International Journal of Pharmaceutical research and Applications
Volume 11, Issue 5, Sep.-Oct.2026,pp:1167-1180 www.ijprajournal.com ISSN:2456-4494

Role of herbal drug in diabetes management: A focus on *Momordica charantia* (karela) and *Syzygium Cumini* (Jamun)

Saumya singh*[1], Mohammad shawwal[2]
[1]*Vijay Pharmacy College (Dept. of Pharmacy) Gulalpur Jaunpur (U.P.), India*
[2]*SamHigginbottom University of Agriculture, Technology and Sciences Prayagraj (U.P.)India*

Date of Submission: 13-10-2026 Date of Acceptance: 25-10-2026

Abstract
Diabetes mellitus (DM) is the most common endocrine disorder and a major global health challenge, characterized by chronic hyperglycemia due to absolute or relative deficiency of insulin or insulin resistance. This persistent hyperglycemia leads to disturbances in carbohydrate, protein and fat metabolism and predisposes to long-term vascular complications. Before the discovery of insulin and modern oral hypoglycemic agents, plant-based traditional medicines were the main source of diabetes management in various indigenous systems of medicine.
Momordica charantia Linn. (Family: Cucurbitaceae), commonly known as Karela or bitter melon, and *Syzygium cumini* (L.) Skeels (Family: Myrtaceae), commonly known as Jamun or Java plum, are among the most extensively studied antidiabetic plants. M. charantia fruit juice has been reported to lower blood glucose, improve glucose tolerance, enhance glucose uptake by skeletal muscle, inhibit intestinal glucose absorption, suppress hepatic gluconeogenesis and protect and restore pancreatic β-cell function and islet architecture through its bioactive constituents such as charantin, polypeptide-p and vicine. Similarly, S. cumini seeds are rich in jamboline, jambosine, ellagic acid and anthocyanins, which exert hypoglycemic action by inhibiting α-amylase and α-glucosidase enzymes, increasing insulin secretion and reducing insulin resistance.
The combination of both plants has shown synergistic and superior antidiabetic activity compared to individual therapy in both preclinical and clinical studies. Therefore, the polyherbal formulation containing M. charantia and S. cumini holds great therapeutic potential as a cost-effective, safe and effective adjunct in the management of type 2 diabetes mellitus.

Key words: *Diabetes mellitus, Momordica charantia, Syzygium cumini, Hypoglycemic, Polyherbal, Synergistic action*

I. Introduction

Diabetes Mellitus (DM) is a metabolic disorder marked by persistent hyperglycemia due to insufficiency of insulin or decreased effectiveness of insulin. This metabolic derangement disturbs carbohydrate, protein and fat metabolism and leads to long term microvascular complications such as retinopathy, nephropathy, neuropathy and macrovascular complications like coronary artery disease, peripheral vascular disease and stroke.[1]

More than 200 million people were suffering from DM in 2010 and it is expected to reach 300 million by 2025, posing a major global health and economic burden. The rising prevalence is attributed to globalization, urbanization and adoption of sedentary lifestyle. The disease has become a pandemic with significant societal implications, particularly in developing countries like India.[2][3][4][5][6]

DM is classified into Type 1 and Type 2. Type 1 DM occurs due to autoimmune destruction of pancreatic β-cells leading to absolute insulin deficiency, often involving mucosal immune dysfunction. Type 2 DM, which accounts for more than 90% of cases, is characterized by both defective insulin secretion and insulin resistance, commonly seen after 40 years of age and strongly associated with obesity, high calorie diet and sedentary lifestyle. Its epidemiology and natural history have been extensively studied in various populations, including South Pacific populations.[7][5][6][8]

While classification is based on etiology and degree of glucose intolerance, the clinical management remains challenging. Type 2 DM is associated with increased risk of hypoglycemia during intensive therapy, and its exact

International Journal of Pharmaceutical research and Applications
Volume 11, Issue 5, Sep.-Oct.2026,pp:1167-1180 www.ijprajournal.com ISSN:2456-4494

pathophysiological defect is still not fully clear. It is managed by diet, exercise, lifestyle modification and oral hypoglycemic drugs. However, conventional drugs are associated with adverse effects and high cost, hence there is a growing interest in herbal drugs which are considered to be safer, cost-effective and having multiple mechanisms of action.[9][10][1]

II. Momordica charantia L. (Bitter Gourd)

Momordica charantia is a tropical vine of family Cucurbitaceae, widely grown for its bitter fruit. English name is bitter melon/gourd. Its original home is tropical regions and it is widely grown in South and Southeast Asia, China, Africa and Caribbean.[11]

2.1 Vernacular Names of *Momordica charantia* [11]

The plant is known by different names in different countries and languages.

