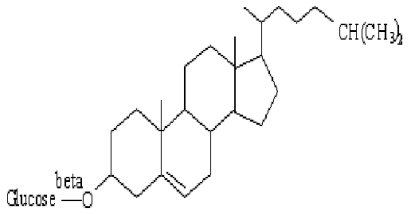
Root –Acrid, astringent, bitter.

Leaf – Antipyretic, bitter, emetic, purgative.

Fruit – Anti-helmintic, acrid, anti-diabetic, anti- inflammatory, depurative.

6.1.4 Chemical constituents[9]:-

The main active constituents of bitter melon (karela) are triterpene, protein, steroids, alkaloids, lipids and phenolic components.



Charantin

6.1.5 Medicinal and traditionaluse[10]:-

Momordica charantia have been used in various Asian traditional medicine systems:-

Roots are used as the treatment of syphilis, rheumatism, ulcers, septic swelling.

Seeds are used in liver and spleen problem, ulcer, diabetes, intestinal parasites, high cholesterol and intestinal gas etc.

Fruits of bitter gourd (karela) used in asthma, inflammation, leprosy, diabetes.

6.1.6 Pharmacological activity:-

***Anti-oxidant activity*:-**Antioxidant activity of extracted phenolic compound from of bitter melon. Antioxidant properties of *Momordica charantia*(Karela) seeds on STZ induced diabetes rats have been studied and result clearly suggested that seeds of *Momordica charantia*(Karela) may be effectively normalize the impaired antioxidant status in STZ induced diabetes[13].

***Anti-diabetic activity*:-**

Many traditional herbal remedies that have been used to treatment for diabetes in Asia and other developing countries.*M. charantia* Karela) are one of the plants that have been investigated thoroughly for the treatment of diabetes. With the traditional and medicinal use supported by modern scientific evidence of the beneficial

functions of the *M. charantia,* it's one of the most promising plants for the diabetes mellitus today. Investigation of the traditional uses of *M. charantia* (Bitter gourd) in India revealed that it is one of the most important for lowering blood glucose levels in patients with the diabetes mellitus[14].

Possible modeof action of *Momordica charantia*(Bitter melon) and their extract [16]:-

The various extracts of *Momordica charantia* and components are believed to exert their hypoglycemic effects by different physiological, pharmacological and biochemical modes. The possible modes of the hypoglycemic actions of *Momordica charantia* (Karela) and its various extracts and its hypoglycemic effects. Stimulates to the peripheral and skeletal muscles glucose utilizations and inhibition of intestinal glucose uptake, prevention of isle β-cells and their functions. Today, over 140 different studies worldwide have been investigated anti-hyperglycemic and hypoglycemic effects of the different extracts of bitter gourd and ingredients of bitter gourdin both human and animal models. Extract of bitter gourd and isolated compoundsare believed to exert their hypoglycemic effects via different physiological and biochemical process. These are includes insulin secretagogue like effect, stimulation of skeletal muscles and peripheral cells glucose utilization, inhibition of intestinal glucose uptake and inhibition of adipocyte differentiation, suppression of key gluconeogenic enzymes and stimulation of key enzymes, HMP pathway and preservation of pancreatic islet cells and their functions.

Preservation of pancreatic β-cells and insulin production:-

It's previously demonstrated viathat oral administration of *M. charantia* could lead to the secretion of insulin from of endocrine pancreatic β-cells. This observation was further confirmed via[17] who investigated the effect of daily oral administration of *M. charantia* fruits juice and distribution of α, β and δ cells in the pancreas of STZ- induced diabetic rats using immune-histochemical methods. The feeding of alcoholic extract from of *M. charantia* showed definite improvement in the islet cells of Langerhans.Physiological experiments have been also shown that *M. charantia* can stimulate to insulin secretion from the endocrine pancreas and elicit glucose uptake in the liver**.** Current evidence therefore, indicates that the

recovery and subsequent increase in the no. of insulin producing cells followed via the release of insulin may be part of the several pathways by which *M. charantia*exert its hypoglycemic effects. In addition, the properties mentioned above, *M. charantia* (Bitter gourd) and its extracts may possess cell-like proliferation and growth like properties similar to that of insulin.