A) Based on Country:

English: Bitter gourd, Bitter melon, Balsam pear
India: Karela
Brazil: Balsamina
China: Ku Gua, Karavila
Japan: Nigauri, Futoreishi
Malaysia: Peria, Priya
Philippines: Ampalaya

B) Based on Language:

Hindi: Karela
Sanskrit: Karavellaka, Karavella
Gujarati: Kareli, Karela
Bengali: Karala, Uchche
Marathi: Karle
Tamil: Pavakkai
Telugu: Kakara
Malayalam: Pavakka

Taxonomical Classification of *Momordica charantia* [11]

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliosida
Order: Cucurbitales
Family: Cucurbitaceae
Genus: Momordica
Species: M. charantia
Binomial Name: *Momordica charantia* L.

2.2 Morphology

It is a herbaceous, slender climber with pubescent stems. Leaves 10-12 cm long, palmately 5-7 lobed, sinuate-dentate. Flowers yellow, corolla 1.5-2 cm. Fruit obovoid or oblong-cylindric, coarsely ridged, bumpy-tuberculate, up to 20 cm, orange or dark yellow when ripe. Seeds black covered with soft red aril, 12-16 mm long. Indian variety is narrower with pointed ends and jagged surface, green or white in color. It is an annual creeper.

2.3 Origin and distribution:

Originally found in old world tropics, now spread throughout tropical regions. Commonly found on fences and hedgerows. Widely found in India, South Africa, Sri Lanka and Mediterranean countries. [12] [13] [14]

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2.4 Phytochemical Profile and Pharmacological Significance of *Momordica charantia*

Momordica charantia is reported to contain a wide variety of biologically active phytoconstituents such as cucurbitane-type triterpenes, steroidal saponins, proteins, alkaloids and steroids.[15]

One of its isolated constituents has shown the ability to inhibit guanylate cyclase enzyme in clinical studies, which is believed to be associated with psoriasis and also essential for the growth and proliferation of leukaemia and cancer cells.

Additionally, a protein isolated from bitter melon, known as momordin, has demonstrated significant anticancer activity against Hodgkin's lymphoma in animal studies. Other bioactive proteins present in the plant like alpha- and beta-momorcharin and cucurbitacin B have also been screened for their possible anticancer potential. A synthetic analogue of these proteins has been developed and patented under the name "MAP-30 (Momordica Anti-HIV Protein of 30 kDa)" and its developers claimed that it can suppress prostate tumour growth.[15]

Alpha- and beta-momorcharin have also been found to inhibit HIV in-vitro. In one investigation, HIV infected cells treated with these proteins exhibited almost complete loss of viral antigen (p24), while normal healthy cells remained unaffected. The inventor of MAP-30 has filed another patent claiming its use in the treatment of tumours and HIV infection. Another study also reported antiviral activity of MAP-30 against herpes simplex virus (HSV) in-vitro.

In several studies, at least three major groups of constituents present in all parts of bitter melon have shown hypoglycaemic activity or other beneficial effects against diabetes mellitus. These blood sugar lowering constituents include:

Steroidal saponins collectively known as **charantins,**
Insulin-like peptides known as **polypeptide-p or plant-insulin,**
Alkaloids like **vicine and charine.**
The hypoglycaemic action is more marked in the fruit part, where these compounds are present in higher concentration as compared to leaves and seeds.[15]

2.5 Table 1.
Bioactive phytochemicals of *Momordica charantia* and their recommended pharmacological properties.[15]

S.No.	Type of Constituent	Mejor Compounds	Biological Activity
1	Triterpenes & Saponins	Charantin, Charine, Momordicins,	Antidiabetic

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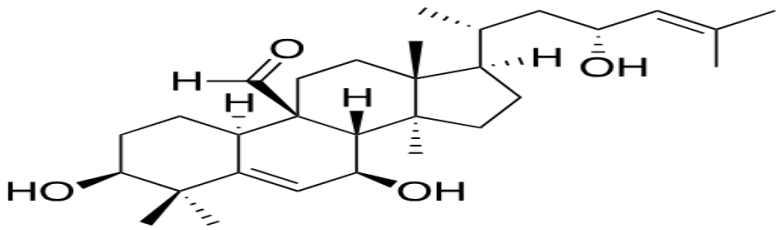
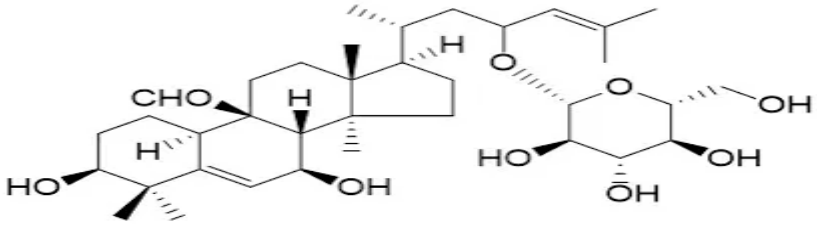
		Momordicosides, Goyaglycosides, Karavilagenins A,B,C, Karavilosides I-V, Cucurbitacins	(hypoglycemic), Anticancer
2	Proteins & Peptides	Momordin, Alpha & Beta-Momorcharin, MAP-30, Polypeptide-p / v-insulin, Trypsin inhibitors	Anticancer (Hodgkin's lymphoma, prostate tumor), Anti-HIV, Anti-herpes, Antidiabetic
3	Steroids & Sterols	Diosgenin, Stigmasterol, Spinasterol, Lanosterol, Taraxerol, Multiflorenol	Blood sugar lowering
4	Flavonoids & Polyphenols	Myricetin, Quercetin, Rutin, Catechin, Gallic acid, Chlorogenic acid, Rosmarinic acid	Antioxidant, Anti-inflammatory
5	Fatty Acids & Others	Lauric acid, Linoleic acid, Oleic acid, Myristic acid, Oleanolic acid, Rosmarinic acid, Zeaxanthin	Antioxidant, Hypoglycemic

Table 2.
2.6 Chemical Structure of Momorcidin-I and Momorcidin-II [16]



IUPAC Name: (3β,7β,23R)-23-(β-D-Glucopyranosyloxy)-3,7-dihydroxycucurbita-5,24-dien-19-al
Molecular Formula: C36H58O9
Mol. Weight: 634.85 g/mol



IUPAC Name: (3β,7β,23R)-3,7,23-Trihydroxycucurbita-5,24-dien-19-al
Molecular Formula: C30H48O4
Mol. Weight: 472.71 g/mol

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III. Marketed formulation *Momordica charantia L.* (Bitter Gourd)

Karela juice

Karela capsule

Karela powder

IV. Folk use of karela *Momordica charantia L.* (Bitter Gourd)

From a medicinal perspective, the plant has been traditionally utilized for centuries by the native tribes of the Amazon basin. Leaf infusion is commonly used as an antidiabetic remedy, as a carminative for colic relief, and externally for healing sores, cuts and infectious wounds. It is also employed both orally and topically as a vermifuge against intestinal worms and parasites, as an emmenagogue, and as an antiviral drug for measles, hepatitis and fever. The drug is described as antidotal, antipyretic, stomachic, appetizing, anti-bilious and laxative in nature.[18]

In addition to Amazonian medicine, it holds a significant place in the traditional systems of Asia and Africa for promoting digestive power, metabolic rate, blood circulation, immunity and overall strength. As per Ayurveda, the Indian traditional medicine, as described in Indian Materia Medica and Medicinal Plants of India, bitter gourd increases Vata dosha, alleviates Kapha and Pitta doshas, and is useful in fever, blood disorders and jaundice. The plant is also reported to be effective against hepatic diseases, skin problems and disorders arising due to vitiated Vata.[17][18]