***Momordica charantia* (Bitter melon) and the glucose metabolism:-**

Insulin plays a major biochemical role in stimulating the uptake of glucose via different cells of the body for the production of energy. Therefore, *Momordica charantia* andits various extracts and components had been reported to exert hypoglycemic effects, and then it is important to understand whether *Momordica charantia* may have a direct effect in including a reduction in blood glucose level studied. Previous studies had been shown that both the aqueous and alcoholic extracts of *Momordica charantia* can inhibit the activities of fructose-1, 6-diphosphatase and glucose-6-phosphatase and at the same time stimulating the action of glucose-6-phosphatase dehydrogenase. It was previously reported that *Momordica charantia* (Karela)and its various extracts can stimulate the peripheral cell glucose uptake[18].

Animal studies of *Momordica charantia* (Bitter melon):-

Various animal studies hasbeen repeatedly shown hypoglycemic effects of the seeds, fruit, pulp, leaves and whole plant of *Momordica charantia* in normal animals. In particular, *Momordica charantia* hasimproved glucose tolerance and suppresses postprandial hypoglycemia in rats and *Momordica charantia* extracts can be enhanced insulin sensitivity and lipolysis. Some studies also claimed that the hypoglycemic effects of bitter melon were compared with orak medication such as tolbutamide, chlorpropamideand glibeclamide. Other studies suggested a role of a- and g- peroxisome proliferator activated (PPARa and PPARg) which are pivotal in lipid and glucose haemostasis and may mitigate insulin resistance[19].The alcoholic extract of *Momordica charantia* was quite effective in lowering blood sugar levels and islets histopathology also showed improvement. The lowered blood sugar and improvement in islets histology remained as such even after discontinuation of extracts feeding for 15 days.

Clinical studies of *Momordica charantia*:- More than 1000 herbal compounds have been used via diverse cultures of the world treat hyperglycemia and among them bitter melon is one of the most popular herbal resource. An earlier studies on the development of diabetic cataracts demonstrated that blood sugar levels dependent cataract formation was showed down by the consumption of *Momordica charantia* extract in association with better glucose homeostasis. Today, processed *Momordica charantia* in the form of capsules or tablets are commonly advertised and sold. The herbal products are marketed under the brand names Gourdin, Karela and Glucobetic in Canada, India, the United Kingdom, the United States and many Asian countries. Compared with animal studies,clinical studies regarding the hypoglycemic effects of *M. charantia*(Bitter gourd) have been sparse and sporadic. Lakholia, a physician, was probably the first to documents the therapeutic effects of *Momordica charantia* 1956 usinghim as the subjects[20].

6.2 *Syzygium cumini:-*

Syzygium cumini L. (family-Myrtaceae) are commonly known as jamun, duhat in Hindi and black plum, black plum tree, Indianblack berry, jambolan, jambolan plum, java plum, Malabar plum in English. *Syzygium cumini* are one of the most widely distributed trees of India, occurs in the major forest groups except in the very arid regions[25].

6.2.1 Scientific classification (*Syzygium cumini*)**:-**

Kingdom:-Plants, planta.
Subkingdom:-Green plants.
Division:-vascular plants.
Subdivision:-Seed plants.
Class:- Magnliopsida.
Superorder:-Rosanae.
Order:-Myrtales.
Family:- Myrtaceae.
Genus:-*Syzygium*
Species:-*Syzygiumcumini* (L.) skeels

Fig.2- *Syzygium cumini* (Jamun)

6.2.2 Taxonomy:-

Syzygium cumini areever green tree to 25m (80ft) tall, with young stems grayish white colors and lower bark coarse and discolored. Leaves opposite, simple, entire, elliptic to broadly oblong, smooth, glossy, somewhat leathery, 5-10cm (2-5 in) long, short pointed at tips; petioles to 3 cm (1.2 in) long; midrib prominent, yellowish colors; blades with many lateral veins closely parallel. Flowers white to pinkish, about cm (0.5 in) across, in branched clusters at stem tips; calyx cup like; 4 petals, fused into a cap; many stamens. Fruits, an ovoid, 1-seeded berry to 2cm (0.8 in) long, purplish red, shiny, with white to lavender flesh[26].

6.2.3 Chemical constituents[27]:-

Various types of active constituents presences in the plant of *Syzygiumcumini*(jamun), such as jambosine, gallic acid, β- sitosterol, ellagic acid, qurecetin, oleanolic acid, anthocyanin, myricetine etc.