V. Pharmacological Activities of *Momordica charantia L.* (Bitter Gourd)

Antidiabetic Activity: The antidiabetic effect is the most extensively studied activity of M. charantia. The fruit contains bioactive compounds such as Charantin (a mixture of β-sitosteryl glucoside and stigmasteryl glucoside), Polypeptide-p (plant insulin) and Vicine which exert hypoglycemic effects through multiple mechanisms including increased insulin secretion from pancreatic β-cells, enhanced peripheral glucose utilization, inhibition of intestinal glucose absorption and suppression of hepatic gluconeogenesis. In alloxan-induced diabetic rat models, ethanolic fruit extract at 200 mg/kg showed significant reduction in fasting blood glucose level.[19][20]

VI. CLINICAL EVIDENCE OF Momordica charantia L. (Bitter Gourd)

The hypoglycemic activity of *Momordica charantia* L. (bitter gourd) that was demonstrated in experimental animal models has been further confirmed through various clinical investigations in human subjects.

Study 1: Leatherdale et al., 1981, United Kingdom
Leatherdale and co-workers studied nine subjects suffering from non-insulin dependent diabetes. They administered a water soluble fraction of bitter gourd together with 50 g of oral glucose. The results

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Volume 11, Issue 5, Sep.-Oct.2026,pp:1167-1180 www.ijprajournal.com ISSN:2456-4494

revealed a marked fall in blood sugar levels and better glucose tolerance after continuous intake of fried bitter melon. Because circulating insulin did not rise, the researchers proposed that the action is extra-pancreatic, mediated by increased peripheral utilization of glucose. [21]

Study 2: Ahmad et al., Bangladesh, Sample Size 100
In this clinical case series, one hundred individuals with moderately controlled type 2 diabetes were treated with a freshly prepared aqueous homogenate of *Momordica charantia*. Both fasting as well as post-meal glucose concentrations showed a highly significant reduction (p value <0.001). [22]

Study 3: Fuangchan et al., Thailand, Sample Size 143
This was a double-blinded, active comparator controlled randomized trial of high methodological quality. One hundred forty-three newly detected type 2 diabetic patients were given bitter melon capsules (500 mg strength, two capsules two times a day) for a period of four weeks. The trial showed a significant lowering of serum fructosamine by 10.2 micromol/L. [23]

Study 4: Cortez-Navarrete et al., 2015, Mexico, RCT, n=24
Twenty-four type 2 diabetic patients who were not receiving any antidiabetic drug were randomly divided to receive Momordica charantia 2000 mg per day or placebo for three months. After completion of therapy, significant decreases in body weight, body mass index, body fat, waist circumference, glycated hemoglobin, two-hour plasma glucose and total glucose area under curve were noted. Additionally, area under curve for insulin increased from 56562 to 65256 pmol/L/min (p=0.043) along with an increase in first-phase and total insulin secretion, which indicates restoration of beta-cell function. [24]

Study 5: Pandey et al., 2021, Nepal, Pilot Add-on Study, n=22
This pilot investigation was performed at B.P. Koirala Institute of Health Sciences, Dharan. Twenty-two patients with uncomplicated type 2 diabetes were enrolled. Group A was managed with conventional antidiabetic agents only, while Group B received conventional agents plus 200 ml of freshly prepared bitter gourd juice every day for 90 days. The add-on group showed a highly significant fall in fasting and post-prandial blood sugar (p<0.0001) compared to the control group. [25]

Study 6: mcIRBP-19 Containing Extract Trial, Taiwan, n=40
A double-blind, placebo-controlled randomized trial was carried out in forty type 2 diabetic subjects whose glycemic control was inadequate despite oral hypoglycemic agents. They were administered 600 mg per day of a standardized bitter gourd extract containing mcIRBP-19, a 19 amino acid peptide having insulin-mimetic action, for three months. In subgroup analysis (n=29), fasting glucose was lowered from 172.5 mg/dL to 159.4 mg/dL (p=0.041) and HbA1c from 8.0% to 7.5% (p=0.010). [26]

VII. *Syzygium cumini* (L.) Skeels (Jamun)

Syzygium cumini is an evergreen tropical tree of family Myrtaceae, widely known for its purple-black edible fruit. English name is Java plum / Black plum. Its original home is Indian Subcontinent and it is widely grown in India, Bangladesh, Pakistan, Indonesia, Sri Lanka and Malaysia. It is also cultivated in Florida, Australia and Africa.[27]

7.1 Vernacular Names of *Syzygium cumini*[27][28][29]

The plant is known by different names in different countries and languages.

A) Based on Country / Common Name:
English: Java Plum, Black Plum, Malabar Plum, Indian Blackberry
Brazil: Jambolão
Philippines: Duhat
Indonesia: Jamblang

B) Based on Language (India):
Hindi: Jamun, Jaman
Sanskrit: Jambu, Raj Jambu, Jambuphala
Gujarati: Jambu
Marathi: Jambhul
Tamil: Naval, Nagal
Telugu: Neredu
Malayalam: Naval
Bengali: Kalajam

7.2 Taxonomical Classification of *Syzygium cumini*[29][30]

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Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Myrtales
Family: Myrtaceae
Genus: Syzygium
Species: cumini
Binomial Name: *Syzygium cumini* (L.) Skeels[29][30]

7.3 Morphology of *Syzygium cumini* (L.) Skeels

It is a large evergreen perennial tree, up to 25-30 meter tall, with dense foliage. Bark is rough, dark grey to pale brown, with irregular scales.[29]

Leaves: Leaves are opposite, 6-12 cm long, oblong-ovate to elliptic, leathery, glossy dark green above, smooth and shining, with numerous lateral nerves converging at margin. Tip is broad and less acuminate.

Flowers: Flowers are fragrant, small, greenish-white to pinkish-white, 7.5-13 mm across, borne in branched panicles (4-6 cm long) mostly from branchlets below the leaves. Calyx is funnel-shaped, cup-shaped, 4 mm long, 4-toothed. Petals are 4, fused into a cap (calyptra). Stamens are numerous.[30]

Fruit: Fruit is an ovoid to elliptic berry, 1.5-3.5 cm long, fleshy, luscious, green when young turning dark purple to nearly black on ripening, with sweet, astringent taste. Contains single large seed.Seeds: Seed is oblong, 18-20 mm long, 11 mm wide, 1.62g average weight, white to pinkish, coarse textured.[31]

7.4 Origin and Distribution of *Syzygium cumini* (L.) Skeels (Jamun)

Originally found in Indian Subcontinent and Indo-Malayan region, now widely distributed throughout tropical regions. It is native to India - Sub-Himalayan tract, Assam, Peninsular India, Burma to Malaya. Found throughout the Philippines, planted and in many regions spontaneous. Also cultivated in Florida, Australia, Caribbean and Africa. Commonly grown as avenue tree and in groves near villages.[29][30][31]

7.5 Phytochemistry of *Syzygium cumini* (L.) Skeels (Jamun)

Jamun is reported to contain a wide variety of biologically active phytoconstituents such as flavonoids, tannins, anthocyanins and essential oils. Seeds are rich in alkaloid Jamboline and glycoside Jambosine which inhibit diastatic conversion of starch into sugar and show potent antidiabetic activity.[32]

Fruit pulp is rich in anthocyanins like delphinidin-3,5-diglucoside, petunidin-3,5-diglucoside and malvidin-3,5-diglucoside which are responsible for its dark purple colour and high antioxidant capacity. Seeds also contain phenolic acids like ellagic acid, gallic acid and corilagin which have demonstrated anticancer and hepatoprotective activity.[33]

Leaves are rich in essential oils containing α-pinene, β-pinene, myrcene and limonene with antimicrobial potential. Bark contains 13-14% tannins including gallotannins and ellagitannins which show anti-diarrheal and anti-inflammatory activity. Seed extract containing antimellin inhibits α-glucosidase and α-amylase enzymes.[34]

At least three groups of constituents - flavonoids (myricetin), tannins and triterpenoids (oleanolic acid, betulinic acid) have shown hypoglycaemic, hypolipidemic and cardioprotective effects. The hypoglycaemic action is more marked in seed and fruit pulp where these compounds are present in higher concentration.[35][36]