6.2.4 Traditional and medicinal uses[27]:-

Traditional and medicinally, the *Syzygium cumini* (jamun) seeds, fruits, leaves and bark are all used in aayurvedic medicine. The bark is acrid, sweet, digestive and astringent to the bowels, anti-helminthes.The bark contains tannins and carbohydrates, accounting for its long term used as an astringent to combat ailments like dysentery and also used in throat, bronchitis, asthma, thirst, biliousness, blood impurities and ulcer. Leaves ash are used to strengthen teeth and gums, seeds are used as astringent, diuretic, stop urinary discharge and remedy for diabetes and the bark is known for its wound healing property. In siddha, jamun are considered to be a haematinic, semen promoting besides thermo-regulant. A traditional medical healer in Madagascar uses of seeds of jambolan to debilitate the complications in diabetes. Jamun leaves are used via women to contract vagina after delivery, reduce mucus and odors. Fruitsare contains many different kinds of anti-oxidant compounds, including flavonoids, phenolic, carotenoids and vitamins, which are all considered beneficial to human health, for decreasing the risk of degenerative diseases by reduction of oxidative stress, and for the inhibition of macromolecules oxidation.

6.2.5 Pharmacological activity:-

***CNS activity*:-**

Ethyl acetate and methanolic extracts of *Syzygium cumini* seeds was undergone for investigating its Central nervous system activity (CNS) of albino mice in rota rod and act photometerat the dose level of 200mg/kg and 400mg/kg. Both the extracts exhibited

significantly CNS activity. The ethyl acetate and methanol extracts of *Syzygium cumini* seeds at the dose level of 200 mg/kg and 400 mg/kg administered orally exhibited significant reduction of activity compared with control group of animals. This study established CNS activity in *Syzygium cumini* seeds [28].

***Anti-diabetic activity*:-**

Extract of *Syzygium cumini* (aqueous suspension) were tested for its anti-diabetic activity at the different dose levels of 1gm, 2gm, 4gm and 6gm/kg body weight. 4gm/kg dose levels were found exhibited maximum hypoglycemic effects (42.64%) in rabbit. It is also produced a significant decreased in the Oral administration of *S. cumini* bark extracts at dose of 300mg/kg body weight exhibited anti-diabetic activity by significantly lowering blood glucose in rats but in case of clinical studies, experiments showing that the tea and extracts prepared from leaves are pharmacologically inert. Patients and physician should be not relying on the putative anti-hyerglycemic effects of this tea and perhaps of other folk medicines, that pretend to have such an effects. The investigation of plants with potential clinical utility could start with a clinical trial testing the effects of folk preparation in order to isolate the active principles of those products blood sugar levels (17.04%) in alloxan diabetic rats. The administration of different doses of aqueous suspension of dried seed kernels in rabbit changes blood sugar levels viz.,1gm, 2gm, 4gm and 6gm/kg body weight indicate that the optimum dose levels are 4gm/kg. The reduction was maximum for the 4gm/kg body weight dose levels being 42.64% as compared to the other dosages[30].

Oral administration of ethyl acetate and methanol extracts of *S. cumini* (200 and 400 mg/kg) was showed significant decreased in blood sugar levels. The isolated compound from of *S. cumini* mycaminose at a dose level of 50mg/kg also showed significant decreased in blood sugar levels. that shown pharmacological activity in this model.

7. CONCLUSION:-

Diabetes mellitus patients in India are increasing day by day probably due to change in life style, change in food patient that is from of traditional fiber rich diet to surgery fast foods diet and also because of genetic basis. The disorder being chromic in nature needed long term treatment to prevent the complications arising due to persistent high blood glucose levels. However, these synthetic anti-diabetic drugs are associated with large no. of side effects. Hence, there is increaseddin tends to use traditional

indigenous plants widely available in India for the treatment of diabetes mellitus. Over 150 plants extract and some of their active principles including reports or documents.

In conclusion, the present study demonstrated that the treatment of diabetes mellitus using, *Syzygium cumini* and *Momordica charantia* has exerted a considerable hypoglycemic effect. We have selected *Momordica charantia* seeds and *Syzygium cumini* seeds, because the anti-diabetic effects are more in both crude drug (i.e. *Momordica charantia* seeds and *Syzygium cumini* seeds). Thus, the synergistic effect produced by the combination of the extracts will be more as compared to individual drug, which will help in better treatment of the disease. The anti-diabetic activity of extract of *Syzygium cumini* may its promote insulin secretion by closure of K^+-ATP channels, membrane depolarization and stimulation of calcium influx, an initial key kept in insulin secretion. In this co-next, no. of other plants also has been reported to the anti-diabetic and insulin stimulatory. Thus, *Momordica charantia* may be also useful for the treatment and prevention of diabetes mellitus and to reduce or replace the use of oral anti-diabetic drugs. These studies and regular use in traditional medicine indicate that *Momordica charantia* and *Syzygium cumini* is effective and as safe for patient as other hypoglycemic agent.

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