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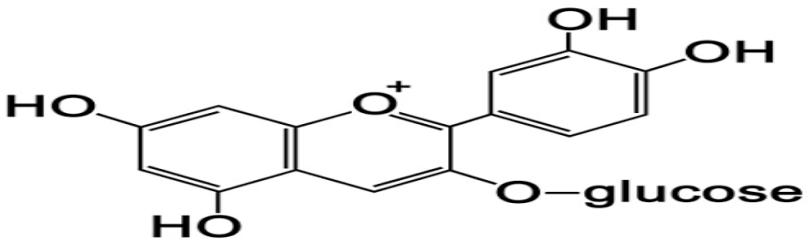
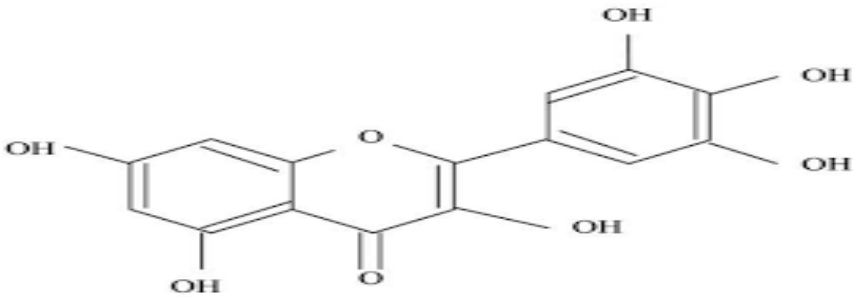
7.6 Table 3.
Bioactive phytochemicals of *Syzygium cumini* and their recommended pharmacological properties.[32][33][34][35]

S.No.	Type of Constituent	Mejor Compounds	Biological Activity
1	Flavonoids & Phenolic acids	Myricetin, Quercetin, Ellagic acid, Gallic acid	Antidiabetic, Antioxidant
2	Anthocyanins & Alkaloids	Delphinidin, Petunidin, Malvidin diglucosides, Jamboline	Antidiabetic, Antioxidant
3	Triterpenes & Sterols	Oleanolic acid, Betulinic acid, β-Sitosterol	Anti-inflammatory, Hypoglycemic
4	Essential oils & Tannins	α-Pinene, Tannins 13-14%	Antimicrobial

7.7 Chemical structure
Table 4: Chemical Structure of *Syzygium cumini* Kuromanin and Myricetin [37][38][39][40]



IUPAC Name (2R,3S,4S,5R,6R)-2-(2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-1-benzopyrylium-3-yloxy)-6-(hydroxymethyl)tetrahydro-2H-pyran-3,4,5-triol chloride
Molecular Formula: C21H21O11
Mol. Weight: 449.38 g/mol



IUPAC Name: 3,5,7-Trihydroxy-2-(3,4,5-trihydroxyphenyl)-4H-1-benzopyran-4-one
Molecular Formula: C15H10O8
Mol. Weight: 318.24 g/mol

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VIII. Marketed product of *Syzygium cumini* (L.) Skeels (Jamun)

IX. Folk and Traditional Uses of *Syzygium cumini* (L.) Skeels (Jamun)

From a medicinal perspective, Jamun has been traditionally utilized for centuries in Ayurveda, Unani and Siddha systems of medicine. The bark is astringent, sweet, carminative and diuretic in nature. Stem bark decoction is commonly used as an antidiabetic remedy, for sore throat, bronchitis, asthma, thirst and dysentery. It is also employed as a blood purifier and externally for healing ulcers and skin wounds.[41]

The drug is described as stomachic, appetizing, antidiarrheal and antibilious in nature. Seeds are highly valued as antidiabetic, with powder taken orally with honey for diabetes and glycosuria. Leaves are used for strengthening teeth and gums, and leaf ash is used for strengthening teeth. Fruit is used as liver tonic, enriches blood and is useful in urinary disorders. In addition to Indian medicine, it holds a significant place in traditional medicine of Africa and Madagascar for treating diarrhea and chronic dysentery.[41][42]

As per Ayurveda, Jamun pacifies Kapha and Pitta doshas, increases Vata dosha, and is useful in diabetes (Madhumeha), diarrhea, skin diseases and leucorrhoea. The plant is also reported to be effective against bleeding disorders, burning sensation and worm infestation arising due to vitiated Pitta and Kapha.[42][43]

X. Pharmacological Activities of *Syzygium cumini* (L.) Skeels (Jamun)

Antidiabetic Activity: The antidiabetic effect is the most extensively studied activity of S. cumini. The seeds contain bioactive compounds such as Jamboline (antimellin), Jambosine and Ellagic acid which exert hypoglycemic effects through multiple mechanisms including inhibition of α-amylase and α-glucosidase enzymes, increased insulin secretion from pancreatic β-cells, enhanced peripheral glucose utilization and suppression of hepatic gluconeogenesis. In alloxan-induced diabetic rat models, ethanolic seed extract at 200 mg/kg showed significant reduction in fasting blood glucose level and improved glucose tolerance.[44][45]

XI. Clinical Evidence of *Syzygium cumini* (L.) Skeels (Jamun)

The hypoglycemic activity of Syzygium cumini (Jamun) that was demonstrated in experimental animal models has been further confirmed through various clinical investigations in human subjects.

Study 1: Sahana et al., 2010, India, n=30

Thirty type 2 diabetic patients were administered 10 g of Jamun seed powder twice daily before meals for three months. The results revealed a significant fall in fasting blood sugar from 193.8 mg/dL to 167.6 mg/dL and post-prandial blood sugar from

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288.4 mg/dL to 229.5 mg/dL. Glycosylated hemoglobin (HbA1c) also reduced significantly from 8.8% to 7.8%.[46]

Study 2: Sidana et al., 2017, India, RCT, n=60
This was a randomized, double-blind, placebo-controlled trial in sixty newly diagnosed type 2 diabetic patients. They were given 5 g of Syzygium cumini seed powder twice daily for three months. Significant reduction in fasting blood glucose, post-prandial glucose and HbA1c was observed compared to placebo group, without any adverse effect on liver and kidney function tests.[47]

Study 3: Ghimire et al., 2021, Nepal, n=50
In this clinical study, fifty patients with type 2 diabetes receiving metformin therapy were given add-on treatment with 500 mg Jamun seed extract capsules twice daily for 90 days. Both fasting as well as post-meal glucose concentrations showed a highly significant reduction ($p < 0.001$) and lipid profile also improved significantly.[48]

Study 4: Anupriya et al., 2022, India, Double-blind RCT, n=40
Forty type 2 diabetic patients were randomly divided to receive Syzygium cumini seed extract 2 g per day or placebo for six months as an adjunct to standard therapy. After completion of therapy, significant decreases in HbA1c from 8.21% to 7.42%, fasting blood sugar and insulin resistance (HOMA-IR) were noted. The extract was well tolerated with no hypoglycemic episodes.[49]

Study 5: Shrestha et al., 2023, Nepal, Add-on Study, n=36
This study was performed at Tribhuvan University Teaching Hospital, Kathmandu. Thirty-six patients with uncomplicated type 2 diabetes were enrolled. Group A was managed with conventional antidiabetic agents only, while Group B received conventional agents plus 5 g of Jamun fruit pulp powder daily for 90 days. The add-on group showed a highly significant fall in fasting blood sugar, post-prandial blood sugar and serum fructosamine ($p<0.001$) compared to control.[50]

Study 6: Teixeira et al., 2006, Brazil, n=30
A randomized, double-blind, placebo-controlled trial was carried out in thirty type 2 diabetic subjects. They were administered tea prepared from 2 g of Syzygium cumini leaves per day for three months. In intention-to-treat analysis, fasting glucose was lowered and glucose tolerance improved, although change in HbA1c was not statistically significant due to short duration. No adverse hepatic or renal effects were observed.[51]

XII. Combined Effect of *Momordica Charantia* and *Syzygium Cumini* In Diabetes

The combination of Momordica charantia (Karela) and Syzygium cumini (Jamun) has shown synergistic antidiabetic effect due to their complementary mechanisms of action. While Charantin, Polypeptide-p and Vicine from Karela enhance peripheral glucose utilization and stimulate β-cell function, Jamboline, Jambosine and Ellagic acid from Jamun inhibit α-amylase and α-glucosidase enzymes and reduce insulin resistance.

Preclinical Evidence:
In alloxan-induced diabetic rat models, combined administration of ethanolic extracts of Momordica charantia fruit (200 mg/kg) and Syzygium cumini seed (200 mg/kg) showed significantly greater reduction in fasting blood glucose (68.42%) compared to individual extracts of Karela (42.12%) and Jamun (48.35%) alone. The combination also significantly improved lipid profile, restored serum insulin level and regenerated pancreatic β-cells, indicating synergistic action.[52][53]

Clinical Evidence: Study 1: Choudhary et al., 2018, India, RCT, n=60
Sixty type 2 diabetic patients were randomly divided into three groups: Group A received Karela powder 2 g/day, Group B received Jamun seed powder 2 g/day and Group C received combination of both (1 g Karela + 1 g Jamun) twice daily for 90 days. Group C showed maximum reduction in fasting blood sugar (31.2%), post-prandial blood sugar (34.8%) and HbA1c (1.4%), which was significantly higher than individual groups ($p<0.001$). No adverse drug reaction was reported.[54]

Study 2: Vaibhav et al., 2023, India, Add-on Trial, n=80
In this double-blind, placebo-controlled trial, eighty type 2 diabetic patients inadequately controlled on metformin 500 mg twice daily were given add-on capsules containing standardized extracts of Momordica charantia 500 mg + Syzygium cumini 500 mg twice daily for 12 weeks. The add-on group showed significant fall in HbA1c from 8.6% to 7.3% ($p<0.0001$), fasting glucose from 182.4 to

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132.6 mg/dL, HOMA-IR and improvement in lipid profile compared to placebo group. The formulation was well tolerated.[55]

XIII. Proposed Synergistic Mechanism of *Momordica charantia* + *Syzygium cumini* Polyherbal Combination

The combination of Karela (*Momordica charantia*) and Jamun (*Syzygium cumini*) is proposed to exert synergistic antidiabetic activity through complementary mechanisms:

13.1 Dual Pancreatic Action: Karela stimulates insulin secretion from pancreatic β-cells via its active constituents Charantin and Polypeptide-p (plant insulin), while Jamun protects β-cells from oxidative damage through Jamboline and Ellagic acid-mediated antioxidant action.

13.2 Dual Extra-Pancreatic Action: Karela increases peripheral glucose uptake and utilization in muscle and adipose tissue, while Jamun inhibits intestinal carbohydrate digestion via α-amylase and α-glucosidase inhibition, thereby reducing postprandial hyperglycemia.

13.3 Anti-oxidant Synergy: Both plants are rich in flavonoids and polyphenols, which scavenge free radicals, reduce oxidative stress, and thereby prevent diabetic complications such as nephropathy, neuropathy and retinopathy.

Therefore, the polyherbal combination is more effective than monotherapy and can be developed as a cost-effective adjunct for type 2 diabetes management.

XIV. CONCLUSION

Jamboline, Jambosine, Ellagic acid, Anthocyanins from S. cumini are responsible for hypoglycemic activity through multiple mechanisms including insulin secretion, enhancement of peripheral glucose utilization, inhibition of α-amylase and α-glucosidase, antioxidant action and regeneration of pancreatic β-cells.

Experimental studies in animal models have consistently demonstrated significant reduction in fasting blood glucose, post-prandial glucose, HbA1c and improvement in lipid profile without major adverse effects.

Clinical evidence including randomized controlled trials, case series and add-on studies in type 2 diabetic patients has further validated the traditional claim. The combination of Karela and Jamun has shown synergistic and superior efficacy compared to monotherapy, with a highly significant reduction in glycemic parameters ($p<0.0001$) and better tolerability as an adjunct to conventional oral hypoglycemic agents.

Thus, the polyherbal formulation containing *Momordica charantia* and *Syzygium cumini* can be considered as a cost-effective, safe and effective adjunct in the management of type 2 diabetes mellitus. However, large-scale, multicentric, long-term randomized controlled trials are warranted to further establish its efficacy, optimal dose and safety for routine clinical use

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